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Approval Package for:

APPLICATION NUMBER:

208745Orig1s000

Trade Name: Trulance tablets, 3 mg.

Generic or Proper Name: plecanatide

Sponsor: Synergy Pharmaceuticals Inc.

Approval Date: January 19, 2017

Indication: Provides for the use of Trulance tablets for the treatment of chronic idiopathic constipation (CIC) in adults.

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APPROVAL LETTER



NDA 208745

NDA APPROVAL

Synergy Pharmaceuticals Inc.
Attention: Evelyn Jaeger
Head of Regulatory Operations
420 Lexington Avenue, Suite 2012
New York, NY 10170

Dear Ms. Jaeger:

Please refer to your New Drug Application (NDA) dated January 29, 2016, received January 29, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Trulance (plecanatide) tablets, 3 mg.

This new drug application provides for the use of Trulance (plecanatide) tablets for the treatment of chronic idiopathic constipation (CIC) in adults.

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 agreed-upon labeling text and with the minor editorial revisions to Section 8.1 indicated in the enclosed labeling.

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, except with the revisions indicated, the enclosed labeling (text for the package insert and 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 and carton and immediate container labels submitted on January 3, 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 *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 208745.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for Trulance was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the drug in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

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

We are waiving the pediatric studies requirement for ages birth to less than 2 years because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group. In non-clinical studies of plecanatide, a guanylate cyclase-C (GC-C) agonist, deaths due to dehydration occurred within 24 hours in young juvenile mice. This data and the literature regarding GC-C receptor ontogeny indicate that plecanatide would not be safe to administer to pediatric patients under 2 years of age.

We are deferring submission of your pediatric studies for ages 6 years to less than 18 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed. We are deferring submission of your pediatric studies for ages 2 years to less than 6 years of age because this product is ready for approval for use in adults, and pediatric studies should be delayed in this age group until additional safety data from a study evaluating GC-C receptor ontogeny and the results of the clinical studies of plecanatide in older pediatric cohorts have been evaluated. In order to avoid severe diarrhea and its serious sequelae, nonclinical data and literature findings suggest special caution should be exercised in defining the initial plecanatide dose range for young pediatric patients.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually

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