Office of Clinical Pharmacology Addendum Review

NDA or BLA Number	21- 572 (SDN#700)
Submission Date	03/02/2017
Submission Type	Pediatric NDA
Brand Name	Cubicin®
Generic Name	Daptomycin
Dosage Form and Strength	500 mg lyophilized powder for reconstitution in a single-dose vial
Route of Administration	IV Infusion
Proposed Indication	*Staphylococcus aureus* bloodstream (SAB) infections (bacteremia) in pediatric patients.
Applicant	Merck
OCP Review Team	Sonia Pahwa, PhD: Primary Reviewer Seong H. Jang, PhD: Team Leader Jeffry Florian, PhD: Team Leader Fang Li, PhD: Pharmacometric Reviewer

1. Executive Summary

This review serves as an addendum to the Clinical Pharmacology review for NDA 21572 SDN # 700 (Cubicin®, daptomycin) entered into DARRTS on August 7, 2017. The purpose of this review addendum is to remove our previous recommendation limiting the dosing regimen of daptomycin 12 mg/kg once daily to pediatric patients aged from 2 to 6 years.

In the original Clinical Pharmacology review of NDA 21572 SDN # 700, we recommended limiting the dosing regimen of Cubicin (daptomycin) 12 mg/kg once daily to pediatric patients aged from 2 to 6 years because the Applicant's proposed dose of 12 mg/kg once daily in pediatric patients aged from 1 to 6 years has been evaluated only in patients ≥2 years of age for pharmacokinetics (PK), safety and efficacy of daptomycin. As such, there is no clinical experience to use 12 mg/kg once daily (up to 42 days) in pediatric patients aged from 1 to 2 years.

Since the initial Clinical Pharmacology review was completed, we had additional discussions with the Clinical review team regarding whether the clinical data in pediatric patients aged from 2 to 6 years receiving 12 mg/kg once daily, together with the PK, safety and efficacy of daptomycin in pediatric patients aged from 1 to 2 years at 10 mg/kg once daily (i.e., the approved dosing regimen for the treatment of complicated skin and skin structure infection), may adequately support the use of daptomycin 12 mg/kg once daily in pediatric patients aged from 1 to 2 years. In addition, the Applicant provided further rationales to support the dosing regimen in this population, including no age- or dose-dependent adverse events from the completed pediatric studies. Finally, simulation conducted by the Clinical Pharmacology review team and corroborated by the Applicant using a previously developed population pharmacokinetic model demonstrated that the AUC_{ss} of daptomycin in pediatric patients ages from 1 to 2 years receiving 12 mg/kg once daily would be comparable to that in adult patients receiving 6 mg/kg once daily and would result in comparable exposures to pediatric patients aged 2 to 17 years

evaluated in the SAB study. Based on all three of these items, the Clinical Pharmacology review team agrees that the Applicant's proposed dosing regimen of daptomycin 12 mg/kg once daily for pediatric patients aged from 1 to 6 years is acceptable.

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/s/

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