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SUPPLEMENT APPROVAL

AstraZeneca AB
C/O AstraZeneca Pharmaceuticals LP
Attention: Craig Zecher
Regulatory Affairs Director
One MedImmune Way
Gaithersburg, MD 20878

Dear Mr. Zecher:

Please refer to your supplemental new drug application (sNDAs) dated and received September 27, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bydureon BCise (exenatide extended release) injectable suspension.

These Prior Approval sNDAs provide for the following:

- S-002 provides for updates to the Prescribing Information (PI) based on DURATION 2 study, BCB106, A Randomized, Double-Blind, Parallel-Group, Multicenter Study to Compare the Glycemic Effects, Safety, and Tolerability of Exenatide Once Weekly to Those of Sitagliptin and Pioglitazone in Subjects with Type 2 Diabetes Mellitus Treated with Metformin.
- S-003 provides for updates to the PI based on DURATION 3 study, H8O-MC-GWBR (GWBR), Efficacy of Once-Weekly Exenatide Long-Acting Release and Once-Daily Insulin Glargine in Patients with Type 2 Diabetes Treated with Metformin Alone or in Combination with Sulfonylurea.
- S-004 provides for updates to the PI based on DURATION 4 study, H8O-MC-GWCH (GWCH), Safety and Efficacy of Exenatide Once Weekly Injection versus Metformin, Dipeptidyl Peptidase-4 Inhibitor, or Thiazolidinedione as Monotherapy in Drug-Naïve Patients with Type 2 Diabetes.
- S-005 provides for updates to the PI based on DURATION 6 study, H8O-MC-GWDE (GWDE), Safety and Efficacy of Exenatide Once Weekly versus

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Liraglutide in Subjects with Type 2 Diabetes and Inadequate Glycemic Control Treated with Lifestyle Modification and Oral Antidiabetic Medications in the Bydureon Prescribing Information.

- S-006 provides for updates to the PI based on DURATION 7 study, (D5553C00002): A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel group, Phase 3 Trial to Evaluate the Safety and Efficacy of Once Weekly Exenatide Therapy Added to Titrated Basal Insulin Glargine Compared to Placebo Added to Titrated Basal Insulin Glargine in Patients with Type 2 Diabetes Who Have Inadequate Glycemic Control on Basal Insulin Glargine with or without Metformin.
- S-007 provides for updates to the PI based on DURATION 8 study, (D5553C00003): A 28-week, multi-centre, randomised, double-blind, active-controlled, phase 3 study with a 24-week extension phase followed by a 52-week extension phase to evaluate the efficacy and safety of concomitant initiation of exenatide once weekly 2 mg and dapagliflozin once daily 10 mg compared to exenatide once weekly 2 mg alone and dapagliflozin once daily 10 mg alone in patients with type 2 diabetes mellitus (T2DM) who have inadequate glycemic control on metformin.
- S-008 provides for reformatting of a table in Section 6 of the PI.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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If you have any questions, call Arati B. Kamath, Ph.D., Regulatory Project Manager, at (301) 796-3159.

Sincerely,

{See appended electronic signature page}

Lisa B. Yanoff, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide
 - Instructions for Use

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LISA B YANOFF
07/25/2019 02:28:17 PM