CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209949Orig1s000

NON-CLINICAL REVIEW(S)

DIVISION OF ANTI-INFECTIVE PRODUCTS
PHARMACOLOGY/TOXICOLOGY REVIEW

DATE: 9/5/2017

Application number:	209949
Supporting document/s:	1
Sponsor's letter date:	12/20/2016
CDER stamp date:	12/20/2016
Product:	Daptomycin Powder for Injection Solution, 350 mg/vial
Indication:	Treatment of complicated skin and skin structure infections (cSSSI) and staphylococcus aureus bloodstream infections (including those with right-sided infective endocarditis)
Sponsor:	Xellia Pharmaceuticals ApS
Review Division:	Division of Anti-Infective Products
Reviewer/Supervisor:	Terry J. Miller, Ph.D.
Division Director:	Sumathi Nambiar, M.D.
Project Manager:	Maureen Dillon Parker

Recommendations:

Pharmacology/Toxicology has no objection to the approval of NDA 209949 for Daptomycin for Injection Solution, 350 mg/vial, submitted by Xellia Pharmaceuticals.

The product labeling for this product is consistent with the currently approved PLR labeling for Cubicin® (daptomycin) with the exception of sponsor's proposed changes to the drug name, dosage forms/strength (i.e. 350 mg versus 500 mg lyophilized powder) and preparation of drug product for injection (b) (4) 0.9% sodium chloride injection to yield a final concentration of 50 mg/mL reconstituted daptomycin for injection). There are no proposed labeling changes to the Pharmacology/Toxicology relevant sections of the package insert.

Information from the NDA Submission:
The Applicant, Xellia Pharmaceuticals, ApS., submitted a 505(b)(2) NDA requesting marketing approval to license Daptomycin for Injection, 350 mg. The proposed drug

product is intended to be a copy of the reference listed drug [RLD] Cubicin® (daptomycin for injection, 500 mg; NDA 21572; Merck and Co., Inc.) with identical active ingredients, excipients, concentration, dosage form, route, and indications. The impurities and degradants detected in the final drug product appear similar to the RLD. Only the total vial contents are different (350 mg vs. 500 mg in Cubicin®). The 350 mg/vial proposed product will be reconstituted to 50 mg/mL, consistent with the 500 mg/vial RLD. The Applicant referenced the approved product labeling for Cubicin® (Merck Sharp & Dohme Corp.) which contains PLR (physician labeling rule)/PLLR (pregnancy and lactation labeling rule) compliant language in Section 8. The Applicant's proposed language for the pharmacology/toxicology relevant sections of the labeling, namely Sections 8 **Use in Specific Populations** and 13 **Nonclinical Toxicology** is consistent with the latest drug product labeling for the RLD Cubicin® as of 9/5/2017.

(Reviewer Comment: The Chemistry review team has confirmed there are no product quality concerns in the latest NDA resubmission that would warrant further nonclinical testing. The Chemistry Reviewer, Dr. Milton Sloan, determined that impurity levels were comparable with other approved daptomycin for injection products, including the RLD (Cubicin®, Merck Sharpe & Dohme, Corp.), supported by stability data up to 24 months. Refer to the product quality review for NDA 209949 by Dr. Milton Sloan in the CDER Informatics Platform for additional information.)

The Applicant did not submit any new relevant pharmacology / toxicology information for review in their 505(b)(2) NDA. No pharmacology/toxicology information was reviewed to support this 505(b)(2) NDA.

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/s/

TERRY J MILLER
09/05/2017