CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208083Orig1s000

SUMMARY REVIEW

Division Director Summary Review for Regulatory Action

Date	(electronic stamp)
From	Sumathi Nambiar MD MPH
Subject	Division Director Summary Review
NDA #	208083
Applicant	Celerity Pharmaceuticals, LLC
Date of Submission	June 30, 2016
PDUFA Goal Date	April 28, 2017
Proprietary Name / Non-Proprietary Name	Clindamycin in 0.9% Sodium Chloride Injection (clindamycin phosphate)
Dosage Form(s) / Strength(s)	Intravenous Solution, 300 mg/50 mL, 600 mg/50 mL, 900 mg/50 mL
Proposed Indication(s)	• Serious infections caused by susceptible anaerobic bacteria • Infections Due to Susceptible Strains of Streptococci, Pneumococci and Staphylococci • Lower Respiratory Tract Infections • Skin and Skin Structure Infections • Gynecological Infections • Intra-abdominal Infections • Septicemia • Bone and Joint Infections
Action	Approval

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Medical Officer Review	Maria Allende, MD
Statistical Review	Karen Higgins, ScD
Pharmacology Toxicology Review	Tessie Alapatt, PhD
OPQ Application Technical Lead Review	Dorota Matecka, PhD
Microbiology Review	Jalal Sheikh, PhD
Clinical Pharmacology Review	Kunyi Wu, Pharm D
OPDP	Puja Shah, PharmD
CDTL Review	Dorota Matecka, PhD
OSE/DMEPA	Deborah Myers, RPh, MBA
Division of Pediatric and Maternal Health	Christos Mastroyannis, MD

OND=Office of New Drugs
OPQ=Office of Pharmaceutical Quality
OPDP=Office of Prescription Drug Promotion
CDTL=Cross-Discipline Team Leader
OSE= Office of Surveillance and Epidemiology
DMEPA=Division of Medication Error Prevention and Analysis

1. Background

NDA 208083 was submitted by Celerity Pharmaceuticals, LLC under Section 505(b)(2) of the Food Drug and Cosmetic Act. The Applicant refers to NDA 50639, CLEOCIN PHOSPHATE IV Solution (clindamycin injection in 5% dextrose) as the listed drug. Clindamycin is a lincosamide antibacterial drug that is approved for the treatment of several serious infections. There are a number of clindamycin drug products approved in the U.S., including injectable and oral formulations. The drug product proposed in this NDA differs from the listed drug in that 0.9% sodium chloride is used as the tonicity adjuster instead of 5% dextrose.

2. Product Quality

The chemistry manufacturing and controls information for clindamycin phosphate drug substance was provided via reference to Type II DMF (b) (4) . DMF (b) (4) was found to be adequate as noted in a review dated May 24, 2016.

The drug product, clindamycin in 0.9% sodium chloride injection, is provided as a premixed, sterile, solution in GALAXY plastic containers and supplied in three strengths, 300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL. Excipients in the proposed formulation include sodium chloride and EDTA. The Applicant has submitted a request for a waiver of the requirement to submit in vivo bioavailability/bioequivalence data for the proposed drug product. The biowaiver request was found acceptable by the Biopharmaceutics Reviewer. The initially proposed acceptance criteria for two specified impurities (b) (4) , any unspecified impurity and total impurities were lowered and an acceptance criterion for total unspecified impurities was added. The drug product specification as revised was found acceptable.

The proposed process controls have been found adequate to mitigate potential risks to product quality. Information provided for the drug product from the product quality microbiology perspective (i.e., the sterilization validation, drug product specification and the container closure integrity) was found acceptable by the Product Quality Microbiology Reviewer.

The container closure system include Baxter's 50 mL single-port PL 2501 Plastic (GALAXY) Container Closure System, which has been used for other FDA approved injectable products and was also found suitable for the currently proposed drug product. Based on the overall stability information provided and the revised acceptance criteria for impurities, the 18-month expiration dating was granted for the drug product to be stored at room temperature.

The manufacturing facilities include [redacted] (b) (4) (drug substance manufacturer) and Baxter Healthcare Corporation (drug product manufacturer). All facilities were found acceptable in support of this NDA.

The Product Quality review team recommends approval of the NDA.

3. Nonclinical Pharmacology/Toxicology

Tessie Alapatt, PhD is the Pharmacology/Toxicology Reviewer for this NDA. No nonclinical toxicology studies were conducted to support this NDA. Dr. Alapatt notes that the acceptance criteria for impurities, including two specified impurities, [redacted] (b) (4) were qualified to support a shelf-life of 18 months. In addition, the quantity of the leachable compound [redacted] (b) (4) from the GALAXY bag for the proposed drug product was found to be acceptable. Dr. Alapatt recommends approval of this NDA and has provided labeling recommendations that have been incorporated in final labeling.

4. Clinical Pharmacology

The Clinical Pharmacology Reviewer for this NDA is Kunyi Wu, PharmD. Dr. Wu notes that no new clinical pharmacology information was submitted in the NDA. Dr. Wu's revisions to the package insert have been incorporated. Dr. Wu recommends approval of the NDA from a clinical pharmacology perspective.

5. Clinical Microbiology

The Clinical Microbiology Reviewer for this NDA is Jalal Sheikh, Ph.D. No new clinical microbiology information was submitted in this NDA. Dr. Sheikh's revisions to the package insert have been incorporated.

6. Clinical/Efficacy-Safety

Maria Allende, MD, is the Clinical Reviewer, and Karen Higgins, ScD is the Statistical Reviewer for this NDA.

Dr. Allende stated that no new information was submitted in the NDA that would alter the favorable risk/benefit assessment of clindamycin for the current labeled indications. The only major labeling change relative to the RLD is that it is consistent with the Pregnancy and Lactation Labeling Rule (PLLR) and is in the Physicians Labeling Rule (PLR) format. Dr. Allende recommends approval of the NDA pending agreement on labeling. Dr. Higgins noted that no statistical review is needed for this NDA as no new data were submitted.

Dr. Allende's review of the literature did not identify any new safety signals. Dr. Allende concluded that the reported adverse events in the published literature are consistent with the adverse reactions listed in the labeling for the listed drug.

7. Advisory Committee Meeting

This NDA was not discussed at an Advisory Committee Meeting.

8. Pediatrics

Under the Pediatric Research and Equity Act (PREA), 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 the requirement is waived, deferred or inapplicable. As none of these criteria are applicable, this NDA is exempt from PREA requirements.

9. Labeling

Labeling recommendations from the various disciplines and from OPDP and DMEPA have been incorporated in labeling. The Division of Pediatric and Maternal Health (DPMH) was consulted and revisions were recommended to comply with the current PLLR requirements. As indicated in the DMEPA review by Deborah Myers, the carton and container labels as currently proposed are acceptable. However, additional revisions will need to be made to the 600 mg/50 mL and 900 mg/50 mL carton and container labels with next printing. These changes have already been incorporated in the 300 mg/50 mL carton and container labels.

10. Regulatory Action

I agree with the recommendations made by the review team and the CDTL that NDA 208083 be approved.

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/s/

SUMATHI NAMBIAR
04/20/2017