

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209210Orig1s000

Trade Name: BYDUREON BCISE injectable suspension

Generic or Proper Name: exenatide extended-release

Sponsor: ASTRAZENECA AB

Approval Date: October 20, 2017

Indication: For the use of BYDUREON BCISE (exenatide extended-release) injectable suspension as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

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APPROVAL LETTER



NDA 209210

NDA APPROVAL

ASTRAZENECA AB
Attention: Craig Zecher
Director, Regulatory Affairs
One Medimmune Way
Gaithersburg, MD 20878

Dear Mr. Zecher:

Please refer to your New Drug Application (NDA) dated and received December 21, 2016, 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.

This new drug application provides for the use of BYDUREON BCISE (exenatide extended-release) injectable suspension as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

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 text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide). 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*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels that were submitted on October 13, and 19, 2017, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 209210.**” Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 through 9 years (inclusive) because necessary studies are impossible or highly impracticable. This is because there are too few children in this age range with type 2 diabetes mellitus to study.

We are deferring submission of your pediatric study for ages 10 to 17 years (inclusive) for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required under section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. This required study is listed below.

Your requirements under the PREA as stated in the approval letter for NDA 022200 for BYDUREON (exenatide extended-release) injectable suspension, dated January 27, 2012, also apply to NDA 209210. We refer to our April 5, 2017, letter granting deferral extension of PMR 1860-1. Accordingly, your requirement under the PREA is as follows:

- 1860-1 A randomized and controlled pediatric study under PREA to evaluate the safety, efficacy, and pharmacokinetics of BYDUREON (exenatide extended-release) injectable suspension for the treatment of type 2 diabetes mellitus in pediatric patients ages 10-17 years (inclusive).

Final Protocol Submission:	April 2012 (completed)
Study Completion:	January 2017
Final Report Submission:	July 2020

We also refer to our letter issued May 9, 2017, which acknowledged your proposed revised Study Completion milestone (February 2020) for PMR 1860-1.

Submit the protocols to your IND 067092, with a cross-reference letter to NDA 022200 and to this NDA.

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

Please cross-reference this NDA when you submit your final report for PMR 1860-1 to NDA 022200.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

- 3274-1 Test samples from clinical studies BCB118 and BCB120 for the presence of anti-GLP-1 and anti-glucagon antibodies using a similar assay used to test samples as described in report REST080154R1. Sample selection criteria will be submitted to and reviewed by the Agency prior to initiation of sample analysis.

The timetable you submitted on October 13, 2017, states that you will conduct this study according to the following schedule:

Study Completion: December 2018
Final Report Submission: May 2019

- 3274-2 Validate the sensitivity of the version of ELISA-0308 method used for the detection of anti-exenatide antibodies (ADA) in patient samples collected in clinical studies BCB118 and BCB120.

The timetable you submitted on October 13, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: January 2019

Submit clinical protocols to your IND 107815 for this product, with a cross-reference letter to this NDA. Alternatively, you may submit clinical protocols to your IND 067092, with a cross-reference letter to NDA 022200 and to this NDA, if applicable. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a

status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert, Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
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 (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

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

If you have any questions, call Richard Whitehead, M.S., Regulatory Project Manager, at (301) 796-4945.

Sincerely,

{See appended electronic signature page}

Jean-Marc Guettier, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling
Carton and Container Labeling

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

/s/

JEAN-MARC P GUETTIER
10/20/2017