CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208385Orig1s000

NON-CLINICAL REVIEW(S)

Memo to the Division File

NDA 208385 Resubmission/Class 2, Submitted 3/24/2017

Daptomycin for Injection, 350 mg (Sagent Pharmaceuticals, Inc.)

From: Terry J. Miller, Ph.D., Pharmacology/Toxicology Reviewer/Supervisor, DAIP

Through: Naseya Minor, M.S., Regulatory Project Manager, DAIP

Date: 8/23/2017

Recommendations:

Pharmacology/Toxicology has no objection to the approval of NDA 208385 for Daptomycin for Injection.

The Applicant referenced the approved product labeling for Cubicin® (Merck Sharp & Dohme Corp.) which contains PLLR compliant language in Section 8. The Pharmacology/Toxicology relevant sections of the Applicant's proposed language are consistent with the latest drug product labeling for the RLD Cubicin®.

Background:

The Applicant, Sagent Pharmaceuticals, Inc., submitted a Class 2 Resubmission of their 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; Merck and Co., Inc.) with identical active ingredients, excipients, concentration, dosage form, route, and indication. 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 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 8/24/2017.

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.

The Applicant had previously received a complete response from this Division on 6/23/2016, for their original NDA submitted 8/25/2016, citing mainly CMC deficiencies. There were no pharmacology/toxicology deficiencies noted in the initial review of the original NDA submission. Labeling recommendations for the pharm/tox relevant

sections were provided in the pharmacology/toxicology review by Dr. Terry Miller (in DARRTS 5/3/2016).

(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. Shrikant Pagay, 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 208385 by Dr. Shrikant Pagay in DARRTS for additional information.)

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

/s/

TERRY J MILLER
08/24/2017

Memo to the Division File

NDA 208385, Submitted 8/25/2015

Daptomycin for Injection, 350 mg (Sagent Pharmaceuticals, Inc.)

From: Terry J. Miller, Ph.D., Pharmacology/Toxicology Reviewer, DAIP

Through: Wendelyn Schmidt, Pharmacology/Toxicology Supervisor, DAIP

Date: May 2, 2016

Background:

The Applicant, Sagent Pharmaceuticals, Inc., 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; Merck and Co., Inc.) with identical active ingredients, excipients, concentration, dosage form, route, and indication. 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 current 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. The labeling for the relevant pharmacology/toxicology sections submitted in the original NDA were identical to previously approved labels. Since this NDA was submitted after the 6/30/2015 deadline and is therefore subject to PLLR labeling requirements, in the 74-day letter to the Applicant, Sagent was required to revise the package insert to ensure compliance with PLLR guidelines. The Applicant submitted the revised package insert to the NDA on 11/23/2015. The Applicant's proposed labeling changes in the pharmacology/toxicology relevant sections of the labeling (Subsections 8.1 and 8.2) can be found in italics and strikethrough below. The reviewer's recommended changes are in bold and strikethrough below.

Labeling:

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

(b) (4)

Risk Summary

(b) (4)

Data

Animal Data

(b) (4)

8.2 (b) (4) Lactation

Risk Summary

(b) (4)

The development and health benefits of breastfeeding should be considered along with the mother's clinical need for daptomycin and any potential adverse effects on the breastfed child from daptomycin or from the underlying maternal condition.

(b) (4)

Recommendation:

There are no pharmacology/toxicology issues with the approval of this NDA.

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

/s/

TERRY J MILLER
05/02/2016

WENDELYN J SCHMIDT
05/03/2016