

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

NDA 22-047 S-006, S-007, and S-008

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 04/30/10
See OMB Statement on Page 3.

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-047

NAME OF APPLICANT / NDA HOLDER

AstraZeneca Pharmaceuticals LP

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

SEROQUEL XR

ACTIVE INGREDIENT(S)

quetiapine fumarate

STRENGTH(S)

50 mg, 200 mg, 300 mg, 400 mg

DOSAGE FORM

Tablet, Extended Release, Oral

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number
4,879,288

b. Issue Date of Patent
11/7/1989

c. Expiration Date of Patent
9/26/2011

d. Name of Patent Owner
AstraZeneca Pharmaceuticals LP

Address (of Patent Owner)
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

FAX Number (if available)
302-886-1578

Telephone Number
(800) 456-3669

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

FAX Number (if available)

Telephone Number
(800) 456-3669

E-Mail Address (if available)

VP, Policy, Legal & Scientific Affairs & Gen Counsel, AstraZeneca Pharmaceuticals, LP

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
****PLEASE NOTE:** Regarding response to 2.2 through 2.4, certain claims of this patent may cover at least one additional polymorph in addition to claiming the drug substance of the pending NDA, amendment or supplement, but the patent is not being submitted for listing on that basis.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 7 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Bipolar Disorder/Bipolar Mania and related references throughout label including but not limited to 1. INDICATIONS AND USAGE 2. DOSAGE AND ADMINISTRATION 3. WARNINGS AND PRECAUTIONS 4. ADVERSE REACTIONS 5. DRUG INTERACTIONS 6. USE IN SPECIFIC POPULATIONS 7. DRUG ABUSE AND DEPENDENCE 8. OVERDOSAGE 9. DESCRIPTION 10. CLINICAL PHARMACOLOGY 11. NONCLINICAL TOXICOLOGY 12. CLINICAL STUDIES 13. HOW SUPPLIED/STORAGE AND HANDLING 14. PATIENT COUNSELING INFORMATION

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

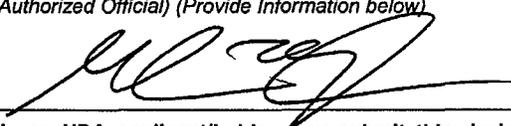
6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



12/3/07

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
Glenn M Engelmann, VP, Policy, Legal & Scientific Affairs & General Counsel

Address
1800 Concord Pike

City/State
Wilmington, DE

ZIP Code
19803

Telephone Number
(302) 886-3244

FAX Number (if available)
(302) 886-1578

E-Mail Address (if available)
glenn.engelmann@astrazeneca.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Appears this way on the original

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

- 4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER
22-047
NAME OF APPLICANT / NDA HOLDER
AstraZeneca Pharmaceuticals LP

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
SEROQUEL XR

ACTIVE INGREDIENT(S)
quetiapine fumarate

STRENGTH(S)
50 mg, 200 mg, 300 mg, 400 mg

DOSAGE FORM
Tablet, Extended Release, Oral

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FDA will not list patent information if you file an Incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number 5,948,437	b. Issue Date of Patent 9/7/1999	c. Expiration Date of Patent 5/28/2017
d. Name of Patent Owner AstraZeneca UK Limited	Address (of Patent Owner) 15 Stanhope Gate	
	City/State London ENGLAND	
	ZIP Code W1K 1LN	FAX Number (if available) 44 20 7304 5113
	Telephone Number +44-20-7304-5000	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) VP, Policy, Legal & Scientific Affairs & Gen Counsel, AstraZeneca Pharmaceuticals, LP	Address (of agent or representative named in 1.e.) 1800 Concord Pike	
	City/State Wilmington, DE	
	ZIP Code 19803	FAX Number (if available)
	Telephone Number (800) 456-3669	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

- 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

- 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number(s) (as listed in the patent) 13 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Bipolar Disorder/Bipolar Mania and related references throughout label including but not limited to 1. INDICATIONS AND USAGE 2. DOSAGE AND ADMINISTRATION 5. WARNINGS AND PRECAUTIONS 6. ADVERSE REACTIONS 7. DRUG INTERACTIONS 8. USE IN SPECIFIC POPULATIONS 9. DRUG ABUSE AND DEPENDENCE 10. OVERDOSAGE 11. DESCRIPTION 12. CLINICAL PHARMACOLOGY 13. NONCLINICAL TOXICOLOGY 14. CLINICAL STUDIES 16. HOW SUPPLIED/STORAGE AND HANDLING 17. PATIENT COUNSELING INFORMATION

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

Appears this way on the original

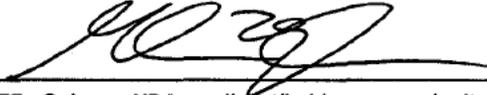
6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



12/3/07

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Glenn M Engelmann, Vice President, Policy, Legal & Scientific Affairs & General Counsel

Address

1800 Concord Pike

City/State

Wilmington, DE

ZIP Code

19803

Telephone Number

(302) 886-3244

FAX Number (if available)

(302) 886-1578

E-Mail Address (if available)

glenn.engelmann@astrazeneca.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

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- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

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First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

- 4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.
 - 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

AstraZeneca Pharmaceuticals LP
1800 Concord Pike
Wilmington, DE 19850-5437

SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets
NDA 22-047

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

EXCLUSIVITY INFORMATION

1. Exclusivity Claim

AstraZeneca Pharmaceuticals LP claims an exclusivity period of three years for this supplemental new drug application.

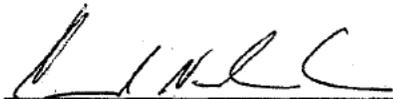
2. Authority for Exclusivity Claim

Exclusivity for this supplemental new drug application is being claimed pursuant to 21 CFR 314.108(b)(5).

3. Information Demonstrating this Supplemental Application Contains New Clinical Investigations Conducted or Sponsored by the Applicant that are Essential to the Approval of this Supplemental New Drug Application.

(a) Certification of New Clinical Investigations

AstraZeneca Pharmaceuticals LP certifies that to the best of its knowledge, each of the clinical investigation(s) included in this supplemental new drug application meets the definition of "new clinical investigation" set forth in 21 CFR Section 314.108(a).



Arvid Nordenhem, M.D., PhD.

(b) Essential to Approval

(i) Literature Search

Attached as Exhibit A is a list of all published studies and publicly available reports of clinical investigations known to AstraZeneca Pharmaceuticals LP through a literature search that are relevant to the conditions for which approval is being sought.

(ii) Certification

AstraZeneca Pharmaceuticals LP certifies that it has thoroughly searched the scientific literature and, to the best of its knowledge, the list of relevant published studies and/or publicly available reports is complete and accurate, and in its opinion, such published studies and/or publicly available reports do not provide a sufficient basis for the approval of the conditions for which approval is being sought without reference to the new clinical investigation(s) in this supplemental new drug application.



Arvid Nordenhem, M.D., PhD.

(iii) Explanation

The listed published studies and/or publicly available reports of clinical investigations do not provide sufficient basis for the approval of the conditions for which the Applicant is seeking approval, without reference to the new clinical investigations in this supplemental new drug application.

The new clinical investigation(s) provide safety and efficacy data regarding the use of SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets for the treatment of bipolar depression that could not be gleaned from published information. Accordingly, these new clinical investigations are essential to the approval of this supplemental new drug application.

(c) Conducted or Sponsored by the Applicant.

AstraZeneca Pharmaceuticals LP, the agent and subsidiary of AstraZeneca UK Limited, is the sponsor named in Form FDA 1571 for IND 76,146 under which the new clinical investigation essential to the approval of this supplemental new drug application was conducted. We believe this fact is sufficient under 21 CFR 314.50(j)(4)(iii) to establish that the clinical investigations were conducted or sponsored by the Applicant.



**Seroquel (quetiapine) SR/XR:
Exclusivity Search – 1996 through Nov 27, 2007**

Bibliography sorted A-Z by first author
Prepared by: Paula Payne-Gallimore, SIS, x62650

**New drugs approved by the FDA: Agents pending FDA approval -
Supplemental applications filed by manufacturer. Significant labeling
changes.**

Baker, D. E.
Hospital Pharmacy.42(7)(pp 648-652), 2007.

Current FDA-related drug information.

Baker, D. E.
Hospital Pharmacy 41(10), 980-982. 2006.

CUSTOM ABSTRACT This article aims to inform the reader on updates pertaining to new drugs, indications, dosage forms and safety-related changes in labeling or use. It is stated that quetiapine (Seroquel) SR is an oral tablet for once daily administration for the treatment of schizophrenia. AUTHOR ABSTRACT This monthly feature will help readers keep current on new drugs, indications, dosage forms, and safety-related changes in labeling or use. Efforts have been made to ensure the accuracy of the information; however, if there are any questions, let us know at hospitalpharmacy@drugfacts.com.

Quetiapine in a controlled release formulation

Brecher, Martin; Chitra, Rohini; Eriksson, Hans; Shaw, Joan; Vaageroe, Maarten; Wilson, Ellis
Astrazeneca AB, Swed.PCT Int. Appl., 182pp.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007058593	A1	20070524	WO 2006-SE1300	20061116
US 2007185080	A1	20070809	US 2006-561306	20061117

The present invention relates to a pharmaceutical controlled release composition comprising quetiapine, 11-[4-[2(2- hydroxyethoxy) ethyl]-1-piperaziny] dibenzo-[b,f][1,4] thiazepine in the treatment of mood disorders, anxiety disorders an symptoms of these disorders. Quetiapine may also be used in combination with a selective serotonin reuptake inhibitor, e.g. paroxetine or fluoxetine, or with a serotonin- norepinephrine reuptake inhibitor, such as duloxetine. (b) (4)



Clinical benefit of switching patients with schizophrenia to once-daily quetiapine sustained release.

Ganesan, S., Agambaram, V., Randeree, F., Eggen, I., Schmidt, M. M., and Meulien, D. European Psychiatry (Paris) 2007;22(Suppl 1):S334-5, P403.

CUSTOM ABSTRACT In this 12 week, multicenter, open-label study of 477 patients with schizophrenia, the authors evaluated the clinical benefit of switching patients who experienced suboptimal efficacy/tolerability with their previous antipsychotic treatment to quetiapine sustained release (SR). Results showed that 62.8% of evaluable patients achieved a clinical benefit upon switching to quetiapine SR with significant improvements observed in mean [SD] change from baseline in CGI-CB (-2.1 [3.62]) and PANSS total (-13.6 [19.23]) (both $p < 0.001$). The mean [SD] CGI-I score at endpoint was 2.8 [1.49] ($p < 0.001$ for mean CGI-I < 4). The authors conclude that switching to quetiapine SR was associated with clinical benefit and was well tolerated in this patient population.

Efficacy and tolerability of once-daily quetiapine sustained release in patients with acute schizophrenia: A randomised, double-blind, 6-week, placebo-controlled study.

Kahn, R., Schulz, C., Palazov, V., Reyes, E., Meulien, D., Brecher, M., Svensson, O., and Andersson, M. H. Biological Psychiatry 2007;61(8) Suppl S:262S, Abs 845.

CUSTOM ABSTRACT In this randomised, double-blind, placebo-controlled study, the authors assessed the safety and efficacy of quetiapine sustained release (SR) once daily or immediate release (IR) twice daily for the treatment of schizophrenia in 588 patients. Psychiatric symptoms improved in a dose dependent manner for SR formulations, with the IR formulation having similar efficacy to the lower dose SR. The main side effects were somnolence and dizziness with a similar incidence of extrapyramidal effects as that seen in placebo-treated patients, and 2 patients taking SR and 1 taking IR quetiapine discontinued due to side effects. The authors conclude that once daily SR quetiapine was safe and effective in patients with schizophrenia.

Efficacy and tolerability of once-daily extended release quetiapine fumarate in acute schizophrenia: A randomized, double-blind, placebo-controlled study.

Kahn, R. S., Schulz, S. C., Palazov, V. D., Reyes, E. B., Brecher, M., Svensson, O., Andersson, H. M., and Meulien, D. Journal of Clinical Psychiatry 68(6), 832-842. 2007.

Objective: To evaluate the efficacy and tolerability of extended release quetiapine fumarate (quetiapine XR) in a 6-week, double-blind, randomized study. Method: Patients with a DSM-IV diagnosis of acute schizophrenia were randomly assigned to fixed-dose quetiapine XR 400, 600, or 800 mg/day (once daily in the evening), quetiapine immediate release (IR) 400 mg/day (200 mg twice daily), or placebo. Dual-matched placebo was used to maintain blinding. Quetiapine XR target doses were reached by day 2 (400 and 600 mg) and day 3 (800 mg). The primary endpoint was least squares mean change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) total score. PANSS response rate (percentage of patients with greater than or equal to 30% reduction in total score), Clinical Global Impressions -Improvement scale (CGI-I) response rate (percentage of patients with

score less than or equal to 3), change in CGI-Severity of Illness (CGI-S), and adverse events (AEs) were also assessed. The study was conducted from November 2004 to December 2005. Results: 588 patients were enrolled and 446 (76%) completed the study. Improvement in PANSS total score at week 6 was significant versus placebo (- 18.8) in all groups: -24.8 (p =.03), -30.9 (p <.00 1), and -31.3 (p <.00 1) for quetiapine XR 400, 600, and 800 mg, respectively, and -26.6 (p =.004) for quetiapine IR. There were also statistically significant differences in PANSS and CGI-I response rates for all active treatments versus placebo (all p <.05). The most common AEs in all quetiapine groups were somnolence and dizziness; there were no unexpected AEs with quetiapine XR. Incidence of AEs potentially related to extrapyramidal symptoms was similar to placebo. Conclusion: Once-daily quetiapine XR (400/800 mg/day) was effective versus placebo in patients with acute schizophrenia. Treatment, including rapid dose escalation, was well tolerated, with a therapeutically effective dose reached by day 2.

Once-Daily Quetiapine Sustained Release (SR) Is Effective And Well Tolerated In Patients With Schizophrenia Switched From Quetiapine Immediate Release (IR).

Moller, H.-J., Johnson, S., Mateva, T., Meulien, D., Brecher, M., Svensson, O., and Miller, F.

In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 202. 1919.

CUSTOM ABSTRACT In this randomized, double-blind study, efficacy and tolerability of switching from quetiapine IR to quetiapine SR, compared with maintaining quetiapine IR treatment in patients with schizophrenia was evaluated. 497 patients were randomized to quetiapine SR (n=331) or quetiapine IR (n=166) with patients receiving quetiapine IR twice daily for 4 weeks, then randomized (2:1) to a once daily equivalent daily dose of quetiapine SR or maintained on quetiapine IR for 6 weeks. The primary endpoint was percent of patients with insufficient efficacy, defined as either discontinuation due to lack of efficacy or $\geq 20\%$ increase in PANSS at any visit. Using the selected non-inferiority margin of 6%, non-inferiority was narrowly missed and non-inferiority was shown in the per-protocol population: 5.3% receiving quetiapine SR showed insufficient efficacy versus 6.2% receiving quetiapine IR. The authors conclude that patients stable on quetiapine IR can be switched to once-daily quetiapine SR without clinical deterioration or compromise in safety/tolerability.

Once-daily quetiapine sustained release (SR) is effective and well tolerated in patients with schizophrenia switched from the same total daily dose of quetiapine immediate release (IR).

Moller, H., Johnson, S., Meulien, D., Brecher, M., Svensson, O., Miller, F., and Study 146 Investigators

Schizophrenia Bulletin 33(2), 449. 2007.

CUSTOM ABSTRACT In this randomized, double-blind, controlled study, the efficacy and safety of once daily quetiapine sustained release (SR) in 630 stable schizophrenic patients switched from same dose twice daily quetiapine immediate release (IR) are described. The rate of discontinuation due to lack of efficacy or adverse effects was 3.3% in patients treated with quetiapine SR and was 1.8% in patients treated with quetiapine IR, the LSM changes in PANSS total score were -3.7 and -4.2 respectively. The incidence of drug-related adverse events was 17.2% for

quetiapine SR and 15.7% for quetiapine IR, however, the type, distribution and intensity of adverse events were similar in the treatment groups. The authors conclude that schizophrenic patients clinically stable on quetiapine IR twice daily can be switched to same dose quetiapine SR once daily without changes in efficacy or safety.

Continued efficacy and tolerability in clinically stable patients switched from quetiapine immediate release (IR) to quetiapine sustained release (SR).

Moeller, H. J., Johnson, S., Mateva, T., Meulien, D., Brecher, M., Svensson, O., and Miller, F.

European Psychiatry (Paris) 2007;22(Suppl 1):S126-7, Abs P089.

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A randomized, placebo-controlled, relapse-prevention study with once-daily quetiapine sustained release in patients with schizophrenia.

Peuskens, J. C., Trivedi, J. K., Malyarov, S., Brecher, M., Svensson, O., Miller, F., and Persson, I.

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CUSTOM ABSTRACT In this randomized, double-blind, placebo-controlled study, the authors assessed the efficacy of sustained release quetiapine for the prevention of recurrence of schizophrenic episodes in 327 patients. Patients initially received open label quetiapine once daily and were then randomized to treatment with flexibly dosed quetiapine or placebo. The relapse rate was reduced in patients continuing quetiapine such that the study was terminated early, with 18% of quetiapine patients and 21% of placebo patients experiencing adverse effects and extrapyramidal symptoms occurring in 1.1% and 1% of patients, respectively. The authors conclude that once daily, sustained release quetiapine prevented relapses in patients with schizophrenia.

Randomised, placebo-controlled, relapse-prevention study with once-daily quetiapine sustained release in patients with schizophrenia.

Peuskens, J., Trivedi, J. K., Malyarov, S., Brecher, M., Svensson, O., Miller, F., Persson, I., and Meulien, D.

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after 90 relapses. Early termination occurred after the first interim analysis as quetiapine was shown to be significantly superior to placebo for time to relapse. The authors conclude that quetiapine SR (400-800 mg/day) given once daily was effective versus placebo in preventing relapse in patients with clinically-stable schizophrenia and was well tolerated during longer-term use.

Efficacy of Once-Daily Quetiapine Sustained Release (SR) in Patients with Acute Schizophrenia.

Schulz, C., Kahn, R., Palazov, V., Reyes, E., Meulien, D., Brecher, M., and Svensson, O. In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 210. 1919.

CUSTOM ABSTRACT In this 6-week, double-blind, randomized, placebo-controlled study the efficacy and safety of once-daily quetiapine SR was evaluated in 588 patients who received either quetiapine SR 400, 600, or 800 mg/day, quetiapine IR 200 mg/day twice daily, or placebo. The primary endpoint was change from baseline to Day 42 in PANSS total score (LOCF) and secondary endpoints included percentage of patients responding at Day 42 with $\geq 30\%$ reduction in PANSS, a CGI-I score ≤ 3 , and changes from baseline to Day 42 in PANSS subscale scores and CGI-S. From the results the authors conclude that once-daily quetiapine SR (400-800 mg/day) was effective versus placebo in patients with acute schizophrenia, and was well tolerated.

Efficacy of Once-Daily Quetiapine Sustained Release across Symptom Domains in Schizophrenia.

Schulz, C., Kahn, R., Palazov, V., Reyes, E., Meulien, D., Brecher, M., and Svensson, O. In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 212. 1919.

CUSTOM ABSTRACT In this 6-week, double-blind, randomized study, quetiapine SR (400, 600, or 800 mg/day) was compared with quetiapine IR (400 mg/day) and placebo for efficacy in a broad range of symptoms in 588 patients with acute schizophrenia. Efficacy was assessed using ANCOVA analyses of the change from baseline to study endpoint for PANSS total score, positive, negative and general psychopathology subscale scores, and aggression and depression cluster scores. From the results the authors conclude that once-daily quetiapine SR is effective across a broad range of symptoms in acute schizophrenia, including positive and negative symptoms, as well as symptoms of general psychopathology, aggression, and depression.

AstraZeneca Pharmaceuticals LP
1800 Concord Pike
Wilmington, DE 19850-5437

SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets
NDA 22-047

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

EXCLUSIVITY INFORMATION

1. Exclusivity Claim

AstraZeneca Pharmaceuticals LP claims an exclusivity period of three years for this supplemental new drug application.

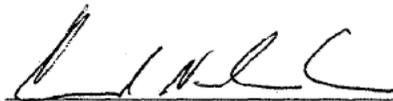
2. Authority for Exclusivity Claim

Exclusivity for this supplemental new drug application is being claimed pursuant to 21 CFR 314.108(b)(5).

3. Information Demonstrating this Supplemental Application Contains New Clinical Investigations Conducted or Sponsored by the Applicant that are Essential to the Approval of this Supplemental New Drug Application.

(a) Certification of New Clinical Investigations

AstraZeneca Pharmaceuticals LP certifies that to the best of its knowledge, each of the clinical investigation(s) included in this supplemental new drug application meets the definition of "new clinical investigation" set forth in 21 CFR Section 314.108(a).



Arvid Nordenhem, M.D., PhD.

(b) Essential to Approval

(i) Literature Search

Attached as Exhibit A is a list of all published studies and publicly available reports of clinical investigations known to AstraZeneca Pharmaceuticals LP through a literature search that are relevant to the conditions for which approval is being sought.

(ii) Certification

AstraZeneca Pharmaceuticals LP certifies that it has thoroughly searched the scientific literature and, to the best of its knowledge, the list of relevant published studies and/or publicly available reports is complete and accurate, and in its opinion, such published studies and/or publicly available reports do not provide a sufficient basis for the approval of the conditions for which approval is being sought without reference to the new clinical investigation(s) in this supplemental new drug application.



Arvid Nordenhem, M.D., PhD.

(iii) Explanation

The listed published studies and/or publicly available reports of clinical investigations do not provide sufficient basis for the approval of the conditions for which the Applicant is seeking approval, without reference to the new clinical investigations in this supplemental new drug application.

The new clinical investigation(s) provide safety and efficacy data regarding the use of SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets for the treatment of bipolar depression that could not be gleaned from published information. Accordingly, these new clinical investigations are essential to the approval of this supplemental new drug application.

(c) Conducted or Sponsored by the Applicant.

AstraZeneca Pharmaceuticals LP, the agent and subsidiary of AstraZeneca UK Limited, is the sponsor named in Form FDA 1571 for IND 76,146 under which the new clinical investigation essential to the approval of this supplemental new drug application was conducted. We believe this fact is sufficient under 21 CFR 314.50(j)(4)(iii) to establish that the clinical investigations were conducted or sponsored by the Applicant.



**Seroquel (quetiapine) SR/XR:
Exclusivity Search – 1996 through Nov 27, 2007**

Bibliography sorted A-Z by first author
Prepared by: Paula Payne-Gallimore, SIS, x62650

**New drugs approved by the FDA: Agents pending FDA approval -
Supplemental applications filed by manufacturer. Significant labeling
changes.**

Baker, D. E.
Hospital Pharmacy.42(7)(pp 648-652), 2007.

Current FDA-related drug information.

Baker, D. E.
Hospital Pharmacy 41(10), 980-982. 2006.

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Clinical benefit of switching patients with schizophrenia to once-daily quetiapine sustained release.

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Efficacy and tolerability of once-daily quetiapine sustained release in patients with acute schizophrenia: A randomised, double-blind, 6-week, placebo-controlled study.

Kahn, R., Schulz, C., Palazov, V., Reyes, E., Meulien, D., Brecher, M., Svensson, O., and Andersson, M. H. Biological Psychiatry 2007;61(8) Suppl S:262S, Abs 845.

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Efficacy and tolerability of once-daily extended release quetiapine fumarate in acute schizophrenia: A randomized, double-blind, placebo-controlled study.

Kahn, R. S., Schulz, S. C., Palazov, V. D., Reyes, E. B., Brecher, M., Svensson, O., Andersson, H. M., and Meulien, D. Journal of Clinical Psychiatry 68(6), 832-842. 2007.

Objective: To evaluate the efficacy and tolerability of extended release quetiapine fumarate (quetiapine XR) in a 6-week, double-blind, randomized study. Method: Patients with a DSM-IV diagnosis of acute schizophrenia were randomly assigned to fixed-dose quetiapine XR 400, 600, or 800 mg/day (once daily in the evening), quetiapine immediate release (IR) 400 mg/day (200 mg twice daily), or placebo. Dual-matched placebo was used to maintain blinding. Quetiapine XR target doses were reached by day 2 (400 and 600 mg) and day 3 (800 mg). The primary endpoint was least squares mean change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) total score. PANSS response rate (percentage of patients with greater than or equal to 30% reduction in total score), Clinical Global Impressions -Improvement scale (CGI-I) response rate (percentage of patients with

score less than or equal to 3), change in CGI-Severity of Illness (CGI-S), and adverse events (AEs) were also assessed. The study was conducted from November 2004 to December 2005. Results: 588 patients were enrolled and 446 (76%) completed the study. Improvement in PANSS total score at week 6 was significant versus placebo (- 18.8) in all groups: -24.8 (p =.03), -30.9 (p <.00 1), and -31.3 (p <.00 1) for quetiapine XR 400, 600, and 800 mg, respectively, and -26.6 (p =.004) for quetiapine IR. There were also statistically significant differences in PANSS and CGI-I response rates for all active treatments versus placebo (all p <.05). The most common AEs in all quetiapine groups were somnolence and dizziness; there were no unexpected AEs with quetiapine XR. Incidence of AEs potentially related to extrapyramidal symptoms was similar to placebo. Conclusion: Once-daily quetiapine XR (400/800 mg/day) was effective versus placebo in patients with acute schizophrenia. Treatment, including rapid dose escalation, was well tolerated, with a therapeutically effective dose reached by day 2.

Once-Daily Quetiapine Sustained Release (SR) Is Effective And Well Tolerated In Patients With Schizophrenia Switched From Quetiapine Immediate Release (IR).

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Once-daily quetiapine sustained release (SR) is effective and well tolerated in patients with schizophrenia switched from the same total daily dose of quetiapine immediate release (IR).

Moller, H., Johnson, S., Meulien, D., Brecher, M., Svensson, O., Miller, F., and Study 146 Investigators

Schizophrenia Bulletin 33(2), 449. 2007.

CUSTOM ABSTRACT In this randomized, double-blind, controlled study, the efficacy and safety of once daily quetiapine sustained release (SR) in 630 stable schizophrenic patients switched from same dose twice daily quetiapine immediate release (IR) are described. The rate of discontinuation due to lack of efficacy or adverse effects was 3.3% in patients treated with quetiapine SR and was 1.8% in patients treated with quetiapine IR, the LSM changes in PANSS total score were -3.7 and -4.2 respectively. The incidence of drug-related adverse events was 17.2% for

quetiapine SR and 15.7% for quetiapine IR, however, the type, distribution and intensity of adverse events were similar in the treatment groups. The authors conclude that schizophrenic patients clinically stable on quetiapine IR twice daily can be switched to same dose quetiapine SR once daily without changes in efficacy or safety.

Continued efficacy and tolerability in clinically stable patients switched from quetiapine immediate release (IR) to quetiapine sustained release (SR).

Moeller, H. J., Johnson, S., Mateva, T., Meulien, D., Brecher, M., Svensson, O., and Miller, F.

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Efficacy of Once-Daily Quetiapine Sustained Release across Symptom Domains in Schizophrenia.

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SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets NDA 22-047

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The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

EXCLUSIVITY INFORMATION

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2. Authority for Exclusivity Claim

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(a) Certification of New Clinical Investigations

AstraZeneca Pharmaceuticals LP certifies that to the best of its knowledge, each of the clinical investigation(s) included in this supplemental new drug application meets the definition of "new clinical investigation" set forth in 21 CFR Section 314.108(a).



Arvid Nordenhem, M.D., PhD.

(b) Essential to Approval

(i) Literature Search

Attached as Exhibit A is a list of all published studies and publicly available reports of clinical investigations known to AstraZeneca Pharmaceuticals LP through a literature search that are relevant to the conditions for which approval is being sought.

(ii) Certification

AstraZeneca Pharmaceuticals LP certifies that it has thoroughly searched the scientific literature and, to the best of its knowledge, the list of relevant published studies and/or publicly available reports is complete and accurate, and in its opinion, such published studies and/or publicly available reports do not provide a sufficient basis for the approval of the conditions for which approval is being sought without reference to the new clinical investigation(s) in this supplemental new drug application.



Arvid Nordenhem, M.D., PhD.

(iii) Explanation

The listed published studies and/or publicly available reports of clinical investigations do not provide sufficient basis for the approval of the conditions for which the Applicant is seeking approval, without reference to the new clinical investigations in this supplemental new drug application.

The new clinical investigation(s) provide safety and efficacy data regarding the use of SEROQUEL® XR (quetiapine fumarate) Extended Release Tablets for the treatment of bipolar mania that could not be gleaned from published information. Accordingly, these new clinical investigations are essential to the approval of this supplemental new drug application.

(c) Conducted or Sponsored by the Applicant.

AstraZeneca Pharmaceuticals LP, the agent and subsidiary of AstraZeneca UK Limited, is the sponsor named in Form FDA 1571 for IND 76,146 under which the new clinical investigation essential to the approval of this supplemental new drug application was conducted. We believe this fact is sufficient under 21 CFR 314.50(j)(4)(iii) to establish that the clinical investigations were conducted or sponsored by the Applicant.



**Seroquel (quetiapine) SR/XR:
Exclusivity Search – 1996 through Nov 27, 2007**

Bibliography sorted A-Z by first author
Prepared by: Paula Payne-Gallimore, SIS, x62650

**New drugs approved by the FDA: Agents pending FDA approval -
Supplemental applications filed by manufacturer. Significant labeling
changes.**

Baker, D. E.
Hospital Pharmacy.42(7)(pp 648-652), 2007.

Current FDA-related drug information.

Baker, D. E.
Hospital Pharmacy 41(10), 980-982. 2006.

CUSTOM ABSTRACT This article aims to inform the reader on updates pertaining to new drugs, indications, dosage forms and safety-related changes in labeling or use. It is stated that quetiapine (Seroquel) SR is an oral tablet for once daily administration for the treatment of schizophrenia. AUTHOR ABSTRACT This monthly feature will help readers keep current on new drugs, indications, dosage forms, and safety-related changes in labeling or use. Efforts have been made to ensure the accuracy of the information; however, if there are any questions, let us know at hospitalpharmacy@drugfacts.com.

Quetiapine in a controlled release formulation

Brecher, Martin; Chitra, Rohini; Eriksson, Hans; Shaw, Joan; Vaageroe, Maarten; Wilson, Ellis
Astrazeneca AB, Swed.PCT Int. Appl., 182pp.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007058593	A1	20070524	WO 2006-SE1300	20061116
US 2007185080	A1	20070809	US 2006-561306	20061117

The present invention relates to a pharmaceutical controlled release composition comprising quetiapine, 11-[4-[2(2- hydroxyethoxy) ethyl]-1-piperazinyl] dibenzo-[b,f][1,4] thiazepine in the treatment of mood disorders, anxiety disorders an symptoms of these disorders. Quetiapine may also be used in combination with a selective serotonin reuptake inhibitor, e.g. paroxetine or fluoxetine, or with a serotonin- norepinephrine reuptake inhibitor, such as duloxetine.

(b) (4)



Clinical benefit of switching patients with schizophrenia to once-daily quetiapine sustained release.

Ganesan, S., Agambaram, V., Randeree, F., Eggens, I., Schmidt, M. M., and Meulien, D. European Psychiatry (Paris) 2007;22(Suppl 1):S334-5, P403.

CUSTOM ABSTRACT In this 12 week, multicenter, open-label study of 477 patients with schizophrenia, the authors evaluated the clinical benefit of switching patients who experienced suboptimal efficacy/tolerability with their previous antipsychotic treatment to quetiapine sustained release (SR). Results showed that 62.8% of evaluable patients achieved a clinical benefit upon switching to quetiapine SR with significant improvements observed in mean [SD] change from baseline in CGI-CB (-2.1 [3.62]) and PANSS total (-13.6 [19.23]) (both $p < 0.001$). The mean [SD] CGI-I score at endpoint was 2.8 [1.49] ($p < 0.001$ for mean CGI-I < 4). The authors conclude that switching to quetiapine SR was associated with clinical benefit and was well tolerated in this patient population.

Efficacy and tolerability of once-daily quetiapine sustained release in patients with acute schizophrenia: A randomised, double-blind, 6-week, placebo-controlled study.

Kahn, R., Schulz, C., Palazov, V., Reyes, E., Meulien, D., Brecher, M., Svensson, O., and Andersson, M. H. Biological Psychiatry 2007;61(8) Suppl S:262S, Abs 845.

CUSTOM ABSTRACT In this randomised, double-blind, placebo-controlled study, the authors assessed the safety and efficacy of quetiapine sustained release (SR) once daily or immediate release (IR) twice daily for the treatment of schizophrenia in 588 patients. Psychiatric symptoms improved in a dose dependent manner for SR formulations, with the IR formulation having similar efficacy to the lower dose SR. The main side effects were somnolence and dizziness with a similar incidence of extrapyramidal effects as that seen in placebo-treated patients, and 2 patients taking SR and 1 taking IR quetiapine discontinued due to side effects. The authors conclude that once daily SR quetiapine was safe and effective in patients with schizophrenia.

Efficacy and tolerability of once-daily extended release quetiapine fumarate in acute schizophrenia: A randomized, double-blind, placebo-controlled study.

Kahn, R. S., Schulz, S. C., Palazov, V. D., Reyes, E. B., Brecher, M., Svensson, O., Andersson, H. M., and Meulien, D. Journal of Clinical Psychiatry 68(6), 832-842. 2007.

Objective: To evaluate the efficacy and tolerability of extended release quetiapine fumarate (quetiapine XR) in a 6-week, double-blind, randomized study. Method: Patients with a DSM-IV diagnosis of acute schizophrenia were randomly assigned to fixed-dose quetiapine XR 400, 600, or 800 mg/day (once daily in the evening), quetiapine immediate release (IR) 400 mg/day (200 mg twice daily), or placebo. Dual-matched placebo was used to maintain blinding. Quetiapine XR target doses were reached by day 2 (400 and 600 mg) and day 3 (800 mg). The primary endpoint was least squares mean change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) total score. PANSS response rate (percentage of patients with greater than or equal to 30% reduction in total score), Clinical Global Impressions -Improvement scale (CGI-I) response rate (percentage of patients with

score less than or equal to 3), change in CGI-Severity of Illness (CGI-S), and adverse events (AEs) were also assessed. The study was conducted from November 2004 to December 2005. Results: 588 patients were enrolled and 446 (76%) completed the study. Improvement in PANSS total score at week 6 was significant versus placebo (- 18.8) in all groups: -24.8 (p =.03), -30.9 (p <.00 1), and -31.3 (p <.00 1) for quetiapine XR 400, 600, and 800 mg, respectively, and -26.6 (p =.004) for quetiapine IR. There were also statistically significant differences in PANSS and CGI-I response rates for all active treatments versus placebo (all p <.05). The most common AEs in all quetiapine groups were somnolence and dizziness; there were no unexpected AEs with quetiapine XR. Incidence of AEs potentially related to extrapyramidal symptoms was similar to placebo. Conclusion: Once-daily quetiapine XR (400/800 mg/day) was effective versus placebo in patients with acute schizophrenia. Treatment, including rapid dose escalation, was well tolerated, with a therapeutically effective dose reached by day 2.

Once-Daily Quetiapine Sustained Release (SR) Is Effective And Well Tolerated In Patients With Schizophrenia Switched From Quetiapine Immediate Release (IR).

Moller, H.-J., Johnson, S., Mateva, T., Meulien, D., Brecher, M., Svensson, O., and Miller, F.

In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 202. 1919.

CUSTOM ABSTRACT In this randomized, double-blind study, efficacy and tolerability of switching from quetiapine IR to quetiapine SR, compared with maintaining quetiapine IR treatment in patients with schizophrenia was evaluated. 497 patients were randomized to quetiapine SR (n=331) or quetiapine IR (n=166) with patients receiving quetiapine IR twice daily for 4 weeks, then randomized (2:1) to a once daily equivalent daily dose of quetiapine SR or maintained on quetiapine IR for 6 weeks. The primary endpoint was percent of patients with insufficient efficacy, defined as either discontinuation due to lack of efficacy or $\geq 20\%$ increase in PANSS at any visit. Using the selected non-inferiority margin of 6%, non-inferiority was narrowly missed and non-inferiority was shown in the per-protocol population: 5.3% receiving quetiapine SR showed insufficient efficacy versus 6.2% receiving quetiapine IR. The authors conclude that patients stable on quetiapine IR can be switched to once-daily quetiapine SR without clinical deterioration or compromise in safety/tolerability.

Once-daily quetiapine sustained release (SR) is effective and well tolerated in patients with schizophrenia switched from the same total daily dose of quetiapine immediate release (IR).

Moller, H., Johnson, S., Meulien, D., Brecher, M., Svensson, O., Miller, F., and Study 146 Investigators

Schizophrenia Bulletin 33(2), 449. 2007.

CUSTOM ABSTRACT In this randomized, double-blind, controlled study, the efficacy and safety of once daily quetiapine sustained release (SR) in 630 stable schizophrenic patients switched from same dose twice daily quetiapine immediate release (IR) are described. The rate of discontinuation due to lack of efficacy or adverse effects was 3.3% in patients treated with quetiapine SR and was 1.8% in patients treated with quetiapine IR, the LSM changes in PANSS total score were -3.7 and -4.2 respectively. The incidence of drug-related adverse events was 17.2% for

quetiapine SR and 15.7% for quetiapine IR, however, the type, distribution and intensity of adverse events were similar in the treatment groups. The authors conclude that schizophrenic patients clinically stable on quetiapine IR twice daily can be switched to same dose quetiapine SR once daily without changes in efficacy or safety.

Continued efficacy and tolerability in clinically stable patients switched from quetiapine immediate release (IR) to quetiapine sustained release (SR).

Moeller, H. J., Johnson, S., Mateva, T., Meulien, D., Brecher, M., Svensson, O., and Miller, F.

European Psychiatry (Paris) 2007;22(Suppl 1):S126-7, Abs P089.

CUSTOM ABSTRACT This randomized, double-blind study compared the efficacy and tolerability of changing treatment of 166 out of a total of 497 patients with clinically stable schizophrenia from fixed doses of quetiapine immediate release (IR) given twice daily for 4 weeks to the same daily dose of quetiapine sustained release (SR) given once daily for 6 weeks. The primary outcome measures of drug discontinuation because of lack of efficacy and increase in psychiatric rating scale were low and similar in both groups of patients, while the occurrence and type of adverse events were also compatible. The authors conclude that schizophrenic patients whose disease had been stabilized on fixed doses of quetiapine IR administered twice daily could be safely and effectively changed to the equivalent daily dose of the SR preparation of quetiapine which was given only once each day in the evening.

A randomized, placebo-controlled, relapse-prevention study with once-daily quetiapine sustained release in patients with schizophrenia.

Peuskens, J. C., Trivedi, J. K., Malyarov, S., Brecher, M., Svensson, O., Miller, F., and Persson, I.

Schizophrenia Bulletin 33(2), 453. 2007.

CUSTOM ABSTRACT In this randomized, double-blind, placebo-controlled study, the authors assessed the efficacy of sustained release quetiapine for the prevention of recurrence of schizophrenic episodes in 327 patients. Patients initially received open label quetiapine once daily and were then randomized to treatment with flexibly dosed quetiapine or placebo. The relapse rate was reduced in patients continuing quetiapine such that the study was terminated early, with 18% of quetiapine patients and 21% of placebo patients experiencing adverse effects and extrapyramidal symptoms occurring in 1.1% and 1% of patients, respectively. The authors conclude that once daily, sustained release quetiapine prevented relapses in patients with schizophrenia.

Randomised, placebo-controlled, relapse-prevention study with once-daily quetiapine sustained release in patients with schizophrenia.

Peuskens, J., Trivedi, J. K., Malyarov, S., Brecher, M., Svensson, O., Miller, F., Persson, I., and Meulien, D.

European Psychiatry (Paris) 2007;(Suppl 1):S132, P107.

CUSTOM ABSTRACT In this randomized, double-blind, placebo-controlled relapse-prevention study, 197 patients with schizophrenia received either quetiapine SR (400-800 mg/day) or placebo following a 16-week stabilization period where patients were switched to open-label, once-daily quetiapine SR dosed at 300 mg on Day 1, 600 mg on Day 2, then 400-800 mg. The primary endpoint was time from randomization to psychiatric relapse with planned analyses at interim, after 45 and 60 relapses, and final,

after 90 relapses. Early termination occurred after the first interim analysis as quetiapine was shown to be significantly superior to placebo for time to relapse. The authors conclude that quetiapine SR (400-800 mg/day) given once daily was effective versus placebo in preventing relapse in patients with clinically-stable schizophrenia and was well tolerated during longer-term use.

Efficacy of Once-Daily Quetiapine Sustained Release (SR) in Patients with Acute Schizophrenia.

Schulz, C., Kahn, R., Palazov, V., Reyes, E., Meulien, D., Brecher, M., and Svensson, O. In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 210. 1919.

CUSTOM ABSTRACT In this 6-week, double-blind, randomized, placebo-controlled study the efficacy and safety of once-daily quetiapine SR was evaluated in 588 patients who received either quetiapine SR 400, 600, or 800 mg/day, quetiapine IR 200 mg/day twice daily, or placebo. The primary endpoint was change from baseline to Day 42 in PANSS total score (LOCF) and secondary endpoints included percentage of patients responding at Day 42 with $\geq 30\%$ reduction in PANSS, a CGI-I score ≤ 3 , and changes from baseline to Day 42 in PANSS subscale scores and CGI-S. From the results the authors conclude that once-daily quetiapine SR (400-800 mg/day) was effective versus placebo in patients with acute schizophrenia, and was well tolerated.

Efficacy of Once-Daily Quetiapine Sustained Release across Symptom Domains in Schizophrenia.

Schulz, C., Kahn, R., Palazov, V., Reyes, E., Meulien, D., Brecher, M., and Svensson, O. In: 160th Annual Meeting of the American Psychiatric Association (APA), San Diego, California, USA, 212. 1919.

CUSTOM ABSTRACT In this 6-week, double-blind, randomized study, quetiapine SR (400, 600, or 800 mg/day) was compared with quetiapine IR (400 mg/day) and placebo for efficacy in a broad range of symptoms in 588 patients with acute schizophrenia. Efficacy was assessed using ANCOVA analyses of the change from baseline to study endpoint for PANSS total score, positive, negative and general psychopathology subscale scores, and aggression and depression cluster scores. From the results the authors conclude that once-daily quetiapine SR is effective across a broad range of symptoms in acute schizophrenia, including positive and negative symptoms, as well as symptoms of general psychopathology, aggression, and depression.

EXCLUSIVITY SUMMARY

Doctype	Number	Supp. Type	Supp. No.	Proprietary Name Generic Name	Dosage Form & Strengths	Claim
NDA #	22047	SE1	006	Seroquel XR (quetiapine fumarate)	extended-release tablets 50, 150, 200, 300, 400 mg	the use of Seroquel XR as monotherapy in the treatment of bipolar depression
NDA #	22047	SE1	007	Seroquel XR (quetiapine fumarate)	extended-release tablets 50, 150, 200, 300, 400 mg	the use of Seroquel XR as monotherapy in the treatment of bipolar mania
NDA #	22047	SE1	008	Seroquel XR (quetiapine fumarate)	extended-release tablets 50, 150, 200, 300, 400 mg	the use of Seroquel XR as adjunctive therapy in the treatment of bipolar mania

Note: SE1-008 relies upon the data from SE1-007, plus extrapolation of efficacy from the IR tablet, which was approved as monotherapy and adjunctive therapy for bipolar mania under NDA 20-639 SE1-016 [monotherapy] and -017 [adjunctive therapy] previously.

Applicant: AstraZeneca Pharmaceuticals LP

Approval Date, If Known PDUFA Goal Date is October 19, 2008 for all three supplements

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

S-006

YES

NO

S-007

YES

NO

S-008

YES

NO

b) If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

S-006: **505(b)(1) SE1 for new indication.**

S-007: **505(b)(1) SE1 for new indication.**

S-008: **505(b)(1) SE1 for new indication.**

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

S-006:

YES

NO

S-007:

YES

NO

S-008:

YES

NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

S-006:	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
S-007:	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
S-008:	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

S-006:	THREE
S-007:	THREE
S-008:	THREE

e) Has pediatric exclusivity been granted for this Active Moiety?

S-006, -007, -008:	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
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If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

The requested studies have not yet been submitted. A Pediatric Exclusivity Determination will be made after these studies are received.

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

S-006, -007, -008:	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
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IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

S-006, -007, -008:

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #	20-639	Seroquel (quetiapine fumarate)	Tablets 25, 50, 100, 200, 300, 400 mg
NDA #	22-047	Seroquel XR (quetiapine fumarate)	Extended Release Tablets, 50, 200, 300, 400 mg

2. Combination product. *Not Applicable.*

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

S-006:	YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>
S-007:	YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>
S-008: yes by right of reference	YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

S-006:	YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>
S-007:	YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>
S-008:	See Question 3a.			

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application

S-006: YES NO
S-007: YES NO
S-008: See Question 3a.

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

S-006: YES NO
S-007: YES NO
S-008: See Question 3a.

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

S-006: YES NO
S-007: YES NO
S-008: See Question 3a.

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

S-006: One Investigation: Study D144CC00002
S-007: One Investigation: Study D144CC00004
S-008: See Question 3a.

Note: the sponsor was permitted to submit results from only one investigation for each of the two indications of bipolar depression and bipolar mania because the results were submitted concurrently and the Immediate Release formulation of the same active moiety is already approved for these indications.

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

S-006:	Study D144CC00002	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
S-007:	Study D144CC00004	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
S-008:	Study D144CC00004 plus extrapolation from NDA 20-639 S-017.	YES <input type="checkbox"/>	NO <input type="checkbox"/>

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

please see above

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

S-006:	Study D144CC00002	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
S-007:	Study D144CC00004	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
S-008:	Study D144CC00004 plus extrapolation from NDA 20-639 S-017.	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

please see above.

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

S-006:	Study D144CC00002
S-007:	Study D144CC00004
S-008:	Study D144CC00004 plus extrapolation from NDA 20-639 S-017.

Exclusivity Summary
NDA 22-047: SE1-006, SE1-007, SE1-008

Investigation #2 !
! YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

S-006, -007, and -008: YES NO

If yes, explain:

Name of person completing form: Doris J. Bates, Ph.D.
Title: Regulatory Health Project Manager
Date: September 17, 2008

Name of Office/Division Director signing form: Thomas P. Laughren, M.D.
Title: Director, Division of Psychiatry Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Doris Bates
10/8/2008 10:21:08 AM

Thomas Laughren
10/8/2008 12:20:17 PM

**Responses below pertain to S-006.
Please see Attachment A for S-007, and Attachment B for S-008.**

S-006 Indication: use of Seroquel XR as monotherapy in the treatment of bipolar depression. Q1 - Q3 are answered in the first section of this form, above.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for some or all pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed): _____

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input checked="" type="checkbox"/>	Neonate	birth	1 mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. 1 mo.	9 yr. 11 mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

Not feasible:

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed): see justification below.

* Not meaningful therapeutic benefit:

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached. See immediately below.

Presently, it is not possible to diagnose bipolar disorder reliably in the above listed pediatric age groups. Therefore, appropriate studies cannot be developed and carried out.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

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IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpmhs@fda.hhs.gov) OR AT 301-796-0700.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):			Reason for Deferral			Applicant Certification †
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/> Other	10 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): June 1, 2015. Deferral certification = pediatric studies in the IR formulation are now completed under a PWR and the sponsor is submitting the required pediatric supplements before the end of 2008. Based on the PK information that should then be available, extrapolation from the IR to the XR dosage form may be possible. On this basis, submission of studies for the XR is presently deferred.						

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: see above

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Additional pediatric subpopulation(s) in which studies have been completed (check below):

Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually

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IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpmhs@fda.hhs.gov) OR AT 301-796-0700.

requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:					
Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

NOTE: S-007 and S-008 information follows this section.

Attachment A: SE1-007

007 Indication: use of Seroquel XR as monotherapy in the treatment of bipolar mania. Q1 - Q3 are answered in the preceding section of this form, for all three supplements.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for some or all pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed): _____

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input checked="" type="checkbox"/>	Neonate	birth	1 mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. <u>1</u> mo.	9 yr. <u>11</u> mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

Not feasible:

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed): see justification below.

* Not meaningful therapeutic benefit:

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached. See immediately below.

Presently, it is not possible to diagnose bipolar disorder reliably in the above listed pediatric age groups. Therefore, appropriate studies cannot be developed and carried out.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received	
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input checked="" type="checkbox"/> Other	10 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Date studies are due (mm/dd/yy): June 1, 2015. Other Reason / Deferral certification = pediatric studies in the IR formulation are now completed under a PWR and the sponsor is submitting the required pediatric supplements before the end of 2008. Based on the PK information that should then be available, extrapolation from the IR to the XR dosage form may be possible. On this basis, submission of studies for the XR is presently deferred.							

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: see above

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:					
Population		minimum	maximum		
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.		
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.		
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.		
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.		
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.		
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.		

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Action F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.

Attachment B: SE1-008

008 Indication: use of Seroquel XR as adjunctive therapy in the treatment of bipolar mania. Q1 - Q3 are answered in the first section of this form, for all three supplements.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for some or all pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed):

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input checked="" type="checkbox"/>	Neonate	birth	1 mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. 1 mo.	9 yr. 11 mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

Not feasible:

Necessary studies would be impossible or highly impracticable because:

Disease/condition does not exist in children

Too few children with disease/condition to study

Other (e.g., patients geographically dispersed): see justification, below

* Not meaningful therapeutic benefit:

Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached. See immediately below.

Presently, it is not possible to diagnose bipolar disorder reliably in the above listed pediatric age groups. Therefore, appropriate studies cannot be developed and carried out.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Version 31-JUL-2008

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpmhs@fda.hhs.gov) OR AT 301-796-0700.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received	
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input checked="" type="checkbox"/> Other	10 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Date studies are due (mm/dd/yy): June 1, 2015.							
Deferral certification = pediatric studies in the IR formulation are now completed under a PWR and the sponsor is submitting the required pediatric supplements before the end of 2008. Based on the PK information that should then be available, extrapolation from the IR to the XR dosage form may be possible. On this basis, submission of studies for the XR is presently deferred.							

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: see above

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Additional pediatric subpopulation(s) in which studies have been completed (check below):

Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 6/2008)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

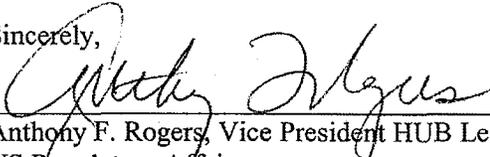
Doris Bates
10/8/2008 10:26:02 AM

1.3.3 DEBARMENT CERTIFICATION

**Re: NDA 22-047 – Supplement for Bipolar Mania
SEROQUEL® XR (quetiapine fumarate) extended-release tablets
Debarment Certification Statement**

In response to the requirements of the Generic Drug Enforcement Act of 1992, I hereby certify on behalf of AstraZeneca LP (AstraZeneca), that we did not use and will not use in connection with this New Drug Application, the services of any person in any capacity debarred under section 306 (a) or (b).

Sincerely,



Anthony F. Rogers, Vice President HUB Leader US
US Regulatory Affairs
AstraZeneca

Table of Contents
NDA 22-047 SE1-006, SE1-007, SE1-008
SEROQUEL® XR (quetiapine fumarate) Extended-Release Tablets
Bipolar Depression [SE1-006]
Bipolar Mania (Acute Monotherapy) [SE1-007]
Bipolar Mania (Maintenance Treatment Adjunctive to Li or (b) (4)
APPROVAL --DUE DATE: October 19, 2008

Approval Action Package:

Table of Contents & Action Package Checklist: Front of File

8. Action Letter & Labeling
 - AP Letter
 - Final Agreed Upon Labeling [PLR] - combined for all three supplements: see AP letter
 - Applicant Proposed Labeling
 - Consolidated labeling that merges indications for S-006, S-007, and S-008, per FDA request
 - PLR Labeling Review Not Required: Approved PLR Label for Seroquel XR Used as Base Document
9. Regulatory Information
 - Patent Information [Orange Book]
 - Patent Certification and Exclusivity Checklist
 - Certification provided for each application separately by sponsor
 - Consolidated Exclusivity Checklist: covers all three supplements
 - User Fee Information, Debarment Certification.
 - Note: Risk Management Plan not Required: Standard Pharmacovigilance is Sufficient.
10. Pediatric Information
 - Consolidated Pediatric Page: covers all three supplements
 - Applicant's Requests for Waivers and Deferrals
11. Administrative Memoranda
 - Division Director Memo
 - Clinical Team Leader Memo
12. Clinical Review
 - Combined Clinical Review of all three supplements
13. Consult Reviews and Technical Reviews
 - Maternal Health Team Review [Labeling]
 - DSI Information: Letters, CIS
 - Statistical Review
 - Clinical Pharmacology Review: Not Required
 - Nonclinical Pharmacology: Communication with Comments on Labeling
 - Chemistry: CMC Review, Confirmation of Categorical Exclusion from Requirement for EA
14. Correspondence, Minutes of Meetings, Submission History
 - Official Correspondence Applicant to FDA
 - Official Correspondence FDA to Applicant
 - Filing Review PM Checklist and Filing Meeting Minutes
 - Milestone Meeting: EOP2 Preliminary Comments, November 6, 2006. Meeting Cancelled by Firm.
 - EDR History
 - DSS History

NDA 22-047 S-006, S-007, S-008
ACTION PACKAGE CHECKLIST -- SUPPLEMENTAL NDA

Application Information		
NDA 22-047	Efficacy Supplement Type SE1	Supplement Number 006, 007, 008
Indication: SE1-006: the use of Seroquel XR as monotherapy in the treatment of bipolar depression SE1-007: the use of Seroquel XR as monotherapy in the treatment of bipolar mania SE1-008: the use of Seroquel XR as adjunctive therapy in the treatment of bipolar mania		
Drug: Seroquel XR (quetiapine fumarate) Extended-Release Tablets		Applicant: AstraZeneca Pharmaceuticals, LP
RPM: Bates	HFD-130	Phone # 301 796 1040
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)		
❖ Application Classifications:		
<ul style="list-style-type: none"> • Review priority 		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority for all three supplements.
<ul style="list-style-type: none"> • Chem class (NDAs only) 		
<ul style="list-style-type: none"> • Other (e.g., orphan, OTC) 		
❖ User Fee Goal Dates		October 19, 2008 - all 3 supplements
❖ Special programs (indicate all that apply)		<input checked="" type="checkbox"/> None Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2
❖ User Fee Information		
<ul style="list-style-type: none"> • User Fee 		<input checked="" type="checkbox"/> Paid UF ID numbers (b) (4) S006 S007 S008
<ul style="list-style-type: none"> • User Fee waiver 		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify)
<ul style="list-style-type: none"> • User Fee exception 		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify)
❖ Application Integrity Policy (AIP) <i>NOT APPLICABLE</i>		
<ul style="list-style-type: none"> • Applicant is on the AIP 		<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP 		<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Exception for review (Center Director's memo) 		

<ul style="list-style-type: none"> OC clearance for approval 	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	(✓) Verified for all three supplements.
❖ Patent	
<ul style="list-style-type: none"> Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. 	(✓) Verified (all 3 supplements)
❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> Exclusivity summary Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	patent on active moiety until 06SEP2011 exclusivity until 20OCT2009
<ul style="list-style-type: none"> Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	() Yes, Application # _____ (✓) No
❖ Administrative Reviews (Project Manager, ADRA)	✓ Filing Checklist
General Information	
❖ Actions	
<ul style="list-style-type: none"> Proposed action 	(✓) AP () TA () AE () NA
<ul style="list-style-type: none"> Previous actions (specify type and date for each action taken) 	none - first cycle approval
<ul style="list-style-type: none"> Status of advertising (approvals only) 	(✓) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
<ul style="list-style-type: none"> Press Office notified of action (approval only) 	(✓) Yes () Not applicable
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	TBD by Press Office
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
<ul style="list-style-type: none"> Final Agreed Upon Labeling 	✓ (see AP Letter)
<ul style="list-style-type: none"> Consolidated applicant-proposed labeling 	✓
<ul style="list-style-type: none"> Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings) 	✓ See Clinical Review, NonClinical Pharm/Tox Communication, Pediatric and Maternal Health Team Review
<ul style="list-style-type: none"> Other relevant labeling (e.g., most recent 3 in class, class labeling) 	NA
❖ Labels (immediate container & carton labels)	
<ul style="list-style-type: none"> Division proposed (only if generated after latest applicant submission) 	NA
<ul style="list-style-type: none"> Applicant proposed 	✓
<ul style="list-style-type: none"> Reviews 	✓ See CMC Review
❖ Post-marketing commitments	
<ul style="list-style-type: none"> Agency request for post-marketing commitments 	PREA ONLY: Partial waiver, partial deferral.
<ul style="list-style-type: none"> Documentation of discussions and/or agreements relating to post-marketing commitments 	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	✓
❖ Memoranda and Telecons	✓

❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	06NOV2006 [IND 45456] - preliminary comments only, meeting cancelled by sponsor
• Pre-sNDA meeting (indicate date)	none requested
• Filing Meeting	30JAN2008
❖ Advisory Committee Meeting	Not Applicable
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	Not Applicable
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader)	✓ Medical Team Leader, Division Director
Clinical Information	
❖ Clinical review	✓
❖ Pediatric Page	✓
❖ Statistical review	✓
❖ Clinical Pharmacology and Biopharmaceutics review(s)	NA
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	✓
• Bioequivalence studies	NA
CMC Information	
❖ CMC review(s)	✓ includes container labeling for 50 mg strength (previously approved, inspected within past 2 years, now to be marketed)
❖ Environmental Assessment	
• Categorical Exclusion	✓
❖ Facilities inspection (provide EER report)	NA
❖ Methods validation	NA
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews	See communication re labeling
❖ Nonclinical inspection review summary	NA
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	NA
❖ CAC/ECAC report	NA

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Doris Bates
10/8/2008 10:24:22 AM

Bates, Doris J

From: Mathis, Mitchell
Sent: Thursday, October 02, 2008 2:53 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Please include my name.

Thank you,
Mitch

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
Importance: High

Under FDAAA we are now required to provide a list of all persons associated with the approval of NDAs or supplements who consent to being listed.

Please reply to this email to let me know if you wish to be included in the list for these supplemental NDAs .

The list will include only the names of those who wish to be included, but the action package must also include copies of your email messages agreeing to be included. So I do need your responses if you wish to be listed.

These three PDUFA actions fall on the same day and are being acted on together. I'm doing a consolidated list, so I only need one response. Thank you!

Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Pinto, Julia
Sent: Monday, September 22, 2008 11:21 AM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Yes, please include me.
Julia

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
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*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Mahjoob, Kooros
Sent: Friday, September 19, 2008 2:40 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Doris,

Yes, I was involved. Please include my name in the list.

Thanks,

Kooros

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
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*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Vidra, James D
Sent: Friday, September 19, 2008 11:31 AM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Doris,
Please include me in your list for this supplement.
Jim Vidra

James D. Vidra, Ph.D.
Branch Chief
Branch VII, Division of Postmarketing Evaluation
Office of New Drug Quality Assessment
Center of Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Telephone No. 301-796-1767
Fax No. 301-796-9749
Email Address: james.vidra@fda.hhs.gov

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
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Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center

Bates, Doris J

From: Bloom, Raanan
Sent: Friday, September 19, 2008 10:57 AM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

OK with me.

Raanan (Ron) A. Bloom, M.S., Ph.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmaceutical Science/HFD-003
Silver Spring, MD 20993-0002
Phone: 301-796-2185
Fax: 301-796-9997
e-mail: raanan.bloom@fda.hhs.go

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
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Best regards,

Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products

*Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Yang, Peiling
Sent: Thursday, September 18, 2008 8:14 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Yes, I do.

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araujo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
Importance: High

Under FDAAA we are now required to provide a list of all persons associated with the approval of NDAs or supplements who consent to being listed.

Please reply to this email to let me know if you wish to be included in the list for these supplemental NDAs .

The list will include only the names of those who wish to be included, but the action package must also include copies of your email messages agreeing to be included. So I do need your responses if you wish to be listed.

These three PDUFA actions fall on the same day and are being acted on together. I'm doing a consolidated list, so I only need one response. Thank you!

Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Feibus, Karen
Sent: Thursday, September 18, 2008 10:58 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

That is fine

Karen B. Feibus, M.D.
Medical Team Leader
Maternal Health Team
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

10903 New Hampshire Ave.
Building 22, Room 6412
Silver Spring, MD 20993
Phone (301)796-0889
karen.feibus@fda.hhs.gov

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
Importance: High

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Best regards,

Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center

Bates, Doris J

From: Laughren, Thomas P
Sent: Thursday, September 18, 2008 9:16 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

Count me in--Tom

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
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Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
Importance: High

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Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:28 PM
To: Bates, Doris J
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List

I consent to being listed in association with these approval actions.

From: Bates, Doris J
Sent: Thursday, September 18, 2008 7:26 PM
To: Bates, Doris J; Laughren, Thomas P; Chidambaram, Nallaperum; Yang, Peiling; Lee, John; Vidra, James D; Kordzakhia, George; Pinto, Julia; Bloom, Raanan; Khin, Ni Aye; Alfaro, Cara; Araojo, Richardae; Mahjoob, Kooros
Cc: Bouie, Teshara; Mathis, Mitchell; Purohit-Sheth, Tejashri; Feibus, Karen; Rosloff, Barry N; Fossom, Linda H; Mathis, Lisa
Subject: RE: NDA 22-047 S-006, -007, and -008: Seroquel XR (quetiapine), bipolar depression and acute mania [monotherapy and adjunctive therapy]- The List
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Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

Bates, Doris J

From: Rosloff, Barry N
ant: Friday, August 22, 2008 12:59 PM
fo: Bates, Doris J
Cc: Fossom, Linda H
Subject: seroquel labeling (suppl. 006-8)

Attachments: seroquellabel.doc

Doris,

Here are my changes (sections 8.1, 12.1, 12.2, and 13.1, track changes).



seroquellabel.doc (321 KB)

Barry

48 pages of draft labeling have been withheld as b(4) immediately following this page



Date: 12 September 2008

Thomas P. Laughren, MD
Division Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 22-047/S-006, -007, and-008
SEROQUEL XR[®] (quetiapine fumarate) Extended Release Tablets
Amendment to a pending application

Dear Dr. Laughren:

Reference is made to NDA 22-047/ S-006, -007, and-008 submitted on 19 December 2007 and to correspondence from Division on 21st and August 26th, 2008 containing questions from the clinical review team on these supplements. The purpose of this submission is to provide the responses to the Division's questions. This same response document was previously sent to the Division on 5 September 2008 by secure electronic mail and is now being submitted formally as an amendment to these supplements.

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 10 September 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

A signed, completed Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j)) is provided as discussed in the April 2008 *Draft Guidance for Sponsors, Industry, Researchers, Investigators, and Food and Drug Administration Staff: Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007*.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

NDA 22-047/S-006, -007, and -008 SEROQUEL XR® (quetiapine fumarate) Extended Release Tablets
Response to FDA Questions 21 and 26 August 2008

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp

Enclosure



Date: 28 August 2008

Thomas P. Laughren, MD
Division Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 22-047/S-006, -007, and-008
SEROQUEL XR[®] (quetiapine fumarate) Extended Release Tablets
Amendment to a pending application

Dear Dr. Laughren:

Reference is made to NDA 22-047/ S-006, -007, and-008 submitted on 19 December 2007 and to correspondence from Division on July 30th and August 15th, 2008 containing questions from the clinical review team on these supplements. The purpose of this submission is to provide the responses to the Division's questions. This same response document was previously sent to the Division on 20 August 2008 by secure electronic mail and is now being submitted formally as an amendment to these supplements.

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 26 August 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

A signed, completed Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j)) is provided as discussed in the April 2008 *Draft Guidance for Sponsors, Industry, Researchers, Investigators, and Food and Drug Administration Staff: Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007*.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

NDA 22-047/S-006, -007, and -008 SEROQUEL XR® (quetiapine fumarate) Extended Release Tablets
Response to FDA Questions 30 July and 15 August 2008

Please direct any questions or requests for additional information to me, or in my absence, to
Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp

Enclosure



Date: 05 June 2008

Thomas P. Laughren, MD
Division Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 22-047/S-007
SEROQUEL XR[®] (quetiapine fumarate) Extended Release Tablets
Amendment to a pending application

Dear Dr. Laughren:

Reference is made to NDA 22-047/S-007 submitted on 19 December 2007 and to correspondence from Dr. Bates on May 9th and 19th, 2008 requesting that AstraZeneca provide an amendment for S-007 which included a request for a categorical exclusion:

The purpose of this submission is to provide the request for a categorical exclusion.

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 2 June 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

AstraZeneca is aware of the provisions of the FDAAA requiring the filing of a completed Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) with, "applications" under section 505 of the FDCA and 351 of the PHSA. AstraZeneca is further aware of the fact that the FDA intends to issue guidance and a Q & A document providing, among other things, greater clarity as to which submissions require such certification. Until FDA issues such guidance, AstraZeneca will make a good faith effort to submit certifications with all submissions under section 505 of the FDCA and section 351 of the PHSA other than safety reports.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

NDA 22-047/S-007: SEROQUEL XR® (quetiapine fumarate) Extended Release Tablets

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

PMP

Enclosure



Date: 28 March 2008

Thomas Laughren, MD, Division Director
Division of Psychiatry Products
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-12666

Re: NDA 22-047/S-007
SEROQUEL[®] XR (quetiapine fumarate) Extended Release Tablets
Amendment to Pending Application: Errata

Dear Dr. Laughren:

Reference is made to NDA 22-047/S-007 for the treatment of Bipolar Mania and to the submission of an errata for this supplement on 28 January 2008 (eCTD Sequence 0014). AstraZeneca has recently become aware that some of the files sent in conjunction with eCTD sequence 0014 dated 28 January 2008 for the above application may not be viewable in FDA's environment. In response to advice from Donovan Duggan from FDA's Office of Business Process Support, AstraZeneca is re-submitting the affected files/documents to ensure that these files are available for review (as needed) and maintained within the lifecycle of the application. Please note that the resubmitted documents/files remain unchanged from the original submission.

This submission includes:

- A completed and signed Form FDA 356h
- A completed and signed Form FDA 3674
- Errata to the Clinical Study Report for Study D144CC00004 and related Appendices, (Appendix 12.2.01-12.2.10).

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 26 March 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

AstraZeneca is aware of the provisions of the FDAAA requiring the filing of a completed Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) with, "applications" under section 505 of the FDCA and 351 of the PHSA. AstraZeneca is further aware of the fact that the FDA intends to issue guidance and a Q & A document providing, among other things,

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp

Enclosure



Date: 27 March 2008

Thomas Laughren, MD, Division Director
Division of Psychiatry Products
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-12666

Re: NDA 22-047/S-006
SEROQUEL[®] XR (quetiapine fumarate) Extended Release Tablets
Amendment to Pending Application: Errata

Dear Dr. Laughren:

Reference is made to NDA 22-047/S-006 for the treatment of Bipolar Depression and to the submission of an errata for this supplement on 28 January 2008 (eCTD Sequence 0013). AstraZeneca has recently become aware that some of the files sent in conjunction with eCTD sequence 0013 dated 28 January 2008 for the above application may not be viewable in FDA's environment. In response to advice from Donovan Duggan from FDA's Office of Business Process Support, AstraZeneca is re-submitting the affected files/documents to ensure that these files are available for review (as needed) and maintained within the lifecycle of the application. Please note that the resubmitted documents/files remain unchanged from the original submission.

This submission includes:

- A completed and signed Form FDA 356h
- A completed and signed Form FDA 3674
- Errata to the Clinical Study Report for Study D144CC00002 and related Appendices, (Appendix 12.2.01-12.2.10).

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 25 March 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

AstraZeneca is aware of the provisions of the FDAAA requiring the filing of a completed Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) with "applications" under section 505 of the FDCA and 351 of the PHSA. AstraZeneca is further aware of the fact that the FDA intends to issue guidance and a Q & A document providing, among other things,

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

greater clarity as to which submissions require such certification. Until FDA issues such guidance, AstraZeneca will make a good faith effort to submit certifications with all submissions under section 505 of the FDCA and section 351 of the PHSA other than safety reports.

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Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp

Enclosure

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.					
DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		PRESCRIPTION DRUG USER FEE COVERSHEET			
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm					
1. APPLICANT'S NAME AND ADDRESS ASTRAZENECA PHARMACEUTICALS LP Gerald Limp 1800 CONCORD PIKE P.O. BOX 8355 Wilmington DE 19803-8355 US		4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 22-047			
2. TELEPHONE NUMBER 302-886-8017		5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: also reference NOA 20-639			
3. PRODUCT NAME SEROQUEL XR Extended Release Tablets - Adjunct Mania (quetiapine fumarate)		6. USER FEE I.D. NUMBER (b) (4)			
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY					
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO					
<p>OMB Statement: Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <table border="0"> <tr> <td>Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448</td> <td>Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852</td> <td>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</td> </tr> </table>			Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.			
SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 		TITLE Regulatory Affairs Director			
		DATE 2-21-08			
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$589,000.00					
Form FDA 3397 (03/07)					

[Close](#) [Print Cover sheet](#)



**SUPPLEMENTAL NDAs ACKNOWLEDGED/FILED:
FILING REVIEW ISSUES IDENTIFIED
(STATISTICAL)**

NDA 22-047 / S-006, S-007, S-008

Gerald Limp
Director, Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike, PO Box 8355
Wilmington, DE 19803-8355

Dear Mr. Limp:

Please refer to your supplemental new drug applications (sNDA), referenced above, which were submitted and received on December 19, 2007 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Seroquel XR (quetiapine fumarate) extended release tablets.

The supplemental applications provide for the use of quetiapine in the treatment of bipolar depression [S-006], as monotherapy in the acute treatment of mania [S-007], and as adjunctive therapy with lithium or (b) (4) in the maintenance treatment of mania [S-008].

We have completed our filing review for these supplemental applications and have determined that your applications are sufficiently complete to permit a substantive review. The applications are filed as of February 15, 2008 under section 505(b) of the Act and in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following review issues:

Statistical

S-006, Indication: Bipolar Depression; Study D144CC00002
S-007, Indication: Bipolar Mania; Study D144CC00004

- For Studies D144CC00002 and D144CC00004, please include SAS programs that produced all efficacy results.
- For Study D144CC00002, the data definition file d144cc0000 does not contain the names of all variables from submitted data sets. For example, the data set -madrs.xpt contains variables _bmadrs and _clmadrs, but these variables are not described in the definition file. Please adjust the definition file correspondingly.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

Please also note that our filing review is only a preliminary evaluation of the application, and is not indicative of all deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have any questions, please contact Doris J. Bates, Regulatory Project Manager, by phone at (301) 796-2260 or via secure electronic mail at doris.bates@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thomas Laughren
2/15/2008 04:57:54 PM



Date: 28 January 2008

Thomas Laughren, MD, Division Director
Division of Psychiatry Products
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-12666

Re: NDA 22-047/Supplement No. Pending
SEROQUEL[®] XR (quetiapine fumarate) Extended Release Tablets
Amendment to a Pending Application: Errata

Dear Dr. Laughren:

Reference is made to NDA 22-047 and the submission of a supplement to NDA 22-047 on 19 December 2007 for the treatment of Bipolar Mania. In accordance with 21 CFR 314.60, AstraZeneca Pharmaceuticals LP (AstraZeneca) is hereby submitting an amendment to this pending application.

It has come to our attention that during a Clinical Quality Assurance review it was discovered that some Appendix Listings (12.2.1 to 12.2.10) were misnumbered and did not correspond to the Section 12.2 cover pages. The Appendix Listings 12.2.1 to 12.2.10 that were misnumbered have been changed. The "Location of supporting data" tables for Section 6, Study Patients, Section 7, Efficacy, and Section 8, Safety have been updated in this errata. None of the data included in the appendices or in the tables derived from them were changed. In addition, minor errors in the Clinical Study Report text were discovered and have been corrected. None of these findings and changes alter the data interpretation or study conclusions. Therefore, we do not consider this a major amendment.

This submission includes:

- A completed and signed Form FDA 356h
- Errata to the Clinical Study Report for Study D144CC00004 and related Appendices, (Appendix 12.2.01-12.2.10).

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 24 January 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

Please note that Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) is not

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

greater clarity as to which submissions require such certification. Until FDA issues such guidance, AstraZeneca has put in place an interim process whereby it will make a good faith effort to submit certifications with all submissions under section 505 of the FDCA and section 351 of the PHSA other than safety reports. Please contact AstraZeneca if it is FDA's opinion that AstraZeneca is not making the certifications required by law.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp

Attachment



Date: 28 January 2008

Thomas Laughren, MD, Division Director
Division of Psychiatry Products
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-12666

Re: NDA 22-047/Supplement No. Pending
SEROQUEL[®] XR (quetiapine fumarate) Extended Release Tablets
Amendment to Pending Application: Errata

Dear Dr. Laughren:

Reference is made to NDA 22-047 and the submission of a supplement to NDA 22-047 on 19 December 2007 for the treatment of Bipolar Depression. In accordance with 21 CFR 314.60, AstraZeneca Pharmaceuticals LP (AstraZeneca) is hereby submitting an amendment to this pending application.

It has come to our attention that during a Clinical Quality Assurance review it was discovered that some Appendix Listings (12.2.1 to 12.2.10) were misnumbered and did not correspond to the Section 12.2 cover pages. The Appendix Listings 12.2.1 to 12.2.10 that were misnumbered have been changed. The "Location of supporting data" tables for Section 6, Study Patients, Section 7, Efficacy, and Section 8, Safety have been updated in this errata. None of the data included in the appendices or in the tables derived from them were changed. In addition, minor errors in the Clinical Study Report text were discovered and have been corrected. None of these findings and changes alter the data interpretation or study conclusions. Therefore, we do not consider this a major amendment.

This submission includes:

- A completed and signed Form FDA 356h
- Errata to the Clinical Study Report for Study D144CC00002 and related Appendices, (Appendix 12.2.01-12.2.10).

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 24 January 2008. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

NDA 22-047/Supplement number pending: SEROQUEL® (quetiapine fumarate) Extended Release Tablets
Submission dated 19 December 2007

Please note that Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) is not included with this submission. We are in the process of identifying procedures to comply with this requirement. We will update the application with the form as soon as we finalize our procedures.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

Please direct any questions or requests for additional information to me, or in my absence, to Pat Patterson, Associate Director, at (302) 885-1539.

Sincerely,

Gerald Limp, Director
Regulatory Affairs
Telephone: (302) 886-8017
Fax: (302) 886-2822

GL/pmp



10 January 2008

Thomas P. Laughren, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-12666

RE: NDA 22-047/ S-006
SEROQUEL XR™ (quetiapine fumarate) Extended-Release Tablets
Amendment to Supplement-50 mg component labels

Dear Dr. Laughren:

In accordance with 21 CFR, 314.60, AstraZeneca Pharmaceuticals LP (AstraZeneca) is submitting an amendment to pending supplement 006. This amendment includes the container labeling for the 50 mg strength of SEROQUEL XR as requested by FDA on January 3, 2008.

This electronic submission has been scanned using Symantec AntiVirus, Version 10.1.5.5001 (Corporate Edition), with a virus definition file dated 07 January 2008, rev 2. No viruses were detected, and AstraZeneca certifies that the submission is virus-free.

Please note that Form FDA 3674, Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C., § 282(j)) is not included with this submission. We are in the process of identifying procedures to comply with this requirement. We will update the application with the form as soon as we finalize our procedures.

This submission contains trade secrets and confidential commercial information exempt from public disclosure pursuant to exemption 4 of the Freedom of Information Act and FDA regulations, and the disclosure of which is prohibited by the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, and other applicable law. Pursuant to FDA regulations, AstraZeneca is entitled to notice, an opportunity to object, and an opportunity to seek pre-release judicial review in the event that FDA determines that all or any part of this submission may be disclosed.

NDA 22-047, SEROQUEL XR™ (quetiapine fumarate) Extended-Release Tablets

Please direct any questions or requests for additional information to me, or in my absence, to Gerald Limp, Director Regulatory Affairs, at (302) 886-8017.

Sincerely,

Kathryn Bradley, Director
Regulatory Affairs
Telephone: (302) 886-5622
Fax: (302) 886-3342

KEB

Bates, Doris J

From: Bates, Doris J
Date: Monday, October 15, 2007 2:26 PM
To: 'Patterson, Pat'
Subject: RE: NDA 22-047 Seroquel XR (quetiapine fumarate) Extended Release Tablets
Importance: High

Dear Ms. Patterson:

I've talked with Dr. Laughren and your formatting proposal is acceptable.

When you send in these supplements please send me an e-copy of the cover letters and User Fee cover sheets, plus WORD files of the proposed labeling - it is a great help to us in setting up our filing meetings to have these available.

Thank you, and I hope this information is helpful,

Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
Washington, DC Federal Research Center

From: Patterson, Pat [mailto:Pat.Patterson@astrazeneca.com]
Sent: Monday, October 01, 2007 5:45 PM
To: Bates, Doris J
Subject: NDA 22-047 Seroquel XR (quetiapine fumarate) Extended Release Tablets

Dear Dr. Bates,

Reference is made to the above NDA and to your November 6, 2006 email providing the Division's preliminary comments from their November 2, 2006 internal meeting regarding our proposed development program for Seroquel XR in the treatment of mania and bipolar depression.

AstraZeneca has completed both the acute mania study and the bipolar depression study in adults earlier than originally estimated. We would like to submit these studies in December 2007 to obtain these indications in our Seroquel XR label. We would like to explore some filing options with the Division to make sure we pursue the best approach. Our current plan is to submit 2 separate sNDAs: 1 for bipolar depression and 1 for acute mania, each with its own user fee and sequence number. Each supplement will contain the pertinent Module 1 components. Since each supplement is supported by only 1 study, there is no information to integrate and therefore we believe that there is no need for a Clinical Summary of Efficacy or a Clinical Summary of Safety. Pooling of the safety data across the two indications is challenging since the designs of the bipolar depression study is so different from the design of the mania study. In 1 of the supplements we will provide some non-clinical information to support a revision of the mechanism of action statement in the labeling. The supportive documentation will be provided for this revision in the appropriate sections for Module 2 and Module 4. Each supplement will also contain a Module 5 that includes the pertinent clinical study report, case report tabulations, patient profiles, case report forms and references.

Since the timing for the submission of these 2 supplements is only a short time away, December 2007, we would like to confirm with the Division that the approach described above would be acceptable. If you require any further clarification, please contact either me or Gerald Limp (302) 886-8017.

12/27/2007

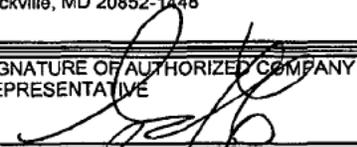
Sincerely,

Pat Patterson
Associate Director, Regulatory Affairs
(302) 885-1539

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION	PRESCRIPTION DRUG USER FEE COVERSHEET			
<p>A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm</p>				
1. APPLICANT'S NAME AND ADDRESS ASTRAZENECA PHARMACEUTICALS LP Gerald Limp 1800 CONCORD PIKE P.O. BOX 8355 Wilmington DE 19803-8355 US	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 22-047			
2. TELEPHONE NUMBER 302-886-8017	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:			
3. PRODUCT NAME SEROQUEL XR Extended Release Tablets - Bipolar Depression (quetiapine fumarate)	6. USER FEE I.D. NUMBER (b) (4)			
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY				
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO				
<p>OMB Statement: Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <table style="width:100%; border:none;"> <tr> <td style="width:33%; vertical-align: top;"> Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448 </td> <td style="width:33%; vertical-align: top;"> Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852 </td> <td style="width:33%; vertical-align: top;"> An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. </td> </tr> </table>		Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	<table border="1" style="width:100%; border-collapse: collapse;"> <tr> <td style="width:50%; padding: 5px;"> TITLE REGULATORY AFFAIRS DIRECTOR </td> <td style="width:50%; padding: 5px;"> DATE 12-10-07 </td> </tr> </table>	TITLE REGULATORY AFFAIRS DIRECTOR	DATE 12-10-07	
TITLE REGULATORY AFFAIRS DIRECTOR	DATE 12-10-07			
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$589,000.00				
Form FDA 3397 (03/07)				

Close Print Cover sheet

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.					
DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		PRESCRIPTION DRUG USER FEE COVERSHEET			
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm					
1. APPLICANT'S NAME AND ADDRESS ASTRAZENECA PHARMACEUTICALS LP Gerald Limp 1800 CONCORD PIKE P.O. BOX 8355 Wilmington DE 19803-8355 US	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 22-047	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:			
2. TELEPHONE NUMBER 302-886-8017	3. PRODUCT NAME SEROQUEL XR Extended Release Tablets - Acute Bipolar Mania (quetiapine fumarate)				
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act		6. USER FEE I.D. NUMBER (b) (4)			
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9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$589,000.00					
Form FDA 3397 (03/07)					

Close Print Cover sheet

Bates, Doris J

From: Bates, Doris J
Sent: Monday, November 06, 2006 2:08 PM
To: 'Patterson, Pat'
Cc: Bates, Doris J
Subject: RE: IND 45,456 Seroquel SR (quetiapine fumarate) Sustained Release Tablets: Preliminary Comments for November 9 Meeting / Teleconference
Importance: High
Attachments: EOP2 Meeting Bipolar Preliminary.pdf

Dear Ms. Patterson:

Attached to this email are the Division's preliminary comments from our November 2, 2006 internal meeting. These comments relate to our meeting scheduled for November 9, 2006.

Please let me know if a change in meeting format [to a teleconference] is needed, or if your firm sees no further need for the meeting upon receipt and review of these comments. Feel free to contact us if there are any questions about the attachment.

Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

FDA Preliminary Responses

IND 45,456 Seroquel SR
AstraZeneca

End of Phase 2 / Type B Meeting: Bipolar Disorder
PreMeeting November 2, 2006; Meeting with Firm November 9, 2006

Participants –

FDA: November 2, 2006: T. Laughren, M.D., Division Director; M. Mathis, M.D., Deputy Director; J. Cai, M.D., Clinical Reviewer; P. Yang, Ph.D., Statistical Team Leader; P. Dinh, Ph.D., Statistical Reviewer; R. Baweja, Ph.D., Biopharmaceutics Team Leader; D. Bates, Ph.D., Regulatory Project Manager.

FDA, November 9, 2006:

AstraZeneca, November 9: 2006: M. Scott, Ph.D., Executive Director, Development; B. Paulsson, M.D., Senior Research Physician; D. Darko, M.D., Director, Clinical Research; H. Winter, Ph.D., Director, Clinical Pharmacology; M Minkwitz, Ph.D., Director, Statistical Sciences; G. Limp, Director, US Regulatory Affairs; S. Fors, Director, Global Regulatory Affairs; P. Patterson, Associate Director, Regulatory Affairs.

Background: Quetiapine immediate release tablets are presently approved for the acute treatment of bipolar mania [monotherapy and adjunctive therapy] and the acute treatment of bipolar depression [monotherapy]. The IR tablets are also being studied as monotherapy and adjunctive therapy in the maintenance treatment of bipolar disorder and in the longer term treatment of bipolar depression [monotherapy]. The purpose of this meeting is to discuss AstraZeneca's (AZ) overall clinical program and study designs for the use of Seroquel SR in treating bipolar disorder.

AZ proposes that, (b) (4)

[REDACTED]

would plan to conduct AZ
(b) (4)

[REDACTED]

Questions:

Question 1:

- a. Does the Division agree that the justification provided above is sufficient to support an approval for quetiapine SR in the treatment of acute mania?
- b. Does the Division agree that the justification provided above is sufficient to support an approval for the quetiapine SR in the treatment of bipolar maintenance?

- c. Does the Division agree that the justification provided above is sufficient to support an approval for quetiapine SR in the treatment of bipolar depression?

Preliminary Comments: No.

From the clinical pharmacology / biopharmaceutics (CPB) perspective, the justification provided is supportive, but there is not a sufficient basis for [REDACTED] (b) (4)

This is because:

- a quantified and validated exposure-response relationship has not been established*
- the exposure (AUC) comparison, across studies, has large variability*

Therefore, from a CPB perspective, a safety and efficacy study is recommended.

From the clinical perspective, a single positive study with Seroquel SR would be needed for each of the indications bipolar mania and depression to support these claims. Once these claims have been established for Seroquel SR, and a claim for bipolar maintenance has been established for Seroquel IR, a claim for bipolar maintenance for Seroquel SR would also be considered established [Phase 4 commitment would not be required].

Discussion at Meeting:

Question 2

Should [REDACTED] (b) (4) not be acceptable, as described in the previous sections, would a single positive clinical efficacy study in acute mania and a single positive efficacy study in bipolar depression be sufficient for approval for each claim with SR tablets?

Preliminary Comments: Yes.

Discussion at Meeting:

General Comments:

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for November 9, 2006 between AstraZeneca and the Division of Psychiatry Products. This material is shared to promote a collaborative and successful discussion at the meeting. If there is anything in it that you do not understand or with which you do not agree, we very much want you to communicate such questions and disagreements. The minutes of the meeting will reflect the discussion that takes place during the meeting and are not expected to be identical to these preliminary comments.

If these answers and comments are clear to you and you determine that further discussion is not required, you have the option of canceling the meeting (please contact the RPM), but this is advisable only if the issues involved are quite narrow. It is not our intent to have our preliminary responses serve as a substitute for the meeting. It is important to remember that some meetings, particularly milestone meetings, are valuable even if pre-meeting communications seem to have answered the principal

questions. It is our experience that the discussion at meetings often raises important new issues.

Please note that if there are any major changes to your development plan / the purpose of the meeting / to the questions, based on our responses here, we may not be prepared to discuss or reach agreement on such changes at the meeting, but we will be glad to discuss them to the extent possible. If any modifications to the development plan or additional questions for which you would like FDA feedback arise prior to the meeting, contact the Regulatory Project Manager to discuss the possibility of including these for discussion at the meeting.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Doris Bates

11/6/2006 02:25:30 PM

CSO

Sent to sponsor on Monday 11-6-06 at 2:08 PM.

Bates, Doris J

From: Bates, Doris J
Sent: Monday, October 15, 2007 2:26 PM
To: 'Patterson, Pat'
Subject: RE: NDA 22-047 Seroquel XR (quetiapine fumarate) Extended Release Tablets
Importance: High

Dear Ms. Patterson:

I've talked with Dr. Laughren and your formatting proposal is acceptable.

When you send in these supplements please send me an e-copy of the cover letters and User Fee cover sheets, plus WORD files of the proposed labeling - it is a great help to us in setting up our filing meetings to have these available.

Thank you, and I hope this information is helpful,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

From: Patterson, Pat [mailto:Pat.Patterson@astrazeneca.com]
Sent: Monday, October 01, 2007 5:45 PM
To: Bates, Doris J
Subject: NDA 22-047 Seroquel XR (quetiapine fumarate) Extended Release Tablets

Dear Dr. Bates,

Reference is made to the above NDA and to your November 6, 2006 email providing the Division's preliminary comments from their November 2, 2006 internal meeting regarding our proposed development program for Seroquel XR in the treatment of mania and bipolar depression.

AstraZeneca has completed both the acute mania study and the bipolar depression study in adults earlier than originally estimated. We would like to submit these studies in December 2007 to obtain these indications in our Seroquel XR label. We would like to explore some filing options with the Division to make sure we pursue the best approach. Our current plan is to submit 2 separate sNDAs: 1 for bipolar depression and 1 for acute mania, each with its own user fee and sequence number. Each supplement will contain the pertinent Module 1 components. Since each supplement is supported by only 1 study, there is no information to integrate and therefore we believe that there is no need for a Clinical Summary of Efficacy or a Clinical Summary of Safety. Pooling of the safety data across the two indications is challenging since the designs of the bipolar depression study is so different from the design of the mania study. In 1 of the supplements we will provide some non-clinical information to support a revision of the mechanism of action statement in the labeling. The supportive documentation will be provided for this revision in the appropriate sections for Module 2 and Module 4. Each supplement will also contain a Module 5 that includes the pertinent clinical study report, case report tabulations, patient profiles, case report forms and references.

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12/27/2007

Sincerely,

Pat Patterson
Associate Director, Regulatory Affairs
(302) 885-1539

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Doris Bates
12/27/2007 04:17:55 PM
CSO

Bates, Doris J

From: Bates, Doris J
Sent: Friday, May 09, 2008 4:52 PM
To: 'Patterson, Pat'
Cc: 'Limp, Gerald L'; Bouie, Teshara
Subject: NDA 22-047, S-006, -007, -008: Seroquel XR, Bipolar Disorder. Please Submit Request for Categorical Exclusion

Importance: High

Good afternoon!

Our chemistry reviewers note that the production volume for direct use of quetiapine drops from (b) (4) kg/yr (June 9, 2006 EA) to (b) (4) kg/yr (Nov 23, 2007 EA; present submission).

Accordingly, these NDA supplements should qualify for categorical exclusion under 21 CFR 25.31a.

Please amend these supplements by submitting a request for categorical exclusion. An electronic desk copy of the request may be forwarded to us [please use the 'reply to all' option], but the official submissions should be also amended [S-006 directly, S-007 and S-008 by cross reference to S-006, if desired].

The Office of Pharmaceutical Sciences has set up a web site with information on categorical exclusions, if you need additional information (http://internet-dev/cder/OPS/EA_exclusions.htm).

Please feel free to contact us if you have any questions,

Sincerely,

Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Doris Bates

5/9/2008 04:56:00 PM

CSO

sent to company on May 9 at time shown in email

Bates, Doris J

From: Bates, Doris J
Sent: Wednesday, July 30, 2008 4:38 PM
To: 'Patterson, Pat'
Cc: Bates, Doris J; Alfaro, Cara
Subject: NDA 22-047, S-006, -007, and -008: Questions from Clinical Reviewer
Importance: High

Good afternoon Ms. Patterson:

As our review of the above cited supplements is progressing, our clinical review team has the following questions:

+++++

1. Please provide an update for the subject in the quetiapine XR group in protocol D144CC00004 who experienced the SAE "vestibular neuronitis".
2. In protocols D144CC00002 and D144CC00004, approximately 2-3% of subjects in both the quetiapine XR and placebo groups were discontinued from the studies for "severe non-compliance to protocol". Please specify which subjects were discontinued and what these protocol violations were.

Additionally, in both studies approximately 7-8% of subjects were discontinued in the category "voluntary discontinuation by subject". Is any additional data available (e.g. comments in CRFs) for these subjects regarding this discontinuation category (e.g. comments suggestive of adverse events, lack of efficacy, etc.)?

3. The current Guidance for Industry: Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products - Content and Format (January 2006) document states that similar events such as somnolence and sedation should be one category rather than separated into two categories. For all tables in currently proposed labeling (including schizophrenia data), please indicate the frequency of somnolence/sedation.

+++++

I have included our clinical reviewer as a CC recipient on this message. A reply by email 'to all' will assure that she receives the information without rerouting delays. Please feel free to respond by email if this is expedient, but note that we will also need a follow up amendment to the supplemental NDAs to keep the official record complete.

Thank you in advance - and as always, if you have any questions please feel free to contact me,

Sincerely,

Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center

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/s/

Doris Bates

7/30/2008 04:44:40 PM

CSO

sent to applicant 30JUL08 at time displayed on email.

Bates, Doris J

From: Bates, Doris J
Sent: Friday, August 15, 2008 10:22 AM
To: 'Patterson, Pat'
Cc: Bates, Doris J
Subject: NDA 22-047 S-006, -007, -008: Two Additional Clinical Questions: Plus Additional Labeling Requests

Good afternoon Pat,

Our clinical reviewer has two further questions regarding the above referenced applications, which are provided below:

1. For study D144CC00002, Table 11.3.7.3.3 lists mean change from baseline for chemistry variables but does not include fasting glucose. Since Table 11.3.7.3.4.1 lists change shifts for chemistry variables and includes fasting glucose, the mean change from baseline data should also be available for fasting glucose. Please submit these data.

2. In section 8.2 (Extent of Exposure) of the clinical study report for D144CC00004, it states that patient E4013003 intentionally took 4000 mg of quetiapine XR. There is a hyperlink for a patient narrative for this case. However, upon review of this narrative, there is no discussion of the clinical symptoms experienced after this overdose. Please provide this information.

I also have two further requests related to labeling - first, though, please convey our thanks to Ms. Tyler for the revisions provided earlier this week:

1. We request that you recalculate the AE frequencies for the combined term somnolence/sedation as a single entity rather than two separate categories. It seems that these two categories are still separated out in the most recent version of labeling.

2. Please incorporate information relevant to the newly approved 150 mg dosage strength.

If at all possible, we need the revisions by August 19 - please let me know if this will be a problem. As always, thank you, Pat, and best regards; if you have any questions about this message, please feel free to contact me.

Sincerely,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research*

*Food and Drug Administration
White Oak Federal Research Center*

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/s/

Doris Bates
8/15/2008 10:27:44 AM
CSO

Bates, Doris J

From: Bates, Doris J
Sent: Thursday, August 21, 2008 10:58 AM
To: 'Patterson, Pat'
Cc: Alfaro, Cara; Bates, Doris J
Subject: RE: NDA 22-047, S-006, -007, and -008: Questions from Clinical Reviewer
Importance: High

Tracking:

Recipient	Delivery
'Patterson, Pat'	
Alfaro, Cara	Delivered: 8/21/2008 10:58 AM
Bates, Doris J	Delivered: 8/21/2008 10:58 AM

Good morning Ms. Patterson,

First I wanted to let you know that your most recent message came through, but the attachment lost its .pdf extension, so thank you for telling us which kind of file it is; if we have any problems opening it I will let you know.

In the meantime, I have received and am forwarding the following additional questions from our clinical reviewer:

1. Under section 8.5 (Use in specific populations: Geriatric use) of your proposed labeling, there is a brief mention of some pharmacokinetic data for the clearance of quetiapine and refers the reader to section 12.3 (pharmacokinetics). However, there is no data for geriatrics/elderly patients in the pharmacokinetics section. Please add these data to this section and any additional pharmacokinetic data relevant to this population for quetiapine or quetiapine XR.
2. In your proposed labeling, dosing for elderly patients and patients with hepatic impairment is to initiate with quetiapine 50 mg/day and increase the dose by 50 mg/day depending on response and tolerance of the patient. Since a 50 mg quetiapine XR tablet is not currently available, currently approved labeling indicates that quetiapine IR 25 mg should be initiated in these populations with dose increases of 25-50 mg/day and, when an effective dose has been reached, the patient can be switched to quetiapine XR.
3. Please provide a comparison of pharmacokinetic data for the quetiapine IR 25 mg tablet and the quetiapine XR 50 mg tablet. Is there any tolerability data that you can provide regarding these populations and initiation of quetiapine XR 50 mg/day?
4. We received your response to our suggestion to combine the terms sedation and somnolence as one adverse event term in product labeling. While you correctly indicate that the lower level terms are different for each of these preferred terms, there is substantial overlap between these terms. Additionally, it is unlikely that a clinician can reliably distinguish between sedation and somnolence, and that splitting these terms actually serves to "dilute" a potentially significant adverse event. You did provide some recalculations combining these terms, however, you may need to recalculate the data. It appears that you may have just

8/25/2008

added the % of patients experiencing these adverse events together - this would potentially overestimate the incidence in the combined term. If some subjects experienced both sedation and somnolence they would currently be counted in both categories but should only be counted once in a combined term. Please recalculate these numbers for the combined term "somnolence" - this would be consistent with what we have asked other Sponsors to do. You may indicate that this term combines both somnolence and sedation terms as a footnote to the adverse event tables.

5. In section 2.1 of labeling (Dosage and Administration: Bipolar depression- usual dose) you have included data for patients receiving (b) (4) mg of quetiapine XR. However, study D144CC00002 was a 300 mg fixed dose design. Please clarify and delete if this was included in error.

6. Also with regard to labeling, for the indication for adjunctive treatment of bipolar disorder with lithium or divalproex, we did not see anything in the proposed labeling discussing the dosing of quetiapine XR that should be used adjunctively. We assume that direct extrapolation from the IR data would give a recommended adjunctive dose between 400 and 800 mg/day. Please add the recommended dosing for adjunctive treatment using the XR into the proposed labeling, or, if the information has been included and we have failed to locate it, indicate where it can be found.

Thank you; if there are any questions regarding these items please feel free to contact us. To facilitate a rapid response, I've included our clinical reviewer as a CC recipient on this message. "Reply to all" should assure that she receives a copy.

Best regards,

*Doris J. Bates, Ph.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Federal Research Center*

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/s/

Doris Bates

8/25/2008 03:53:14 PM

CSO

See email for date and time of transmittal to applicant.

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Office/Division): OPS, Staff (HFD-354) Attn: Bai Nguyen (301-796-1531) WO21 RM3523		FROM (Name, Office/Division, and Phone Number of Requestor): Teshara G. Bouie, ONDQA, Division of Post-Marketing Assessment, 301-796-1649		
DATE February 19, 2008	IND NO.	NDA NO. 22-047	TYPE OF DOCUMENT SE1-006 SE1-007 SE1-008	DATE OF DOCUMENT December 19, 2007
NAME OF DRUG Seroquel XR	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE May 19, 2008	
NAME OF FIRM: Astrazenea				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> PRE-NDA MEETING	<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER		
<input type="checkbox"/> PROGRESS REPORT	<input type="checkbox"/> END-OF-PHASE 2a MEETING	<input type="checkbox"/> FINAL PRINTED LABELING		
<input type="checkbox"/> NEW CORRESPONDENCE	<input type="checkbox"/> END-OF-PHASE 2 MEETING	<input type="checkbox"/> LABELING REVISION		
<input type="checkbox"/> DRUG ADVERTISING	<input type="checkbox"/> RESUBMISSION	<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE		
<input type="checkbox"/> ADVERSE REACTION REPORT	<input type="checkbox"/> SAFETY / EFFICACY	<input type="checkbox"/> FORMULATIVE REVIEW		
<input type="checkbox"/> MANUFACTURING CHANGE / ADDITION	<input type="checkbox"/> PAPER NDA	<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):		
<input type="checkbox"/> MEETING PLANNED BY	<input type="checkbox"/> CONTROL SUPPLEMENT			
II. BIOMETRICS				
<input type="checkbox"/> PRIORITY P NDA REVIEW	<input type="checkbox"/> CHEMISTRY REVIEW			
<input type="checkbox"/> END-OF-PHASE 2 MEETING	<input type="checkbox"/> PHARMACOLOGY			
<input type="checkbox"/> CONTROLLED STUDIES	<input type="checkbox"/> BIOPHARMACEUTICS			
<input type="checkbox"/> PROTOCOL REVIEW	<input type="checkbox"/> OTHER (SPECIFY BELOW):			
<input type="checkbox"/> OTHER (SPECIFY BELOW):				
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION	<input type="checkbox"/> DEFICIENCY LETTER RESPONSE			
<input type="checkbox"/> BIOAVAILABILITY STUDIES	<input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS			
<input type="checkbox"/> PHASE 4 STUDIES	<input type="checkbox"/> IN-VIVO WAIVER REQUEST			
IV. DRUG SAFETY				
<input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL	<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY			
<input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES	<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE			
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)	<input type="checkbox"/> POISON RISK ANALYSIS			
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP				
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL	<input type="checkbox"/> NONCLINICAL			
COMMENTS / SPECIAL INSTRUCTIONS: These supplements provide for a new indication, bipolar depression (S-006), bipolar mania (S-007), and acute bipolar mania (S-008). Please review the Environment Assessment.				
These supplements can be found in the EDR.				
SIGNATURE OF REQUESTOR Teshara G. Bouie		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
PRINTED NAME AND SIGNATURE OF RECEIVER		PRINTED NAME AND SIGNATURE OF DELIVERER		

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/s/

Teshara Bouie
2/19/2008 04:03:41 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD-710 (Dr. Yang, Dr. Kordzakhia)		FROM: HFD-130 (Dr. Bates)		
DATE January 2, 2008	IND NO. 32,132; 45,456; 73,864; 76,146	NDA NO. 22-047, SE1-006, SE1-007, SE1-008	TYPE OF DOCUMENT Efficacy supplements	DATE OF DOCUMENT December 19, 2007
NAME OF DRUG Seroquel XR (quetiapine fumarate) Extended Release Tablets	PRIORITY CONSIDERATION Ten month, due October 19, 2008 [three on same day]	CLASSIFICATION OF DRUG S-006: bipolar depression S-007: acute mania monotherapy S-008: acute mania adjunctive therapy		DESIRED COMPLETION DATE: Jan. 30, 2008 filing meeting Feb. 29, 2008 74-day letter Oct. 19, 2008 PDUFA date
NAME OF FIRM: AstraZeneca Pharmaceuticals LP				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input checked="" type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS:				
Three new efficacy supplements submitted on same date. – see filing meeting notice. EDR link: \\CDSESUB1\EVSPROD\NDA022047\022047.enx				
Medical reviewer is Dr. Cara Alfaro. Please note: as of today, AZ has paid for only two of three submissions. The third submission, for bipolar mania adjunctive therapy, contains no efficacy data at present. However. labeling submitted with S-007 includes both indications.				
SIGNATURE OF REQUESTER see electronic signature		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Doris Bates

1/3/2008 01:49:13 PM

Three efficacy supplements submitted as two. Third does not
include efficacy data. See consult request - will
be discussed at filing meeting.



**SEROQUEL® XR (quetiapine fumarate)
Extended Release Tablets**

Statement of Pediatric Use Information

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1. STATEMENT OF WAIVER OF PEDIATRIC STUDIES3

2. STATEMENT OF DEFERRAL OF PEDIATRIC STUDIES.....3

1. STATEMENT OF WAIVER OF PEDIATRIC STUDIES

Under authority of 21 CFR 314.55 ©AstraZeneca Pharmaceuticals LP (AstraZeneca) is hereby providing a statement for waiver of investigations in pediatric patients under 12 years of age for this SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets Supplemental New Drug Application (sNDA) for Bipolar Depression.

SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets

sNDA 22-047

AstraZeneca Pharmaceuticals LP (AstraZeneca)

Indication: SEROQUEL XR is indicated for the treatment of bipolar depression as monotherapy.

Ages Addressed in Waiver: Children under 10 years of age

Rationale: The prevalence of bipolar disorder under the age of 10 years is very low. In addition, the literature suggests that bipolar disorder may be difficult to diagnose reliably under 10 years of age.

2. STATEMENT OF DEFERRAL OF PEDIATRIC STUDIES

AstraZeneca is hereby providing a statement of deferral for conducting pediatric studies for this SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets sNDA.

SEROQUEL XR (quetiapine fumarate) Extended-release Tablets

sNDA 22-047

AstraZeneca Pharmaceuticals LP (AstraZeneca)

Indication: SEROQUEL XR is indicated for the treatment of bipolar depression as monotherapy.

Ages Addressed in Deferral: Adolescents (ages 10-17 years)

Rationale: AstraZeneca is awaiting the delivery of results of our pediatric studies, as part of our fulfilment of the written request for NDA 20-639. These studies are designed to address the efficacy and safety of quetiapine fumarate in the pediatric population. We anticipate filing the results mid-2008.

The written request program currently consists of the following four studies that have been endorsed by FDA:

- A Study to Characterize the Steady-State Pharmacokinetics, Safety and Tolerability of Quetiapine Fumarate (SEROQUEL) in Children and Adolescents with Selected Psychotic Disorders” (Study D1441C00028)
- A 6-week, Multicenter, Double-blind, Parallel-group, Placebo-controlled Study of the Efficacy and Safety of Quetiapine Fumarate (SEROQUEL) in the Treatment of Adolescents with Schizophrenia” (Study D1441C00112)
- A 3-week, Multicenter, Double-blind, Parallel-group, Placebo-controlled Study of the Efficacy and Safety of Quetiapine Fumarate (SEROQUEL) in the Treatment of Children and Adolescents with Acute Bipolar I Mania” (Study D1441C00149)
- A 6-Month, Multicenter, Open-label study of the Safety and Tolerability of Quetiapine Fumarate (SEROQUEL) in Children and Adolescents with Bipolar I Disorder and Adolescents with Schizophrenia” (Study D1441C00150)

S007
S008



**SEROQUEL® XR (quetiapine fumarate)
Extended Release Tablets**

Statement of Pediatric Use Information

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2.	STATEMENT OF DEFERRAL OF PEDIATRIC STUDIES.....	3

1. STATEMENT OF WAIVER OF PEDIATRIC STUDIES

Under authority of 21 CFR 314.55 ©AstraZeneca Pharmaceuticals LP (AstraZeneca) is hereby providing a statement for waiver of investigations in pediatric patients under 12 years of age for this SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets Supplemental New Drug Application (sNDA) for Bipolar Mania.

SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets

sNDA 22-047

AstraZeneca Pharmaceuticals LP (AstraZeneca)

Indication: SEROQUEL XR is indicated for the treatment of bipolar mania as both adjunct and monotherapy.

Ages Addressed in Waiver: Children under 10 years of age

Rationale: The prevalence of bipolar disorder under the age of 10 years is very low. In addition, the literature suggests that bipolar disorder may be difficult to diagnose reliably under 10 years of age.

2. STATEMENT OF DEFERRAL OF PEDIATRIC STUDIES

AstraZeneca is hereby providing a statement of deferral for conducting pediatric studies for this SEROQUEL XR (quetiapine fumarate) Extended-Release Tablets sNDA.

SEROQUEL XR (quetiapine fumarate) Extended-release Tablets

sNDA 22-047

AstraZeneca Pharmaceuticals LP (AstraZeneca)

Indication: SEROQUEL XR is indicated for the treatment of bipolar mania as both adjunct and monotherapy.

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- A 6-Month, Multicenter, Open-label study of the Safety and Tolerability of Quetiapine Fumarate (SEROQUEL) in Children and Adolescents with Bipolar I Disorder and Adolescents with Schizophrenia” (Study D1441C00150)