CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-692 S001/002

ADMINISTRATIVE DOCUMENTS

NDA 20-692

Serevent® (salmeterol xinafoate)
Diskus Inhalation Powder
sNDA

DEBARMENT CERTIFICATION

Glaxo Wellcome hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this application.

Shelly A Schiff for Charles Mueller 22SEP98

Charles E. Mueller
Head, International Compliance Services
World Wide Compliance

Date

.....

The list of Glaxo Wellcome Principal Investigators for the above titled submission has been compared with the 08Apr97 Food and Drug Administration Debarment List and the 01Jan97 Disqualified, Restricted, and Given Assurances lists.

Shelly A Schiff for Jeanne Kistler 22SEP98

Jeanne Kistler
Compliance Services Coordinator
World Wide Compliance

Date

NDA 20-692

Supplemental New Drug Application

Serevent® (salmeterol xinafoate) Diskus Inhalation Powder

DEBARMENT CERTIFICATION

Glaxo Wellcome hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this application.

Shelly A Schiff for Charles Mueller 22 SEP 98

Charles E. Mueller
Head, International Compliance Services
World Wide Compliance
Date

.....

The list of Glaxo Wellcome Principal Investigators for the above titled submission has been compared with the 12Aug97 Food and Drug Administration Debarment List and the 18Apr97 Disqualified, Restricted, and Given Assurances lists.

Shelly A Schiff for Jeanne Kistler 22SEP98

Jeanne Kistler
Compliance Services Coordinator
World Wide Compliance
Date

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20692	**Trade Name:**	SEREVENT DISKUS 50MCG INHALATION POWDER
Supplement Number:	2	**Generic Name:**	SALMETEROL XINAFOATE
Supplement Type:	SE5	**Dosage Form:**	Powder; Inhalation
Regulatory Action:	PN	**Proposed Indication:**	maintenance treatment of asthma and in the prevention of EIB in patients 4 years of age and older with reversible obstructive airway disease.

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? YES

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days)____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-18 Years)

Label Status	ADEQUATE Labeling for SOME PEDIATRIC ages
Formulation Status	NO NEW FORMULATION is needed
Studies Needed	No further STUDIES are needed
Study Status	

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:
The supplement will be approved.

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, PARINDA JANI

/S/
Signature

9-23-98
Date

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20692	**Trade Name:**	SEREVENT DISKUS 50MCG INHALATION POWDER
Supplement Number:	1	**Generic Name:**	SALMETEROL XINAFOATE
Supplement Type:	SE1	**Dosage Form:**	Powder; Inhalation
Regulatory Action:	PN	**Proposed Indication:**	EIB for adults and children 4 years of age and older

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? YES

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days)
____Infants (1-24 Months)
_X_Other Age Groups (listed): 4 - 11 years of age
____Children (25 Months-12 years)
____Adolescents (13-18 Years)

Label Status	ADEQUATE Labeling for SOME PEDIATRIC ages
Formulation Status	NO NEW FORMULATION is needed
Studies Needed	No further STUDIES are needed
Study Status	-

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:
The supplement is due September 26, 1998 and will be approved. Sponsor has submitted a separate supplement for pediatric indication (S-002, for children 4 years of age and older) which will be approved on the same date.

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, PARINDA JANI

Signature

Date

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY for NDA # 20-692 SUPPL # 002

Trade Name Serevent Diskus
Generic Name Salmeterol xinafoate inhalation powder
Applicant Name Glaxo Wellcome HFD- 570

Approval Date: September 25, 1998

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain 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 an original NDA?

YES /_ _/ NO /_ X _/

b) Is it an effectiveness supplement?

YES /_ X _/ NO /__/

If yes, what type? (SE1, SE2, etc.) SE5

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 /_X_/ 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 /_X_/ NO /___/

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

3 years

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 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 /_X_/ NO /___/

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

NDA # 20-236 Serevent Inhalation Aerosol

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 /___/

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

NDA #_____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S 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 /_X_/ 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.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(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 /_X_/ 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 /_X__/ 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 /_X_/

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:

Investigation #1, Study # SLGA 2016

Investigation #2, Study # SLD-390

Investigation #3, Study # SLGA 3014

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_/
Investigation #2	YES /___/	NO /_X_/
Investigation #3	YES /___/	NO /_X_/
Investigation #4	YES /___/	NO /_X_/
Investigation #5	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:

NDA #_____ Study #
NDA #_____ Study #

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_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /_X_/

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

NDA #_____ Study #
NDA #_____ Study #
NDA #_____ Study #

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"):

Investigation #1, Study # SLGA 2016

Investigation #2, Study # SLD-390

Investigation #3, Study # SLGA 3014

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 through #3
IND # [redacted] YES /_X_/ NO /___/ _____

(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 /___/ Explain _____ NO /___/ Explain _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ 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: _____

_____

/S/

Parinda Jani
Project Manager

9.23.98
Date

/S/

John K. Jenkins, M.D., F.C.C.P.
Division Director

9/25/98
Date

cc:
Original NDA 20-692
Division File HFD-570
HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY for NDA # 20-692 SUPPL # 001

Trade Name Serevent Diskus
Generic Name Salmeterol xinafoate inhalation powder
Applicant Name Glaxo Wellcome HFD- 570

Approval Date: September 25, 1998

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain 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 an original NDA?

YES /_ _/ NO /_ X _/

b) Is it an effectiveness supplement?

YES /_ X _/ NO /__/

If yes, what type? (SE1, SE2, etc.) SE1

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 /_X_/ 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 /_X_/ NO /___/

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

3 years

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 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 /_X_/ NO /___/

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

NDA # 20-236 Serevent Inhalation Aerosol

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 /___/

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

NDA #_____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S 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 /_X_/ 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.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(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 /_X_/ 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 /_X__/ 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 /_X_/

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:

Investigation #1, Study # SLGA 2013

Investigation #2, Study # SLGA 2017

Investigation #3, Study # SLGA 2002

Investigation #4, Study # SLGA 2003

Investigation #5, Study # SLGA 2014

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_/
Investigation #2	YES /___/	NO /_X_/
Investigation #3	YES /___/	NO /_X_/
Investigation #4	YES /___/	NO /_X_/
Investigation #5	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:

NDA #_____ Study #
NDA #_____ Study #

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_/
Investigation #2	YES /___/	NO /_X_/
Investigation #3	YES /___/	NO /_X_/
Investigation #4	YES /___/	NO /_X_/
Investigation #5	YES /___/	NO /_X_/

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

NDA #_____ Study #
NDA #_____ Study #
NDA #_____ Study #

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"):

Investigation #1, Study # SLGA 2013

Investigation #2, Study # SLGA 2017

Investigation #3, Study # SLGA 2002

Investigation #4, Study # SLGA 2003

Investigation #5, Study # SLGA 2014

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 through #5
IND # [redacted] YES /_X_/ NO /___/ _____

(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?

APPEARS THIS WAY
ON ORIGINAL

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____ NO /___/ 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: _____

/S/

Parinda Jani
Project Manager

9.23.98
Date

/S/

John K. Jenkins, M.D., F.C.C.P.
Division Director

9/25/98
Date

cc:
Original NDA 20-692
Division File HFD-570
HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL

III. Marketing Exclusivity

NDA 20-692

Serevent® (salmeterol xinafoate) Diskus® Inhalation Powder

Request for Marketing Exclusivity

Pursuant to Section 505(c)(3)(D)(iv) and 505(j)(4)(D)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.108(b)(4), Glaxo Wellcome Inc. requests three years of exclusivity from the date of approval of Serevent® (salmeterol xinafoate) Diskus® Inhalation Powder for long-term twice daily (morning and evening) administration in the prevention of exercise-induced bronchospasm (EIB) in patients 4 years of age or greater.

We hereby certify as to the following:

Section 7, Item VIII of this application contains a list of published studies or publicly available reports of clinical investigations known to Glaxo Wellcome through a literature search that are relevant to the use of Serevent Diskus Inhalation Powder for long-term twice daily (morning and evening) administration in the prevention of exercise-induced bronchospasm in patients 4 years of age or greater. This search is comprehensive in that it includes data for the use of salmeterol xinafoate dry powder in patients 4 years of age or greater with EIB and covers the period of October 1, 1995 until January 15, 1997.

Glaxo Wellcome has thoroughly searched the literature and to the best of our knowledge, the list is complete and accurate and, in our opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of Serevent Diskus Inhalation Powder for such use.

Thus, Glaxo Wellcome Inc. is entitled to exclusivity as this application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and sponsored by Glaxo Wellcome Inc. The following investigations are "essential to the approval of the application" in that there are insufficient data available in the public domain to support FDA approval of the indication.

SLGA2013	A randomized, double-blind, double-dummy, single-dose, four-way crossover comparison of salmeterol 50mcg and 100mcg via the Diskus™, salmeterol 50mcg via the metered-dose inhaler and placebo for the prevention of exercise-induced bronchospasm and adolescent and adult subjects with asthma (RM1996/00095/00)

SLGA2017	A randomized, double-blind, double-dummy, single-dose, four-way crossover comparison of salmeterol 50mcg and 100mcg via the Diskus™, salmeterol 50mcg via the metered-dose inhaler and placebo for the prevention of exercise-induced bronchospasm and adolescent and adult subjects with asthma (RM1996/00163/00)
SLGA2003	A randomized, double-blind, double-dummy, single-dose, three-way crossover comparison of salmeterol xinafoate 50mcg and placebo given by the multi-dose powder inhaler and Diskhaler for the prevention of exercised-induced bronchospasm in pediatric subjects with asthma (UCR/95/014)
SLGA2014	A randomized, double-blind, double-dummy, single-dose, four-way crossover comparison of salmeterol 25mcg and 50mcg given by the multidose powder inhaler (Diskus®), Albuterol 180mcg given by the metered-dose inhaler, and placebo for the prevention of exercise-induced bronchospasm in pediatric subjects with asthma (RM1996/00350/00)

The clinical investigations are defined as "new" as they have not been relied on by the FDA to demonstrate substantial evidence of effectiveness of previously approved drug products for any indication or of safety for a new patient population and do not duplicate the results of any such investigation.

The investigations were "conducted or sponsored by Glaxo Wellcome" in that Glaxo Wellcome Inc. was the sponsor of the investigational new drug applications (IND salmeterol xinafoate multi-dose powder inhaler, IND and IND under which these investigations were conducted.

/S/

Ramona Krailler, Ph.D
Product Director, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

SLGA2016 A randomized, double-blind, double-dummy, five-way crossover comparative clinical trial of single-doses of salmeterol 25, 50 and 100 mcg via the Diskus™ (multidose powder inhaler), albuterol 200mcg rotacaps via [redacted] and placebo in pediatric subjects aged 4-11 years with asthma (RM1996/00351/00)

SLD-390 A randomized, double-blind, comparative clinical trial of the effects of twelve week courses of salmeterol xinafoate [redacted] versus placebo in pediatric patients aged 4-11 years with mild-to-moderate asthma (UCR/95/028)

SLGA3014 A randomized, double-blind, double-dummy, parallel-group, comparative clinical trial of the effects of twelve week courses of 50mcg and 25mcg salmeterol powder via the Diskus™ BID versus Ventolin rotacaps® 200mcg QID versus placebo in pediatric subjects aged 4-11 years with mild to moderate asthma (RM1997/00414/00)

The clinical investigations are defined as "new" as they have not been relied on by the FDA to demonstrate substantial evidence of effectiveness of previously approved drug products for any indication or of safety for a new patient population and do not duplicate the results of any such investigation.

The investigations were "conducted or sponsored by Glaxo Wellcome" in that Glaxo Wellcome Inc. was the sponsor of the investigational new drug applications (IND [redacted] salmeterol xinafoate multi-dose powder inhaler, and IND [redacted] under which these investigations were conducted.

/S/

Ramona Krailler, Ph.D
Product Director, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Patent Information for
SEREVENT® DISKUS® Inhalation Powder
NDA 20-692

Active Ingredient:	Salmeterol Xinafoate
Strength of Drug Product:	50 micrograms of salmeterol (as xinafoate) per blister
Dosage Form:	Inhalation Powder
Route of Administration:	Oral Inhalation
Applicant Firm Name:	Glaxo Wellcome Inc.

Patent Number:	**4,992,474**
Coverage:	Salmeterol and Salmeterol Xinafoate per se, compositions and various methods of use
Issue Date:	February 12, 1991
Expiration Date:	February 12, 2008

Patent Number:	**5,225,445**
Coverage:	covers the use of salmeterol in patients with reversible airways obstruction
Issue Date:	July 6, 1993
Expiration Date:	February 12, 2008 (the portion of the patent term subsequent to February 12, 2008 has been disclaimed)

Patent Number:	**5,380,922**
Coverage:	covers micronisable microcrystals of salmeterol xinafoate and a process for its production
Issue Date:	January 10, 1995
Expiration Date:	January 10, 2012

Patent Number:	**5,590,645**
Coverage:	covers the product administration system
Issue Date:	January 7, 1997
Expiration Date:	March 1, 2011

Patent Number:	**Des. 342,994**
Coverage:	covers the product administration system
Issue Date:	January 4, 1994
Expiration Date:	January 4, 2008

The Undersigned certifies to the best of his knowledge and belief the above listed patents are valid patents, claiming salmeterol xinafoate or its administration system, the subject of a New Drug Application.

01/17/97
Date

Charles E. Dadswell
Registered Patent Attorney
United States Registration No. 35,851