CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022544Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 022544 SUPPL # 000 HFD # 170

Trade Name Gralise Tablets

Generic Name Gabapentin

Applicant Name Abbott Products

Approval Date, If Known January 28, 2011

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?

YES ☒ NO ☐

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

505(b)(2)

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.")

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.

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?

YES ☒ NO ☐

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

3 years

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

YES ☒ NO ☐

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? NO

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?

YES ☐ NO X

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 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.

YES ☒ NO ☐

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

NDA# 020882

NDA# 021129

NDA# 020235

And several ANDAs (see Orange Book)

2. Combination product.

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 X

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.

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.

YES ☒ NO

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?

YES ☒ NO ☐

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:

(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?

YES ☒ NO ☐

(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.

YES ☐ NO ☒

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?

YES ☐ NO X

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:

Study 62

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 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.")

Investigation #1 YES ☐ NO X

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

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?

Investigation #1 YES ☐ NO X

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

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"):

Study 62

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		
IND # 071439	YES ☐	NO X Explain: Depomed was the sponsor of the IND. The ownership of the IND was transferred to Abbott prior to the NDA submission.

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
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.)

YES ☐ NO X

If yes, explain:

Name of person completing form: Allison Meyer
Title: Regulatory Project Manager
Date: January 25, 2011

Name of Office/Division Director signing form: Bob Rappaport, MD
Title: Director, HFD-170

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/

ALLISON MEYER
01/28/2011

BOB A RAPPAPORT
01/28/2011

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 22544 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Gralise Established/Proper Name: gabapentin Dosage Form: tablets		Applicant: Abbott Pharmaceuticals Agent for Applicant (if applicable):
RPM: Allison Meyer		Division: HFD-170

NDAs:
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

NDA 20235, 20882, and 21129 - Neurontin

Provide a brief explanation of how this product is different from the listed drug.

This product is indicated for management of post-herpetic neuralgia and is dosed as a once-daily use product.

If no listed drug, explain.
- ☐ This application relies on literature.
- ☐ This application relies on a final OTC monograph.
- ☐ Other (explain)

Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☒ No changes ☐ Updated Date of check: 1-13-2010

If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

❖ Actions	
• Proposed action • User Fee Goal Date is 1/30/11	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None

[1] The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics [2]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS: ☒ MedGuide
☐ Communication Plan
☐ ETASU
☐ REMS not required

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Press Office notified of action (by OEP)	☐ Yes ☒ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

[2] Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic 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.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric 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.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☒ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☒ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☒ Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

  Answer the following questions for **each** paragraph IV certification:

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☒ Yes ☐ No

  (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).

  *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).*

  (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

  *If "**No**," continue with question (3).*

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ Yes ☐ No

  (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

  *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

  (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☒ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).*

  *If "**No**," continue with question (5).*

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☐ Yes ☒ No
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist[3]	January 28, 2011
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s) AP 1/28/11
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	January 28, 2011
• Original applicant-proposed labeling	March 30, 2010
• Example of class labeling, if applicable	

[3] Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☒ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	
• Original applicant-proposed labeling	3/30/10
• Example of class labeling, if applicable	
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	1/28/11
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s))*	 7/13/10, 1/27/11 Accepted, 7/13/10
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☐ RPM ☒ DMEPA 1/7/11 ☒ DRISK 12/17/10 ☒ DDMAC 1/14/11 ☐ CSS ☐ Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[4]/Memo of Filing Meeting) (indicate date of each review)* ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	1/25/11 ☐ Not a (b)(2) 1/18/11 ☐ Not a (b)(2) 1/14/11
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	X Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC 11/3/10 If PeRC review not necessary, explain: _____ • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	 ☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent *(include certification)*	☒ Verified, statement is acceptable
❖ Outgoing communications *(letters (except action letters), emails, faxes, telecons)*	**4/14/10, 4/20/10. 4/21/10, 5/4/10, 5/25/10, 6/17/10, 7/14/10, 7/20/10, 7/23/10, 7/28/10, 8/6/10, 8/12/10,**

[4] Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

	8/19/10, 8/27/10, 9/1/10, 9/8/10, 9/28/10, 10/1/10, 11/8/10, 11/16/10, 12/1/10, 12/3/10, 12/7/10, 1/6/11, 1/7/11, 1/18/11, 1/19/11, 1/21/11, 1/24/11
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☐ No mtg 12/15/09
• EOP2 meeting *(indicate date of mtg)*	☐ No mtg 4/6/06
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	12/19/05
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None 1/28/11
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None 12/18/10
PMR/PMC Development Templates *(indicate total number)*	☒ None
Clinical Information[5]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	See CDTL review
• Clinical review(s) *(indicate date for each review)*	12/7/10, 12/13/10
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	Included in clinical review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not applicable
❖ Risk Management • REMS Documents and Supporting Statement *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	3/30/10, 1/27/11 12/17/10, 1/21/11 ☐ None 12/17/11
❖ DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☐ None requested 11/30/10, 12/1/10, 12/15/10(2)

[5] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☒ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☒ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None 12/6/10
Statistical Review(s) *(indicate date for each review)*	☐ None 12/6/10
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ None 12/6/10
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 5/26/10, 12/6/10
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of DSI letters)*	☒ None
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ None
• Supervisory Review(s) *(indicate date for each review)*	☐ None 12/2/10
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None 5/17/10, 12/2/10
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary *(include copies of DSI letters)*	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☐ None 1/13/11
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None 12/3/10, 1/13/11
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) *(indicate date of each review)*	☒ Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None

❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	12/3/10
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout) *(date completed must be within **2 years** of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[6])*	Date completed: 5/26/10 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☒ Completed ☐ Requested ☐ Not yet requested ☐ Not needed (per review)

[6] I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
(3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
(3) **And** all other “criteria” are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE’s ADRA.

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

/s/

ALLISON MEYER
01/31/2011

Meyer, Allison

From: Jani, Parinda
Sent: Thursday, January 27, 2011 2:30 PM
To: Meyer, Allison
Subject: RE: NDA 022544 Gralise Labeling

Please DARRT this email. You can revise the comment and send it to the sponsor. If you want me to look over everything one more time, let me know.

From: Meyer, Allison
Sent: Thursday, January 27, 2011 2:29 PM
To: Mena-Grillasca, Carlos; Fields, Ellen; Rappaport, Bob A; Jani, Parinda; Doddapaneni, Suresh
Subject: RE: NDA 022544 Gralise Labeling

From: Mena-Grillasca, Carlos
Sent: Thursday, January 27, 2011 2:23 PM
To: Meyer, Allison
Subject: RE: NDA 022544 Gralise Labeling

Hi Allison,

That recommendation came from other members of the team, I thought that was the consensus from earlier emails and was trying to capture it in my comments. Bottom line is that I am ok with the statement "Take with evening meal".

Carlos

Carlos M Mena-Grillasca | Team Leader | DMEPA/OSE/CDER/FDA | ☎ 301.796.4073 | ✉ carlos.mena-grillasca@fda.hhs.gov

---

From: Meyer, Allison
Sent: Thursday, January 27, 2011 2:15 PM
To: Mena-Grillasca, Carlos
Subject: FW: NDA 022544 Gralise Labeling

From: Rappaport, Bob A
Sent: Thursday, January 27, 2011 2:15 PM
To: Fields, Ellen; Doddapaneni, Suresh; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

You need to find out why Carlos wants this and whether there's a good reason. Otherwise we'd be overriding their concerns without adequate Equal Voice discussion.

From: Fields, Ellen
Sent: Thursday, January 27, 2011 2:14 PM
To: Rappaport, Bob A; Doddapaneni, Suresh; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

Ok, so should we just leave it “take with evening meal”?

From: Rappaport, Bob A
Sent: Thursday, January 27, 2011 2:11 PM
To: Fields, Ellen; Doddapaneni, Suresh; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

Agree. We don't usually put that in labeling unless there's an issue and it may just be confusing here.

From: Fields, Ellen
Sent: Thursday, January 27, 2011 2:11 PM
To: Doddapaneni, Suresh; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

Nope, we didn’t have any indication that the (b) (4) is an issue

---

From: Doddapaneni, Suresh
Sent: Thursday, January 27, 2011 2:10 PM
To: Fields, Ellen; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

(b) (4)

From: Fields, Ellen
Sent: Thursday, January 27, 2011 2:07 PM
To: Doddapaneni, Suresh; Meyer, Allison; Jani, Parinda; Naraharisetti, Suresh
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

(b) (4)

From: Doddapaneni, Suresh
Sent: Thursday, January 27, 2011 2:04 PM
To: Meyer, Allison; Jani, Parinda; Fields, Ellen; Naraharisetti, Suresh
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

This has to be viewed little bit differently than other products we typically encounter. The ER characteristics were the best with high fat meal and taking it with the evening meal may approach that as dinner can be expected to be more elaborate and may approach the high fat meal conditions. So, we don't want to use the generic word 'food' as food can mean anything ranging from a cookie... Take it with evening meals seems appropriate.

(b) (4)

From: Meyer, Allison
Sent: Thursday, January 27, 2011 1:45 PM
To: Jani, Parinda; Fields, Ellen; Naraharisetti, Suresh; Doddapaneni, Suresh
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

From: Jani, Parinda
Sent: Thursday, January 27, 2011 1:44 PM
To: Fields, Ellen; Meyer, Allison
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

Need to check with Clinpharm.

From: Fields, Ellen
Sent: Thursday, January 27, 2011 1:43 PM
To: Jani, Parinda; Meyer, Allison
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

We went back and forth w/ CMC and DMEPA about this this morning. We will have to let them know if we don't want to include (b) (4) on the container.

From: Jani, Parinda
Sent: Thursday, January 27, 2011 1:41 PM

To: Meyer, Allison; Fields, Ellen
Cc: Rappaport, Bob A; Roca, Rigoberto A
Subject: RE: NDA 022544 Gralise Labeling

Comment A.2 below

Nowhere in the label it says take it with [redacted] (b) (4). It says take with evening meal. So the statement should be take with [redacted] (b) (4). patients can just end up taking it with [redacted] (b) (4)

From: Fields, Ellen
Sent: Thursday, January 27, 2011 1:24 PM
To: Mena-Grillasca, Carlos; Meyer, Allison
Cc: Peri, Prasad; Marroum, Patrick J; Hu, Yong; Christodoulou, Danae D; Holquist, Carol A; Toyer, Denise P
Subject: RE: NDA 022544 Gralise Labeling

Carlos, one question,
On the unit of use bottles, why don't they need the statement [redacted] (b) (4) ?

From: Mena-Grillasca, Carlos
Sent: Thursday, January 27, 2011 1:22 PM
To: Meyer, Allison
Cc: Peri, Prasad; Marroum, Patrick J; Fields, Ellen; Hu, Yong; Christodoulou, Danae D; Holquist, Carol A; Toyer, Denise P
Subject: RE: NDA 022544 Gralise Labeling

The following are DMEPA's comments to the revised labels/labeling submitted by the Applicant:

A. General comments:

1 Increase the prominence of the established name (i.e. boldness relative to the proprietary name).
2 Include the statement [redacted] (b) (4) preceding the "swallow tablet whole statement".
3 Using bold font should be reserved for highlight important information. Therefore, remove bolding from the "each tablet contains... " statement. Use bold font for the following statements: [redacted] (b) (4) Swallow tablet whole. Do not crush, split or chew."

B. Container labels (300 mg, bottles of 30, 90, and 300 tablets; 600 mg, bottles of 90 and 300 tablets)

1 The addition of multiple patent numbers on the container labels is not required and crowds the labels. Especially on the 300 mg x 30 tablets label. Delete or relocate to the left side of the label to provide space for implementation of the general comments.

2 Delete the statement [redacted] (b) (4). The unit of use bottles should

be CRC and the bulk bottles should not be dispensed to patients. Therefore, this statement is not necessary.

C. Sample pack (15 days)

1 Increase the prominence (i.e. size) of the net quantity statement:

This 30 days starter pack of Gralise includes the following:
Nine 300 mg tablets
Twenty four 600 mg tablets

D. Starter Pack (30 days)

1 The statement "StarterPack" is fanciful and of greater prominence than more relevant information (e.g. established name, net quantity, etc.). Reduce the size and use regular font.

2 Make the net quantity statement (see comment C.1) identical to that of the 15 days sample pack with regards to location and prominence. To achieve this you might need to delete or relocate the information below the area reserved for the pharmacy label and the company logo.

Carlos

Carlos M Mena-Grillasca | Team Leader | DMEPA/OSE/CDER/FDA | ☎ 301.796.4073 | ✉ carlos.mena-grillasca@fda.hhs.gov

---

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

/s/

ALLISON MEYER
01/27/2011

Meyer, Allison

From: Meyer, Allison
Sent: Monday, January 24, 2011 7:46 AM
To: 'Hare, Michael'
Subject: Patent information

Michael,
You may send in new patent information for patents that are held by Abbott. If you are trying to establish patent certification to someone else's patent, that would be another issue.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, January 21, 2011 3:49 PM
To: 'Hare, Michael'
Subject: FW: Finalized - NDA 22544 Information Request (COR-NDAIR-01)

Attachments: NDA 022544.rems ir.final.01212011.pdf

NDA 022544.rems ir.final.01212...

Michael,
Please respond by Tuesday at noon.
Thanks,

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258

301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, January 19, 2011 12:57 PM
To: 'Hare, Michael'
Subject: label

Attachments: label to sponsor.doc

Michael,
Here is the label. There may be additional edits, as our DDMAC division comments have not been incorporated yet, and Dr. Rappaport may have additional comments.
Allison

label to sponsor.doc (297 KB

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, January 18, 2011 7:37 PM
To: 'Hare, Michael'
Subject: FW: Gralise label/labeling comments to applicant

Attachments: Glacier Bkgrd.jpg

Glacier Bkgrd.jpg (3 KB)

Michael, Please address these asap. The package insert will get to you tomorrow, however Dr. Rappaport may have additional comments.

Comments To The Applicant

A. General Comments

1. The actual proprietary name was not included in the labels and labeling, therefore, we will not comment on the presentation of the proprietary name until the final version of the labels and labeling with the proprietary names are submitted for review.

2. Per 21 CFR 201.10(g)(2), ensure that the established name is at least half the size of the proprietary

name and have the prominence commensurate with the prominence of the proprietary name, taking into account all pertinent factors, including typography, layout, contrast, and other printing features

3. Remove all (b) (4) dosage form references. The dosage form designation for Gralise is "tablets".

4. Increase the prominence of the strength (i.e. font size). Also, consider revising the font type used, the current 'condensed' font used is difficult to read.

5. Remove the inactive ingredients list as this information is not required for oral products and crowds the label.

6. Revise the statement (b) (4) to "See prescribing information…"

7. Provide adequate color differentiation between the 15 days sample pack and the 30 days starter pack. As currently presented they look almost identical and could be a source of confusion and selection error.

(b) (4)

C. Sample Pack (15 days) and Starter Pack (30 days) Labels

1. Revise the color scheme used for the presentation of the days of the week and the "professional sample not for resale" statements. As currently presented, the yellow font over an orange background color scheme is difficult to read.

2. Delete the list of inactive ingredients as this is not required for solid oral dosage forms. This will provide space for implementation of comments E.3., E.4., and E.5.

3. Add the trade name and established name as it appears on "Days 1 to 7" to the other cards (i.e. "Days 7 to 14", "Days 15 to 22", and "Days 23 to 30"). In case the cards get separated this will ensure that the product will remain labeled.

4. Include the statement "Do not use Gralise interchangeably with other gabapentin products because of differing pharmacokinetic profiles that affect frequency of administration" on the Principal Display Panel.

5. Delete the strength statement "300 mg & 600 mg" from the established name and place below the established name as presented in the following example:

This 15 days sample pack of Gralise includes the following:
(b) (4) 300 mg tablets
Twenty-four 600 mg tablets

6. Place the strength next to each blister on the card so that every tablet is identified.

D. Container Label (300 mg and 600 mg; bottles of 90 and 300 tablets)

1. If space permits, include the statement "Do not use Gralise interchangeably with other gabapentin products because of differing pharmacokinetic profiles that affect frequency of administration." At a minimum you should include the statement "Do not use Gralise interchangeably with other gabapentin products" on the Principal Display Panel.

2. Decrease the prominence and relocate the "Rx only" statements to the side panel. As currently presented it competes in prominence with other more important information such as the strength.

3. Include the statements, "Swallow table whole. Do not crush, split or chew the tablet."

4. Consider deleting the inactive ingredients information to allow for the implementation of comments C.1. and C.3.

E. Blister Labels

See general comments

F. Blister Carton Labeling (5 cards/10 tablets each)

1. Include the statement "Do not use Gralise interchangeably with other gabapentin products because of differing pharmacokinetic profiles that affect frequency of administration" on the Principal Display Panel.

2. Include a statement on the principal display panel for pharmacists to dispense Medication Guides with the product (e.g. "Dispense the enclosed Medication Guide to each patient"). Also, make sure that enough Medication Guides are provided with each packaging presentation.

3. Include the statements, "Swallow tablet whole. Do not crush, split or chew the tablet."

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue

Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, January 07, 2011 1:14 PM
To: 'Hare, Michael'
Subject: FW: Gabapentin NDA22-544

This is to remind the you to revise the drug product dissolution specification in the NDA as requested by the Biopharm team. You have agreed on the dissolution spec in the pre-telecon document for the 20-Dec-2010 telecon, but you need to revise the spec in the NDA. Thanks.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Thursday, January 06, 2011 11:01 AM
To: 'Hare, Michael'
Subject: RE: Debarment certification

Attachments: Abbott.gif

Abbott.gif (2 KB)

Michael,
We will need one from Abbott.
Allison

From: Hare, Michael [mailto:michael.hare@abbott.com]

Sent: Thursday, January 06, 2011 10:10 AM
To: Meyer, Allison
Subject: RE: Debarment certification

Allison,

Solvay Pharmaceuticals, Inc. simply changed it's name to Abbott Products, Inc. There is a Debarrment Certification for Solvay in 1.3.3 Section of the NDA along with the original (Seq 0000) cover letter that states Abbott acquired Solvay. Will this suffice? If not, I can quickly generate a certification for the legal entity of Abbott Products, Inc. and submit by Friday. Just let me know.

Thanks.

Michael F. Hare
Asst. Director
Global Regulatory Affairs
Abbott
901 Sawyer Road
Marietta GA 30062
United States Tel: 770 578 5620
Mobile/Cell: 678 938 8942
Fax: 770 578 5864
michael.hare@abbott.com

From: Meyer, Allison [mailto:Allison.Meyer@fda.hhs.gov]
Sent: Thursday, January 06, 2011 9:27 AM
To: Hare, Michael
Subject: Debarment certification

Michael,
I need a debarment certification from Abbott ASAP.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993

301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, December 03, 2010 3:23 PM
To: 'Hare, Michael'
Subject: FW: Cmc issues for gabapentin

Importance: High

- **In accordance with the ICH Q1D guideline with respect to bracketing in stability testing, we recommend that you test the product stability in the bottle configurations with the lowest and the highest headspace/volume ratio for each strength in your post-approval stability programs.**

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, December 01, 2010 2:00 PM
To: 'Hare, Michael'
Subject: Cmc issues for gabapentin

Michael, Please respond as soon as possible.

- **The acceptance limit for the total impurities in the drug product should be tightened to (b) (4) based on the stability data of your drug product.**
- **You have not provided adequate information to justify the omission of particle size in your drug substance specification. Include particle size test (method and acceptance limits) in your drug substance specification for both the primary and alternate suppliers.**
- **Provide a comparison of the particle size distribution for the drug substance from the primary and alternate suppliers.**
- **Provide dimensional information and pictures of the phase 3 tablets before and after swelling in mSGF for 6-8 hours.**

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, November 16, 2010 12:20 PM
To: 'Hare, Michael'

We would just like to inform you that we have gotten approval for the use of the specification of the (b) (4) impurity, therefore the qualification will not be necessary for approval.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research

10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Monday, November 08, 2010 8:57 AM
To: 'Hare, Michael'
Subject: FW: NDA22-544 CMC IR

Importance: High

Michael,
I will need a response to this within a week.

Provide confirmation that the materials of construction for your blister and bottle packaging components conform to the requirements in the applicable sections of the Code of Federal Regulations, Title 21, Indirect Food Additives.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, October 01, 2010 11:23 AM
To: 'Hare, Michael'
Subject: FW: NDA 22-544 Gabapentin drug substance impurity

Importance: High

At our last tcon, we told you that you need to revise the drug substance impurity limits in accordance to the identification and qualification thresholds in ICH Q3A. Thanks.

That seems to be the only additional outstanding requests besides the ones you mentioned.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, October 01, 2010 10:19 AM
To: 'Hare, Michael'
Subject: Outstanding requests

Michael,
I believe we have outstanding CMC and Clinical Pharmacology/Biopharm requests. Please let me know when we should expect a response.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993

301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, October 01, 2010 9:35 AM
To: 'Hare, Michael'
Subject: Receipt for paragraph IV

Michael,
Have you submitted the registered receipt of proof that you have sent the paragraph IV information to the patent holders?

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, September 28, 2010 3:04 PM
To: 'Hare, Michael'
Subject: Biopharmaceutics Re-assignment for NDA 22-544 for Gabapeptin ER Tablets

Michael,

These comments need to be addressed as soon as possible:

1. Submit dissolution method report including the complete dissolution profile data (individual, mean, SD, profiles) collected during the development and validation of the proposed dissolution method.
2. (b) (4)
3.
4.
5.

6. (b) (4)

7.

8.

Thanks,

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, September 08, 2010 8:40 AM
To: 'Hare, Michael'
Subject: FW: Information request for NDA 22544 (Gabapentin)

Importance: High

Michael,

Clarification on simulation results in Report 85-0010R2

You conducted simulations to show the impact of type of meal (moderate-fat, high-fat) and renal function on the pharmacokinetics of gabapentin. The following are the clarification questions:

1. The median Cmax of simulated gabapentin concentrations in a patient with CrCL=15 mL/min receiving 300 mg dose with moderate fat meal in Figure 4 at steady-state (post-dose at 240h) is similar to that in a patient with CrCL of 120 mL/min. However, the median Cmax of simulated gabapentin concentrations in a patient with CrCL=15 mL/min receiving 300 mg dose with high fat meal in Figure 8 at steady-state (post-dose at 240h) is lower than that in a patient with CrCL of 120 mL/min. This is opposite to the observed findings that Cmax, AUC of gabapentin increase with high-fat meal in comparison to moderate and low fat meal. The simulations do not reflect the observed impact of type of meal on pharmacokinetics of gabapentin.

2. Simulations as shown in Figure 5 vs Figure 9 also have similar issues as mentioned above.

3. Simulations as shown in Figure 2 vs Figure 6 also have similar issues as mentioned above.

4. The label for Figure 5 mentions the type of food as high-fat. However, based on calories it appears to be moderate-fat food. Please clarify.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, September 01, 2010 9:30 AM
To: 'Hare, Michael'
Subject: FW: Information Request for NDA 22544

Importance: High

Please submit datasets (only names if already submitted) and SAS program files for non-compartmental analysis as well as bioequivalence testing in Studies 81-008, 81-0040, 81-0044, 81-0048, 81-0049.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, August 27, 2010 1:34 PM
To: 'Hare, Michael'
Subject: Tcon for Tuesday 8/31

I have scheduled a tcon for Tuesday at 11:30 am eastern time to discuss the (b) (4) issue and some CMC comments. Please provide a call-in number.

Also, please send me a word version of your label.
Thanks,
Allison

Meyer, Allison

From: Meyer, Allison
Sent: Friday, August 27, 2010 8:59 AM
To: 'Hare, Michael'
Subject: FW: NDA 22-544 (G-ER) clinical inquiry

Attachments: NDA22544-3rd inquiry.doc

NDA22544-3rd inquiry.doc (28 K...

Allison Meyer
Division of Anesthesia and Analgesia
ODE 2
CDER

Meyer, Allison

From: Meyer, Allison
Sent: Thursday, August 19, 2010 1:01 PM
To: 'Hare, Michael'
Subject: FW: (b) (4) clarification w/Sponsor (N22-544)

You asked why we are changing our recommendation/requirement on the duration of the qualification study for the (b) (4) impurity. This relates to the duration of proposed clinical use - that initially during the teleconference we momentarily thought the indication sought would result in chronic use - for which we require a 3-month study. However, we do not consider PHN to represent chronic use and therefore a shorter (1-month) qualification study is acceptable.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Thursday, August 12, 2010 2:43 PM
To: 'Hare, Michael'
Subject: FW: 2nd clinical inquiry/G-ER NDA 22544

Attachments: 2nd inquiry.doc

2nd inquiry.doc (29 KB)

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Friday, August 06, 2010 2:58 PM
To: 'Hare, Michael'
Subject: FW: IR for NDA 22-544

Attachments: IR for NDA 022544.doc

IR for NDA 022544.doc (57 KB)

Thanks,

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II

Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, July 28, 2010 9:15 AM
To: 'Hare, Michael'
Subject: RE: NDA 022544 - Gabapentin Extended Release Tablets

Michael,
You will need to provide the 120-day safety update submission, even if it says that you do not have anything to report.
Allison

From: Hare, Michael [mailto:Michael.Hare@solvay.com]
Sent: Wednesday, July 28, 2010 8:43 AM
To: Meyer, Allison
Subject: NDA 022544 - Gabapentin Extended Release Tablets

Allison,
I just wanted to follow up with you on my response to your email last week regarding the status of the Day 74 Filing communication letter and your email dated 17 June. Last week, I responded that Abbott would provide a response by this week on these questions. This response is going through our internal management approval process this week. The earliest that we will be able to provide the Agency the responses will be next week.

In addition, I also wanted to let you know that Abbott would not be providing a Day 120 Safety Update. There are currently no on-going clinical studies and therefore no additional safety data to provide to the NDA. Does the Agency require a formal submission to the NDA stating that no new safety data will be provided for Day 120? Or will this email suffice?

Best regards,

Michael F. Hare
Assistant Director, Regulatory Affairs
Abbott (formerly Solvay Pharmaceuticals, Inc.)
Marietta, GA 30062
T: 770-578-5620
C: 678-938-8942
E: michael.hare@solvay.com

d'informer immediatement l'expediteur par messagerie electronique et d'ensuite detruire ce message.

Meyer, Allison

From: Meyer, Allison
Sent: Friday, July 23, 2010 11:04 AM
To: 'Hare, Michael'
Subject: FW: Information request for NDA 22-544 Gabapentin

Your proposed Level 2 acceptance value of NMT (b) (4) in the determination of drug product content uniformity does not meet the requirement in USP <905> (i.e. NMT (b) (4) for 30 units). Revise the Level 2 acceptance value to meet the USP <905> requirement. Update the content uniformity results in the batch analysis and stability data tables according to the USP <905> acceptance criteria.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, July 20, 2010 9:28 AM
To: 'Hare, Michael'
Subject: Outstanding information requests 22544

Michael,
We are still waiting on information requests that are clinical and clin pharm questions. When will we get a response to these?
Thanks,

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue

Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, July 14, 2010 12:32 PM
To: 'Hare, Michael'
Subject: FW: NDA 022544 Administrative Question

I think it is required for only certain submissions and not all submissions

http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm

New drug applications (NDAs), supplemental NDAs, biologics license applications (BLAs), supplemental BLAs, abbreviated new drug applications (ANDAs), premarket approval applications (PMAs), PMA "panel track" supplements, humanitarian device exemptions (HDEs), and resubmissions of these, are all "applications" under their respective sections of the Act or the PHS Act. Similarly, 510(k)s are "submissions of a report" under that section of the Act. Thus, all of these specified applications and submissions fall within the plain language of the statutory provision.Additionally, they all represent the initiation of the regulatory review process through which clinical investigations supporting approval of a previously unapproved medical product are submitted to FDA for marketing approval of that product. Because amendments to pending applications, pending supplemental applications, or pending submissions of 510(k)s are not independently "applications" or "submissions of a report under 510(k)," such amendments need not be accompanied by a certification.

We believe that the statutory requirement to submit a certification also applies to investigational new drug applications (INDs) and the submissions of new protocols to INDs. INDs are authorized under § 505(i) of the Act (*see also* 21 C.F.R. § 312.3 (defining "IND" as "an investigational new drug application")). We also have concluded that a certification must accompany the submission of a new clinical protocol to an IND as described in 21 CFR § 312.30(a). There are a number of different types of submissions to an IND that are referred to as "amendments" under FDA's regulations, but these types of submissions are varied as to their purpose and the role they play in the regulatory process. One type of submission is that of a new protocol submitted to a pending IND. A new clinical protocol that is submitted to a pending IND, for a study not already included in an existing protocol, is the investigational stage analog to an efficacy supplement to an NDA or BLA for a new indication not already covered by the existing application. New protocols are referred to as amendments to INDs, and are submitted to existing INDs, as a matter of regulatory process; FDA could have required that new protocols filed with the Agency be submitted to a new IND, but for administrative ease chose to have them submitted to the existing IND. In contrast, other types of amendments to pending INDs are more analogous to amendments to NDAs, BLAs, and PMAs; as such, consistent with our interpretation of the statute with regard to amendments to NDAs, BLAs, and PMAs, certifications need not be submitted with IND amendments other than submission of a new protocol to an existing IND.

FDA intends to exercise enforcement discretion with regard to submission of certifications with four categories of applications and submissions: 1) a supplement to an approved NDA, BLA, or PMA other than an efficacy supplement (for NDAs and BLAs) or a panel track supplement (for PMAs), 2) a supplement to an approved ANDA, 3) INDs that fall within the types of INDs described in section 561 of the Act (21 U.S.C. § 360bbb), and 4) submission of a 510(k) if that submission does not refer to, relate to, or include information on or from a clinical trial. FDA believes that, in contrast to the types of applications and submissions discussed above, the majority of supplements to approved NDAs, BLAs, and PMAs do not refer to, relate to, or include information on or from a clinical trial. Furthermore, even to the extent that, for example, a labeling supplement to an approved NDA may refer to, relate to, or include information on or from one or more clinical trials, those clinical trials in all likelihood were conducted under an IND, and therefore the sponsor would already

have submitted a certification regarding those trials during the investigational phase. It would be repetitive and would serve little or no purpose to have a sponsor repeatedly certify to having complied with the requirements of Title VIII of FDAAA with regard to the same clinical trial.

With regard to supplements to approved ANDAs, even when such supplements are intended to add an additional indication (such as when existing patents or exclusivities have expired), such supplements would not ordinarily refer to, relate to, or include information on or from any clinical trial other than those which were referenced or referred to in the original ANDA submission. Thus, as with non-efficacy supplements to approved NDAs and BLAs, and non-panel track supplements to approved PMAs, certification with a supplemental ANDA would be repetitive, and would serve little or no purpose with regard to ensuring that the requirements of Title VIII had been met.

With regard to INDs that fall within the types of INDs described in section 561 of the Act (21 U.S.C. § 360bbb), none of the clinical trials conducted under such INDs will meet the definition of applicable drug clinical trial in section 402(j)(1)(A)(iii) of the PHS Act (42 U.S.C. § 282(j)(1)(A)(iii)), and thus none of those trials will be subject to the registration and reporting requirements as set forth in Title VIII of FDAAA. One of the criteria for being an applicable drug clinical trial is that the trial at issue is a "controlled clinical investigation." Trials conducted under INDs that fall within the types of INDs described in section 561 of the Act are not controlled. Because none of the clinical trials conducted under an IND of the type described in section 561 of the Act would be subject to the requirements of Title VIII of FDAAA, certification with regard to such clinical trials when submitting an IND for such a clinical trial would serve little or no purpose with regard to ensuring that the requirements of Title VIII had been met.

Finally, with regard to 510(k)s, the majority of 510(k) submissions do not refer to, relate to, or include information on or from a clinical trial. Accordingly, FDA believes that certification with regard to 510(k) submissions that do not refer to, relate to, or include information on or from a clinical trial would serve little or no purpose with regard to ensuring that the requirements of Title VIII had been met.

Because FDA believes that the statutory purposes of Title VIII would not be furthered by the submission of certifications with these four categories of applications and submissions, the Agency intends to exercise enforcement discretion regarding certification with these applications and submissions.

Based on these considerations and as described above, FDA recommends that a certification accompany the following types of applications and submissions:

Applications/Submissions (including Resubmissions)
IND
New Clinical Protocol Submitted to an IND
NDA
Efficacy Supplement to an Approved NDA
BLA
Efficacy Supplement to an Approved BLA
ANDA
PMA
PMA Panel Track Supplement
HDE
510(k) that refers to, relates to, or includes information on a clinical trial

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176

Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

From: Hare, Michael [mailto:Michael.Hare@solvay.com]
Sent: Tuesday, July 13, 2010 8:44 AM
To: Meyer, Allison
Subject: NDA 022544 Administrative Question

Allison,
How is the divison interpreting the use of Form 3674. Should it be submitted with every NDA amendment regardless of content (i.e. clinical data or not)? We are recieving conflicting inputs from various divisions within CDER regarding the use of this form.

I would be happy to put a 3674 in every submission but want to confirm with you before submitting extraneous information.

Best regards,

Michael F. Hare
Assistant Director, Regulatory Affairs
Abbott (formerly Solvay Pharmaceuticals, Inc.)
Marietta, GA 30062
T: 770-578-5620
C: 678-938-8942
E: michael.hare@solvay.com

Meyer, Allison

From: Meyer, Allison
Sent: Thursday, June 17, 2010 7:01 AM
To: 'Hare, Michael'
Subject: 22544

Michael,
Please address asap.

1. In study 81-0062, it is not clear whether the subjects who took rescue medications were required to be discontinued from the trial or was discontinuation at the discretion of the investigator. The protocol states that the investigator "should have considered discontinuation of the patients from the trial (Page 17 of the 81-0062 Clinical Study Report)." Please clarify.

2. Regarding the disposition of patients for study 81-0062, readjudicate those patients who discontinued due to the reasons "withdrew consent" or "other reasons" (Page 28 of the 81-0062 Clinical Study Report) by reviewing the CRFs to determine whether any of these subjects actually discontinued due to adverse events or lack of efficacy. Also, submit the CRFs to the NDA.

3. For study 81-0062, perform an exploratory subgroup efficacy analysis of the three key secondary endpoints for the US population and the non-US population, and submit results to the FDA

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, May 25, 2010 1:06 PM
To: 'Hare, Michael'
Subject: FW: question

Michael

They just need to certify for the patents listed in the Orange Book .
Allison

From: Hare, Michael [mailto:Michael.Hare@solvay.com]
Sent: Tuesday, May 25, 2010 12:36 PM
To: Meyer, Allison
Subject: RE: question

Allison,
The question is...Are there additional patents that are not listed on the electronic version of the Orange Book that we should certify? The history of Neurontin is quite complex from looking at the number of NDA's submitted by the Sponsor. There are patents that were associated with these NDAs that are not Orange Book listed. How do we know if we should certify a patent if they are not Orange Book listed? Is there another database?

There is currently one Orange Book listed patent for Neurontin. Abbott Products Inc will be amending the current 022544 application with a certification regarding this patent within the next day or so. However, we want to ensure that this in the only patent to certify and not others.

Michael F. Hare
Assistant Director, Regulatory Affairs
Abbott (formerly Solvay Pharmaceuticals, Inc.)
Marietta, GA 30062
T: 770-578-5620
C: 678-938-8942
E: michael.hare@solvay.com

From: Meyer, Allison [mailto:Allison.Meyer@fda.hhs.gov]
Sent: Tuesday, May 25, 2010 12:07 PM
To: Hare, Michael
Subject: question

Michael,
Got your voicemail but couldn't hear you very well. Could you send your question to me in an email please?

Allison Meyer

Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, May 04, 2010 1:34 PM
To: 'Hare, Michael'
Subject: FW: NDA 22-544

Importance: High

Michael,

Submit chemical structures of all known impurities for the drug substance and drug product to NDA 22-544.

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Wednesday, April 21, 2010 1:56 PM
To: 'Hare, Michael'
Subject: FW: another request for Gabapentin ER

Michael

"For studies all Phase 2 and 3 studies for the PHN indication, provide narrative summaries for all subjects who dropped out of the study due to an adverse event".

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

Meyer, Allison

From: Meyer, Allison
Sent: Tuesday, April 20, 2010 2:32 PM
To: 'Hare, Michael'
Subject: RE: Proprietary name review

Yes, it was received. Please respond to the following request ASAP:
Provide a list of all study sites for study 81-0062 that includes for each site:

The name and address of the investigator

The number of patients screened, enrolled, and randomized

The number of major and minor protocol deviations

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and
Analgesia Products
Office of New Drugs II
Center for Drug Evaluation and Research

10903 New Hampshire Avenue
Bldg. 22, Rm. 3176
Silver Spring, MD 20993
301-796-1258
301-796-9713 (fax)

From: Hare, Michael [mailto:Michael.Hare@solvay.com]
Sent: Tuesday, April 20, 2010 1:19 PM
To: Meyer, Allison
Subject: RE: Proprietary name review

Allison,
Just wanted to confirm that the submission was recieved per your request below. The amendment was submitted via the gateway on 16 April.
Best regards,

Michael F. Hare
Assistant Director, Regulatory Affairs
Abbott (formerly Solvay Pharmaceuticals, Inc.)
Marietta, GA 30062
T: 770-578-5620
F: 770-579-7339
E: michael.hare@solvay.com

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

/s/

ALLISON MEYER
01/25/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022544 **INFORMATION REQUEST**

Abbott Products, Inc.
901 Sawyer Road
Marletta, GA 30062

Attention: Michael Hare
Assistant Director, Regulatory Affairs

Dear Mr. Hare:

Please refer to your new drug application (NDA) dated March 30, 2010, received March 30, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Gabapentin Extended Release (G-ER).

We have reviewed the proposed Risk Evaluation and Mitigation Strategy (REMS) section of your submission and have the following comments and information requests. In order to continue our evaluation of your NDA, we request a prompt written response.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. Additional revisions maybe needed so that the REMS and REMS supporting documents are consistent with the final labeling. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

GOAL

a. Revise your goal as follows:

The goal of this REMS is to inform patients about the serious risks associated with the use of gabapentin extended release tablets.

b. Your Medication Guide distribution plan appears to be acceptable. Your detailed plan for how you plan to distribute the Medication Guide in accordance with 21 CFR 208.24 is more appropriate for the REMS Supporting Document. See our editorial comments on this section of the proposed REMS (see Appendix A)

- We remind you that under 21 CFR 208.24, you are responsible for ensuring that sufficient numbers of Medication Guides are provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription. You state that you plan to contract with a third-party fulfillment group responsible for the following activities: identification of all Pharmacies/dispensers in the US, timely printing of Medication Guide tear pads, timely shipment of the tear pads and timely fulfillment of re-ordering of the Medication Guide tear pads in quantities to meet the needs of each dispenser, as specified by the dispenser. We find this distribution plan acceptable.
- We remind you that under 21 CFR 208.24, you are responsible for ensuring that the gabapentin extended release tablet carton or container label contains a prominent statement that the Medication Guide should be dispensed to each patient. We suggest the following language if the product is enclosed in the carton. "Dispense accompanying Medication Guide to each patient."

c. Your proposed element, (b) (4) is fine for the REMS Supporting Document but is not a required element of the REMS and has been removed. See Appendix.A.

d. Your proposed timetable for submission of assessments (18 months, 3 years and 7 years) is acceptable. We have some editorial comments on this section of the REMS.

e. Regarding your REMS Assessment Plan

The submitted methodology lacks sufficient detail to complete a review.

1. Submit for review the detailed plan that will be used to evaluate patients' understanding about the risks associated with and safe use of [Tradename]. This information **does not** need to be submitted for FDA review prior to approval of your REMS, however it should be submitted at least 90 days before the evaluation will be conducted. The submission should be coded "REMS Correspondence." If the plan is to conduct the required assessment using a survey, the submission should include all methodology and instruments that will be used to evaluate the patients' knowledge about the risks associated with and safe use of [Tradename].
2. We encourage you to recruit respondents using a multi-modal approach. For example, patients could be recruited online, through physicians' offices, through pharmacies, managed care providers, or through consumer panels.
   - Explain how often non-respondent follow-up or reminders will be completed.
   - Explain how an incentive or honorarium will be offered, and the intended amount.
   - Explain how recruitment sites will be selected.
   - Submit for review any recruitment advertisements.
3. Define the sample size and confidence intervals associated with that sample size.
4. Define the expected number of patients to be surveyed to obtain the final proposed sample size, and how the sample will be determined (selection criteria)

5. The patient sample should be demographically representative of the patients who use [Tradename].
   If possible and appropriate, sample should be diverse in terms of: age, race, ethnicity, sex, socio-economic status, education level, geography.

6. Explain the inclusion criteria; that is, who is an eligible respondent. For example, *patient* respondents might be:
   - Age 18 or older
   - Currently taking [Tradename] or have taken in past 3 months
   - Not currently participating in a clinical trial involving [Tradename]
   - Not a healthcare provider

   Submit any screener instruments, and describe if any quotas of sub-populations will be used.

7. Explain how surveys will be administered, and the intended frequency.
   We encourage you to offer respondents multiple options for completing the survey. This is especially important for inclusion of the lower literacy population. For example, surveys could be completed online or through email, in writing or by mail, over the phone, or in person.
   Explain how surveyors will be trained.

8. Explain controls used to compensate for the limitations or bias associated with the methodology.

9. Submit for review the introductory text that will be used to inform respondents about the purpose of the survey.
   Potential respondents should be told that their answers will not affect their ability to receive or take [Tradename], and that their answers and personal information will be kept confidential and anonymous.

10. Respondents should not be eligible for more than one wave of the survey.

11. The assessment is to evaluate the effectiveness of the REMS in achieving the REMS goal by evaluating patients' knowledge of the serious risks associated with use of [Tradename]. The assessment is not to evaluate consumer comprehension of the Medication Guide.
    Other than when the patient received the Medication Guide at the time the prescription was filled/dispensed, respondents should not be offered an opportunity to read or see the Medication Guide again prior to taking the survey.

12. Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in the Medication Guide.

13. The patient knowledge survey should include a section with questions asking about the specific risks or safety information conveyed in the Medication Guide to see if the patient not only understands the information, but knows what to do if they experience the event.
    Most of the risk-specific questions should be derived from information located in the "What is the Most Important Information I should know about [Tradename]?"

section of the Medication Guide. The questions should be about understanding the risk, the symptoms, and what to do if the event occurs.
The risk-specific questions should be non-biased, non-leading, multiple choice questions with the instruction to "select all that apply." Each question should have an "I don't know" answer option.
The order of the multiple choice responses should be randomized on each survey.

14. The order of the questions should be such that the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Demographic questions should be collected last or as part of any screener questions.
Respondents should not have the opportunity or ability to go back to previous questions in the survey.
Explain if and when any education will be offered for incorrect responses.

15. Include questions about receipt of the Medication Guide in the patient survey as a way to fulfill the obligation to report on the distribution of the Medication Guide.

16. Just prior to the questions about receipt of the Medication Guide, include text that describes a Medication Guide. For example,
Now we are going to ask you some questions about the Medication Guide you may have received with [Tradename]. The Medication Guide is a paper handout that contains important information about the risks associated with use of [Tradename] and how to use [Tradename] safely. Medication Guides always include the title "Medication Guide" followed by the word [Tradename] and its pronunciation. The Medication Guide usually has sections titled "What is the most important information I should know about [Tradename]," "What is [Tradename]," and "Who should not take [Tradename]."

17. Use the following (or similar) questions to assess receipt and use of the Medication Guide.

- Who gave you the Medication Guide for [Tradename]? (Select all that apply)
  a) My doctor or someone in my doctor's office
  b) My pharmacist or someone at the pharmacy
  c) Someone else - please explain: _____
  d) I did not get a Medication Guide for [Tradename]

- Did you read the Medication Guide?
  - All,
  - Most,
  - Some,
  - None

- Did you understand what you read in the Medication Guide?
  - All,
  - Most,
  - Some,
  - None

- Did someone offer to explain to you the information in the Medication Guide?
  - Yes, my doctor or someone in my doctor's office
  - Yes, my pharmacist or someone at the pharmacy
  - Yes, someone else please explain: _____
  - No
- Did you accept the offer? Yes or No
- Did you understand the explanation that was given to you?
  - All,
  - Most,
  - Some,
  - None
- Did or do you have any questions about the Medication Guide? Yes or No (If Yes, list your question(s) below) Note: This is an open text field that should be grouped/coded by the sponsor prior to submitting to FDA

18. Results should be analyzed on an item-by-item or variable-by-variable basis. The data may be presented using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).

19. Data may be stratified by any relevant demographic variable, and also presented in aggregate. We encourage you to submit with your assessments all methodology and instruments that were used to evaluate the effectiveness of the REMS.

If you have any questions, call Allison Meyer, Regulatory Project Manager, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Parinda Jani
Chief, Project Management Staff
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Attachments:
Marked-up copy of the proposed REMS
Clean copy of the proposed REMS

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

/s/

PARINDA JANI
01/21/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022544 **DISCIPLINE REVIEW LETTER**

Abbott Products, Inc.
901 Sawyer Road
Marletta, GA 30062

Attention: Michael Hare
Assistant Director, Regulatory Affairs

Dear Mr. Hare:

Please refer to your new drug application (NDA) dated March 30, 2010, received March 30, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Gabapentin Extended Release (G-ER).

We also refer to your submission dated October 28, 2010.

The Office of New Drugs Quality Assessment has completed the review of the biopharmaceutics section of your submission, and have identified the following deficiencies:

1. Your proposed IVIVC models for Gabapentin ER tablets are not acceptable for the following reasons:

(b) (4)

a.

b.

c.

d.

2. (b) (4) Since you failed to demonstrate the extended release characteristics as outline in 21 CFR 320.25(f), this proposed formulation of gabapentin should not be classified as an extended release product.

3. (b) (4)

4. Using the dissolution method; USP Apparatus 1 (basket), 100 rpm, 900 ml of pH 1.2 Buffer, modified Simulated Gastric Fluid without pepsin, at 37°C, the following dissolution acceptance criteria are recommended for gabapentin ER tablets:

Acceptance Criteria	
1 hour:	(b) (4)
4 hours:	(b) (4)
8 hours:	(b) (4)
12 hours:	(b) (4)

In the absence of an acceptable IVIVC, the recommended specification ranges are based on the mean dissolution values (b) (4) from the registration, clinical and stability batches. Revise the dissolution specifications accordingly.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Allison Meyer, Regulatory Project Manager, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Parinda Jani
Chief, Project Management Staff
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
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/

PARINDA JANI
12/07/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: OSE

FROM: Allison Meyer, ODE II/DAAP/301 796 1258

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
November 19, 2010		22544	New NDA	3/30/2010

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Gabapentin ER	Standard	Analgesic	12/19/2010

NAME OF FIRM: Abbott

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL BIOPHARMACEUTICS
- ☐ IN VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: \\CDSESUB1\EVSPROD\NDA022544\022544.enx

Please provide us with an AERs search for post marketing data for Neurontin. Crude counts are sufficient.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

ALLISON MEYER
11/19/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022544

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Abbott Products, Inc.
901 Sawyer Road
Marietta, Georgia 30062

ATTENTION: Michael F. Hare
Assistant Director, Regulatory Affairs

Dear Mr. Hare:

Please refer to your New Drug Application (NDA) dated March 30, 2010, received March 30, 2010, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for Gabapentin Extended-release Tablets, 300 mg and 600 mg.

We also refer to your April 16, 2010, correspondence, received April 16, 2010, requesting review of your proposed proprietary name, Gralise. We have completed our review of the proposed proprietary name, Gralise and have concluded that it is acceptable.

The proposed proprietary name, Gralise, will be re-reviewed 90 days prior to the approval if the NDA. If we find the name unacceptable following re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your April 16, 2010 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Bola Adeolu, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4264. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Allison Meyer at (301) 796- 1258.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22544	ORIG-1	ABBOTT PRODUCTS INC	GABAPENTIN E-R TABLETS

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

/s/

CAROL A HOLQUIST
07/13/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 22544

FILING COMMUNICATION

Abbott Products, Inc.
901 Sawyer Road
Marletta, GA 30062

Attention: Michael Hare
Assistant Director, Regulatory Affairs

Dear Mr. Hare:

Please refer to your new drug application (NDA) dated March 30, 2010, received March 30, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Gabapentin Extended Release (G-ER).

We also refer to your submissions dated April 16, 20, and 30, and May 26, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is January 30, 2011.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by December 17, 2010.

During our filing review of your application, we have identified the following potential review issues:

1. Utilization of the 505(b)(2) approval pathway only allows reliance on the Agency's finding of safety and/or effectiveness as it is reflected in the approved labeling of the Reference Listed Product. You cannot rely on innovator studies or specifications described in the Summary Basis of Approval for the RLD to support your proposed drug

product specifications. Additionally, the specifications that need to be in compliance with ICHQ3B (drug product) are those at the end of the shelf-life of the product. Your stability data showed that the qualification threshold (0.2% or 3 mg total daily intake [TDI], whichever is lower) is exceeded for multiple impurities on the basis of TDI. Reduce specifications to comply or you will need to provide impurity qualification studies to support the proposed specifications.

We also request that you submit the following information:

2. Based on the simulations for the "moderate renally impaired group" (Study Report 85-0010), you proposed that a dosing of 600 mg is appropriate for any fed condition and a 1200 mg dose is considered the upper limit. However in the final annotated label, your dosing recommendation for this group of patients is 600 to1800 mg. Explain the discrepancy and propose the appropriate dosing schedule for this group along with supportive information.

3. Unlike in Neurontin products, you have not proposed the dosing scheme for patients with creatinine clearance <15 ml/min or for patients undergoing hemodialysis. Propose the dosing scheme for patients with creatinine clearance <15 ml/min or patients undergoing hemodialysis, or provide an explanation if dosing in these patients is not practically feasible with your product.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of 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 not already done so, you must submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

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.

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Allison Meyer, Regulatory Project Manager, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22544	ORIG-1	ABBOTT PRODUCTS INC	GABAPENTIN E-R TABLETS

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

/s/

BOB A RAPPAPORT
06/09/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: OSE

FROM: Allison Meyer, ODE II/DAAP/301 796 1258

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
May 5, 2010		22544	New NDA	3/30/2010

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Gabapentin ER	Standard	Analgesic	11/19/2010

NAME OF FIRM: Abbott

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL BIOPHARMACEUTICS
- ☐ IN VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: \\CDSESUB1\EVSPROD\NDA022544\022544.enx
We have received a new NDA 22-544. This product will have a MG-only REMS (class labeling), which needs to be reviewed by DRISK. I have scheduled Planning, MC and WU meetings. We would like the labeling to be reviewed by DMEPA.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22544	ORIG-1	ABBOTT PRODUCTS INC	GABAPENTIN E-R TABLETS

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

/s/

ALLISON MEYER
05/11/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:	FROM: (Name/Title, Office/Division/Phone number of requestor)
CDER-DDMAC-RPM	Allison Meyer, ODEII/DAAP/301-796-1258

REQUEST DATE	IND NO.	NDA/BLA NO.	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
May 5, 2010		22544	New NDA

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE (Generally 1 week before the wrap up meeting)
Gabapentin ER	Standard	Analgesic	11/19/10

NAME OF FIRM:	
Abbott	PDUFA Date: 1/30/11

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)
x PACKAGE INSERT (PI)
☐ PATIENT PACKAGE INSERT (PPI)
☒ CARTON/CONTAINER LABELING
☒ MEDICATION GUIDE
☐ INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION
☒ ORIGINAL NDA/BLA
☐ IND
☐ EFFICACY SUPPLEMENT
☐ SAFETY SUPPLEMENT
☐ LABELING SUPPLEMENT
☐ PLR CONVERSION

REASON FOR LABELING CONSULT
☒ INITIAL PROPOSED LABELING
☐ LABELING REVISION

EDR link to submission: \\CDSESUB1\EVSPROD\NDA022544\022544.enx

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: 7/19/10

Labeling Meetings: TBD

Wrap-Up Meeting: 11/30/10

SIGNATURE OF REQUESTER

SIGNATURE OF RECEIVER	METHOD OF DELIVERY (Check one) ☐ eMAIL ☐ HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22544	ORIG-1	ABBOTT PRODUCTS INC	GABAPENTIN E-R TABLETS

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

/s/

ALLISON MEYER
05/11/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022544 **NDA ACKNOWLEDGMENT**

Abbott Products Inc.
901 Sawyer Road
Marietta, GA 30062

Attention: Michael Hare
Assistant Director, Regulatory Affairs

Dear Mr. Hare:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Gabapentin Extended Release (G-ER) Tablets, 300 mg and 600 mg

Date of Application: March 30, 2010

Date of Receipt: March 30, 2010

Our Reference Number: NDA 022544

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 29, 2010 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

Please note that you are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 USC §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been

met. Where available, the certification must include the appropriate National Clinical Trial (NCT) control numbers. 42 USC 282(j)(5)(B). You did not include such certification when you submitted this application. You may use Form FDA 3674, *Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank,* to comply with the certification requirement. The form may be found at http://www.fda.gov/opacom/morechoices/fdaforms/default.html.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trials referenced in this application. Additional information regarding the certification form is available at: http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm. Additional information regarding Title VIII of FDAAA is available at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information on registering your clinical trials is available at the Protocol Registration System website http://prsinfo.clinicaltrials.gov/.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anesthesia and Analgesia Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm

If you have any questions, call me, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Allison Meyer
Sr. Regulatory Health Project Manager
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22544	ORIG-1	ABBOTT PRODUCTS INC	GABAPENTIN E-R TABLETS

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

/s/

ALLISON MEYER
04/14/2010