CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 203433s002

Name: Fluticasone Propionate and Salmeterol Inhalation Powder USP, 100 mcg/50 mcg and 250 mcg/50 mcg

Sponsor: Hikma Pharmaceuticals USA Inc

Approval Date: December 17, 2020

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA203433Orig1s002

CONTENTS

Reviews / Information Included in this Review

Approval Letter	**X**
Tentative Approval Letter	
Labeling	
Labeling Review(s)	
Medical Review(s)	
Chemistry Review(s)	**X**
Pharm/Tox Review	**X**
Bioequivalence Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Other Review(s)	
Administrative & Correspondence Documents	

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APPLICATION NUMBER:

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APPROVAL LETTER

ANDA 203433/S-002

PRIOR APPROVAL SUPPLEMENT
APPROVAL

Hikma Pharmaceuticals USA Inc.
1809 Wilson Road
Columbus, OH 43228
Attention: Chrysoula Koukoutsis
Associate Director, Drug Regulatory Affairs

Dear Chrysoula Koukoutsis:

This letter is in reference to your supplemental abbreviated new drug application (sANDA) received for review on February 2, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Fluticasone Propionate and Salmeterol Inhalation Powder USP, 100/50 µg and 250/50 µg.

The sANDA, submitted as “Prior Approval Supplement," provides for:

(b) (4)
(b) (4) for Fluticasone Propionate and Salmeterol Inhalation Powder USP, 100/50 µg and 250/50 µg.

We have completed the review of this sANDA and it is approved.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

If your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts we remind you that you must comply with the postmarking safety reporting requirements for an approved combination product (21 CFR Part 4, Subpart B). Additional information on combination product postmarketing

safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions [1] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

If you have further questions regarding this supplement, you may contact Avani Patel, Regulatory Business Process Manager, at (240) 402 - 1845.

Sincerely yours,

{See appended electronic signature page}

For:
Paul Schwartz, Ph.D.
Director, Division of Post Marketing Activities II
Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

[1] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Niles Ron

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA203433Orig1s002

CHEMISTRY REVIEW(s)

DISCIPLINES INVOLVED	REVIEW OUTCOME	DISCIPLINES INVOLVED	REVIEW OUTCOME
Chemistry	Adequate	Bioequivalence	NA
Microbiology	NA	Facility	NA
Labeling	NA	DMF	NA
SUBMISSIONS REVIEWED			
Submission Date:	2/2/2021		
Amendment(s) Date:	NA		

OFFICE OF PHARMACEUTICAL QUALITY

REVIEW OF SUPPLEMENT TO ABBREVIATED NEW DRUG APPLICATION

1. CHEMIST'S REVIEW NUMBER 1

2. sANDA NUMBER 203433/S-002

3. NAME AND ADDRESS OF APPLICANT

Hikma Pharmaceuticals USA Inc.
Attention: Jerald Andry, PharmD, MS
Senior Director, Drug Regulatory Affairs
1809 Wilson Road
Columbus, OH 43228
Tel: (614) 241-4154
Fax: (614) 276-2470
Email: dra-columbus@Hikma.com

4. PURPOSE OF AMENDMENT/SUPPLEMENT (b) (4) (b) (4) (b) (4) for Fluticasone Propionate and Salmeterol Inhalation Powder USP, 100/50 µg and 250/50 µg.

5. DATE(S) OF SUBMISSION(S) 2/2/2021

6. PHARMACOLOGICAL CATEGORY Treatment of asthma in patients aged 4 years and older

7. NAME OF DRUG NA

8. NONPROPRIETARY NAME Fluticasone Propionate & Salmeterol Inhalation Powder

9. DOSAGE FORM Dry Powder Inhaler

10. POTENCY 100/50 µg and 250/50 µg

11. HOW DISPENSED Rx

12. RELATED IND/NDA/DMF(s) NA

13. STERILIZATION NA

14. LABELING NA

15. ESTABLISHMENT INSPECTION NA

16. BIOEQUIVALENCE STATUS NA

17. COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

The applicant (Hikma Pharmaceuticals USA Inc.) submitted this PAS to provide for (b) (4) (b) (4) (b) (4) for Fluticasone Propionate and Salmeterol Inhalation Powder USP, 100/50 µg and 250/50 µg.

The detailed proposed changes are described below.

(b) (4) (b) (4) (b) (4)

(b) (4)

In support of the proposed changes, the applicant provided following information and studies as in section 3.2.P.7.

1) (b) (4)
2)
3)
4)
5)

6) (b) (4)

7)

As the conclusion, the applicant stated that:

(b) (4)

The report will be reviewed by Pharm/Tox team.

Reviewer's Comments:

(b) (4)

Therefore, it is believed that the applicant provided sufficient information and study data for the proposed changes, which are approvable per CMC perspective.

18. PACKAGING NA

19. STABILITY NA

20. REMARKS AND CONCLUSIONS approvable

21. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt?

■ Yes or ☐ No. If no, explain reason(s) below:

Special Product Online Tracking (SPOT)?

☐ Yes or ■ No. If yes, complete a SPOT form.

22. REVIEWER AND DATE COMPLETED Jianxin Yang 4/15/2021

23. DMF CHECK LIST

DMF No.	DMF	Action Code	Result of Review	Date Review Completed
	Comment			
	Comment			
	Comment			
	Comment			
	Comment			
	Comment			

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows: (2) Type 1 DMF; (3) Reviewed previously and no relevant revision since last review; (4) Sufficient information in application; (5) Authority to reference not granted; (6) DMF not available; (7) Other (explain under "Comments").

Reviewer _____ Signature _____ Date _____

cc: ANDA 203433/S-002
Division File
Field Copy
HFD-600/Reading File

Jianxin Yang

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Date: 4/16/2021 01:20:46PM
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Dipak Chowdhury

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Date: 4/16/2021 01:27:53PM
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA203433Orig1s002

PHARM/TOX REVIEW(s)

PHARMACOLOGY-TOXICOLOGY CONSULTATION REVIEW
Division of Clinical Review (DCR)
Office of Bioequivalence (OB), Office of Generic Drugs (OGD)
Center for Drug Evaluation & Research (CDER)

Drug Product:	Fluticasone propionate and salmeterol inhalation powder, 100/50 µg and 250/50 µg strengths
ANDA#: **Applicant:**	ANDA 203433/Supplement-002 Hikma Pharmaceuticals USA Inc.
RLD#/Approval Date: **Sponsor:**	Advair Diskus (NDA 021077, fluticasone propionate and salmeterol inhalation powder), for oral inhalation use, approved on 08/24/2000 Glaxo Group Ltd England Dba Glaxosmithkline
Pharmacology-Toxicology Primary Reviewer:	Chanchal Gupta, Ph.D. Staff Fellow
Pharmacology-Toxicology Secondary Reviewer:	Richard Houghtling, Ph.D. Lead Pharmacologist
Tertiary Reviewer:	Sruthi King, Ph.D. Associate Director of Pharmacology/Toxicology, OGD
To:	Jianxin Yang, Ph.D. Division of Post-Marketing Activities (DPMA) II Office of Pharmaceutical Quality (OPQ)
Reason for Consult:	(b) (4)
Date of Submission:	02/02/2021
Date Consult Received:	02/09/2021
Date of Completion:	04/15/2021
Conclusion:	OGD-Pharmacology/Toxicology concludes that the proposed (b) (4) generic fluticasone propionate and salmeterol inhalation powder is acceptable. There is nothing to be conveyed to the applicant.
Deficiency Classification:	☐ Major ☐ Minor ☒ N/A (Review is Adequate)

1 Executive Summary:

This OGD-Pharmacology/Toxicology (Pharm/Tox) review addresses a consult request from the Division of Post-Marketing Activities (DPMA) II in the Office of Pharmaceutical Quality (OPQ) regarding the (b) (4) in a generic fluticasone propionate and salmeterol inhalation powder, 100/50 µg and 250/50 µg strengths.

The reference listed drug (RLD) is Advair Diskus (NDA 021077, fluticasone propionate and salmeterol inhalation powder, 100/50 µg, 250/50 µg, and 500/50 µg strengths). Advair Diskus is indicated for asthma in patients 4 years and older and for maintenance treatment of airflow obstruction and reducing exacerbations in patients with chronic obstructive pulmonary disease (COPD).

(b) (4)

2 Internal Recommendation:

The proposed specification (b) (4) (b) (4) in the generic fluticasone Pharm/Tox perspective.

3 Comments to be conveyed by the RPM to the ANDA applicant as written:

There is nothing to be conveyed to the applicant.

4 Regulatory Background:

Hikma Pharmaceuticals USA Inc. submitted ANDA 203433 on 02/11/2016, for the generic fluticasone propionate and salmeterol inhalation powder (100/50 µg and 250/50 µg strengths). ANDA 203433 was approved by the FDA on 12/17/2020. The RLD is marketed by Glaxo Group Ltd England Dba Glaxosmithkline and approved on 08/24/20000.

(b) (4)

DPMA II consulted OGD-Pharm/Tox to (b) (4)

(b) (4)

proposed specification limit is the subject of the current review.

5 Labeling:

The current product label for the RLD (NDA 021077) was approved on 01/07/2019.[8]

5.1 Indications

Advair Diskus is a combination product containing a corticosteroid and a long-acting β_2-adrenergic agonist, indicated for asthma in patients 4 years and older and for maintenance treatment of airflow obstruction and reducing exacerbations in patients with COPD. It is not indicated for relief of acute bronchospasm.

(b) (4)

[7] ANDA 203433, Panorama, 203433_S-002 (Pharm Tox Consult)-05Feb21; https://panorama.fda.gov/task/view?ID=601d58a20018d73abe2acc5dd52cbf98, dated 02/09/2021.
[8] Advair Diskus label, Drugs@FDA; https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021077s061lbl.pdf, accessed on 03/20/2021.

5.2 Dosage and Administration

Advair Diskus is administered as one inhalation twice daily by oral inhalation route. The maximum daily dose (MDD) of fluticasone propionate and salmeterol inhalation powder is 1000/100 µg/day in adults and adolescents 12 years and older and 200/100 µg/day in children 4-11 years.

6 Discussion:

The generic fluticasone propionate and salmeterol drug product is a pre-metered dry powder inhaler, containing a foil blister strip of powder formulation. (b) (4)

(b) (4)

6.1 Applicant's Justification

(b) (4)

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Chanchal Gupta

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Sruthi King

Digitally signed by Sruthi King
Date: 4/15/2021 02:09:10PM
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Comments: Dr. Richard Houghtling completed secondary review on this consult. I completed tertiary review and am signing on his behalf while he is on leave.