CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213645Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	September 13, 2021
Requesting Office or Division:	Division of Anti-Infectives (DAI)
Application Type and Number:	NDA 213645
Product Name and Strength:	Dapzura RT (daptomycin) for Injection, 500 mg/vial
Applicant/Sponsor Name:	Baxter Healthcare Corporation (Baxter)
OSE RCM #:	2021-1515
DMEPA 1 Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 PURPOSE OF MEMORANDUM

On July 30, 2021, Baxter submitted their Class 2 Resubmission[a] to provide their responses to the deficiencies included in the Agency's Complete Response Letter (CRL), dated April 29, 2021.[b] Thus, the Division of Anti-Infectives (DAI) requested that we review the proposed prescribing information (PI), container label, and carton labeling for Dapzura RT (Appendix A) to determine if they are acceptable from a medication error perspective.

2 BACKGROUND/REGULATORY HISTORY

On August 18, 2021, the Agency provided Baxter confirmation that we consider their July 30, 2021, resubmission a complete class 2 response to the Agency's CRL dated April 29, 2021.[c]

[a] Baxter Healthcare Corporation. Resubmission – Response to Complete Response Letter for Dapzura RT (daptomycin) for Injection (NDA 213645). Deerfield (IL): Baxter; 2021 JUL 30. Available from: \\CDSESUB1\evsprod\nda213645\0022\m1\us\cover-letter-2021jul30.pdf.

[b] DeBellas, C. Communication: Complete Response Letter for Dapzura RT (daptomycin) for Injection. Silver Spring (MD): FDA, CDER, OND, OAP, DAI (US); 2021 APR 29. NDA 213645. Available from: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af805ebced&_afrRedirect=212311791847 2336.

[c] Rosenberger, J. FDA Communication: Acknowledge – Class 2 Resubmission for Dapzura RT. Silver Spring (MD): FDA, CDER, OND, OAP, DAI (US); 2021 AUG 18. NDA 213645. Available from: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af8060cc0d&_afrRedirect=239259720146 5087.

3 DISCUSSION

Prior to the issuance of the April 29, 2021 CRL, we reviewed the proposed Dapzura RT PI, container label, and carton labeling and we found the proposed container label and carton labeling acceptable.[d] Baxter's resubmission includes both draft and annotated PI, as well as container label and carton labeling identical to that included in their submission dated February 22, 2021[e,f] that we previously reviewed and found acceptable from a medication error perspective.[d]

Additionally, we note that we provided no recommendations for the PI in our review.[g]

4 CONCLUSION

Our evaluation of the proposed Dapzura RT PI, container label and carton labeling included in the resubmission dated July 30, 2021, did not identify additional areas of vulnerability that may lead to medication errors. Therefore, we have no additional recommendations at this time.

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[d] Myers D. Label and Labeling Review Memo for Dapzura RT (NDA 213645). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 FEB 25. RCM No.: 2020-1382-1.

[e] Draft Carton and Container Labels Received on FEB 22, 2021 (Dapzura NDA 213645) Deerfield (IL): Baxter Healthcare Corporation; 2021 FEB 22. Available from: \\CDSESUB1\evsprod\nda213645\0014\m1\us\container-carton-original-draft-v3-c.pdf.

[f] Annotated Container and Carton Labeling Received on FEB 22, 2021 (Dapzura NDA 213645) Deerfield (IL): Baxter Healthcare Corporation; 2021 FEB 22. Available from: \\CDSESUB1\evsprod\nda213645\0014\m1\us\annotated-comparison-container-carton.pdf.

[g] Myers D. Label and Labeling Review for Dapzura RT (NDA 213645). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 FEB 10. RCM No.: 2020-1382.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON JULY 30, 2021

Prescribing Information (PI) (image not shown):

- Cleaned proposed (Draft) PI available at the following link: \\CDSESUB1\evsprod\nda213645\0022\m1\us\pi-draft-labeling-text-original-draft-v4-c.docx.
- Annotated PI available at the following link: \\CDSESUB1\evsprod\nda213645\0022\m1\us\annotated-draft-pi.docx.

Container label

Carton labeling

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/s/

DEBORAH E MYERS
09/13/2021 09:32:56 AM

VALERIE S VAUGHAN
09/13/2021 09:38:41 AM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Pharmacovigilance Memorandum

Date:	April 9, 2021
Reviewer:	Ronald Wassel, PharmD, Safety Evaluator Division of Pharmacovigilance II
Team Leader:	Rachna Kapoor, PharmD, MBA Division of Pharmacovigilance II
Product Name:	Daptomycin for Injection
Subject:	Reports of hypoglycemia, hypophosphatemia, lactic acidosis, hyperuricemia, proximal and distal renal tubulopathy, and hepatic failure (prolongation of coagulation time, increased hepatic enzymes, and increased bilirubin) associated with Cubicin® RF, and in particular, occurring in patients with Hereditary Fructose Intolerance
Application Type/Number:	NDA 213645
Applicant:	Baxter Healthcare
OSE RCM #:	2021-623

1 INTRODUCTION

The Division of Anti-infectives (DAI) requested a search of the FDA Adverse Event Reporting System (FAERS) for reports of hypoglycemia, hypophosphatemia, lactic acidosis, hyperuricemia, proximal and distal renal tubulopathy, and hepatic failure (prolongation of coagulation time, increased hepatic enzymes, and increased bilirubin) associated with Cubicin® RF, and in particular, these events occurring in patients with Hereditary Fructose Intolerance (HFI).

DAI is reviewing a 505(b)(2) application submitted by Baxter Healthcare for Daptomycin for Injection, which makes reference to the listed drug CUBICIN® RF (daptomycin for injection), lyophilized powder containing 500 mg of daptomycin per single-dose 10 mL vial container, NDA 021572 held by CUBIST PHARMS LLC (currently owned by Merck Sharp & Dohme Corp.). Baxter's proposed Daptomycin for Injection, lyophilized powder containing 500 mg daptomycin per single-dose 10 mL vial container is qualitatively and quantitatively similar to the approved CUBICIN® RF drug product, with differences in excipients. Baxter's Daptomycin for Injection contains the excipients 238 mg sorbitol, 238 mg of mannitol, and hydrochloric acid and/or sodium hydroxide as a pH adjuster, whereas CUBICIN® RF contains 713 mg sucrose and sodium hydroxide as a pH adjuster.

Fructose, sorbitol, and sucrose are used as excipients in a variety of formulations including oral, topical, and parenteral drugs. However, patients with the rare genetic disorder of HFI may develop a life-threatening hypoglycemia, hypophosphatemia, lactic acidosis, and hepatic failure when exposed to fructose, sorbitol, and sucrose. Patients with HFI develop a natural defense mechanism against fructose, sorbitol, and sucrose by vomiting any food containing these substances. Since this defense mechanism is bypassed with parenteral delivery, a much higher risk is associated with drug formulations with parenteral (especially intravenous) use.

2 METHODS AND MATERIALS

Division of Pharmacovigilance (DPV) searched the FAERS database with the strategy described in Table 1.

Table 1. FAERS Search Strategy*	
Date of Search	March 30, 2021
Time Period of Search	All reports through March 29, 2021 (For the Quick Query search of the MedWatch narrative for Cubicin RF, we used a "From Date" of July 6, 2016, which was the date of approval for Cubicin RF)
Search Types	FAERS Business Intelligence Solution (FBIS) Quick Query (QQ) FBIS Product-Manufacturer Reporting Summary (PMRS)
Search Prompts	Search #1: QQ with Product Verbatims CUBICIN RF; CUBICIN RF 500MG VIAL; CUBICING RF Search #2: PMRS with Product Verbatims CUBICIN 500MG PF PWD VL MERCK SHARP & DOHME; CUBICIN RF; CUBICIN RF 500MG VIAL Search #3: QQ narrative search with "cubicin rf" Search #4: QQ with Product Active Ingredient Daptomycin and narrative "HFI" Search #5: QQ with Product Active Ingredient Daptomycin and narrative "fructose intolerance"
* See Appendix A for a description of the FAERS database.	

3 RESULTS

The FAERS searches retrieved **96** reports. Of note, there were no reports with the narrative searches that included HFI or fructose intolerance. After merging the results and removing duplicate case ID numbers there were **47** total reports.

There were no reports of hypoglycemia, hypophosphatemia, lactic acidosis, or hyperuricemia. There were no reports with the specific terms proximal and distal renal tubulopathy, and hepatic failure; however, there were several preferred terms related to the renal and hepatic systems and included Acute kidney injury, Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased, Blood creatinine abnormal, Blood thromboplastin abnormal, Hepatic enzyme increased, Hepatic function abnormal, Hepatitis, Liver function test increased, and Renal impairment. We reviewed those cases that included any of those terms, which was a total of 5 unique cases. None of these cases described a patient with HFI and none provided enough information to make adequate assessments.

4 REVIEWER'S COMMENTS

A review of FAERS data found no case reports of interest related to patients with HFI receiving Cubicin RF.

5 APPENDICES

5.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

FDA Adverse Event Reporting System (FAERS)

FAERS is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

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/s/

RONALD T WASSEL
04/11/2021 09:56:06 AM

RACHNA KAPOOR
04/11/2021 09:10:07 PM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: March 17, 2021

To: Jae Hong, M.D.
Division of Anti-Infective Products (DAIP)

Carmen DeBellas, Regulatory Project Manager, DAIP

Abimbola Adebowale, Associate Director for Labeling, DAIP

From: David Foss, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jim Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for DAPZURA RT (daptomycin for injection), for intravenous use

NDA: 213645

In response to DAIP's consult request dated November 12, 2020, OPDP has reviewed the proposed product labeling (PI) and carton and container labeling for the original NDA for DAPZURA RT.

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling received by electronic mail from DAIP on March 11, 2021, and are provided below.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by electronic mail from DAIP on March 12, 2021, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact David Foss at (240) 402-7112 or david.foss@fda.hhs.gov.

45 Pages of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

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/s/

DAVID F FOSS
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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	February 25, 2021
Requesting Office or Division:	Division of Anti-Infectives (DAI)
Application Type and Number:	NDA 213645
Product Name and Strength:	Dapzura RT (daptomycin) for Injection, 500 mg/vial
Applicant/Sponsor Name:	Baxter Healthcare Corporation (Baxter)
OSE RCM #:	2020-1382-1
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Division Director (Acting):	Lubna Merchant, MD, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted their revised container label and carton labeling received on February 22, 2021 for Dapzura RT. The Division of Anti-Infectives (DAI) requested that we review the revised container label and carton labeling for Dapzura RT (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review, as well as a comment from our Office of Pharmaceutical Quality (OPQ) colleagues.[a,b]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Myers D. Label and Labeling Review for Dapzura RT (NDA 213645). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 FEB 10. RCM No.: 2020-1382.
[b] DeBellas C. FDA Communication: NDA 213645 Information Request Carton and Container Recommendations: FDA, CDER, OND, DAI (US); 2021 FEB 11. Available from: https://darrts.fda.gov/darrts/ViewDocument?documentId=090140af805d183f.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON FEBRUARY 22, 2021

- Baxter's responses to our February 11, 2021 recommendations available at the following link: \\CDSESUB1\evsprod\nda213645\0014\m1\us\labeling-history-ir-comments-dated-2021feb11-responses.pdf.
- Annotated Container and Carton Labeling available at the following link: \\CDSESUB1\evsprod\nda213645\0014\m1\us\annotated-comparison-container-carton.pdf.

Container label

Carton labeling

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/s/

DEBORAH E MYERS
02/25/2021 08:59:46 PM

LUBNA A MERCHANT
02/26/2021 08:26:22 AM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	February 10, 2021
Requesting Office or Division:	Division of Anti-Infectives (DAI)
Application Type and Number:	NDA 213645
Product Name and Strength:	Dapzura RT (daptomycin) for Injection, 500 mg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Baxter Healthcare Corporation (Baxter)
FDA Received Date:	June 30, 2020, September 11, 2020, September 18, 2020, and December 16, 2020
OSE RCM #:	2020-1382
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Deputy Director:	Irene Z. Chan, PharmD, BCPS

1 REASON FOR REVIEW

As part of the approval process for Dapzura RT (daptomycin) for Injection, the Division of Anti-Infectives (DAI) requested that we review the proposed Dapzura RT prescribing information (PI), container label, and carton labeling for areas of vulnerability that may lead to medication errors.

2 REGULATORY HISTORY

On December 9, 2020, we found the proposed proprietary name, Dapzura RT, conditionally acceptable.[a]

3 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Label and Labeling	F

N/A=not applicable for this review

*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

4 FINDINGS AND RECOMMENDATIONS

Table 2 below include the identified medication error issues with the submitted prescribing information (PI), container label, and carton labeling, our rationale for concern, and the proposed recommendation to minimize the risk for medication error.

[a] Myers, D. Proprietary Name Review for Dapzura RT*** (NDA 213645). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 DEC 09. Panorama No. 2020-42743080.

Table 2. Identified Issues and Recommendations for Baxter Healthcare Corporation (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label and Carton Labeling			
1.	As currently presented, the "Usual Dose" statement is not included.	Per 21 CFR 201.55, "…labels for prescription drugs bear a statement of the recommended or usual dosage."	Add the "Usual Dose" statement on the container label (if space permits) and carton labeling of the package. For example; "Recommended Dosage: See Prescribing Information."
Container Label			
1.	As currently presented, the format for the expiration date is not defined.	Clearly defining the expiration date will minimize confusion and risk for deteriorated drug medication errors.	Identify the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to

Table 2. Identified Issues and Recommendations for Baxter Healthcare Corporation (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			separate the portions of the expiration date.
2.	As currently presented, you note the location for "Barcode (FPO)," however the product linear barcode is not included on your proposed container label.	It is not clear what type of "Barcode" (i.e., linear barcode that contains the national drug code (NDC) and/or 2D data matrix barcode) is intended for your currently notated "Barcode (FPO)" location (on the side panel). The drug linear barcode is often used as an additional verification before drug administration in the inpatient setting; therefore, it is an important safety feature that should be part of the label whenever possible. Reference 21CFR 201.25(c)(2)	Provide clarification regarding what type of "Barcode" (i.e., linear barcode that contains the national drug code (NDC) and/or 2D data matrix barcode) is intended for your currently notated "Barcode (FPO)" location (on the side panel) and submit the product linear barcode for our review. Additionally, we recommend that the container label linear barcode be oriented in a vertical position, as a barcode placed in a horizontal position may be difficult to scan due to the curvature of the vial.
Carton Labeling			
1.	As currently presented, you note the location for "1D Barcode," however the product linear barcode is not included on your proposed carton labeling.	It is not clear what type of "Barcode" (i.e., linear barcode that contains the national drug code (NDC) and/or 2D data matrix barcode) is intended for your currently notated location for "1D Barcode" (on the bottom of the principal display panel). The drug linear barcode is often used as an additional verification before drug	Provide clarification regarding what type of "Barcode" (i.e., linear barcode that contains the national drug code (NDC) and/or 2D data matrix barcode) is intended for your currently notated location (on the bottom of the principal display panel) and submit the product linear barcode for our review.

Table 2. Identified Issues and Recommendations for Baxter Healthcare Corporation (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		administration in the inpatient setting; therefore, it is an important safety feature that should be part of the carton labeling whenever possible.	
2.	As currently presented, you note two locations as "FPO 2D Barcode location." However, the intended location of the human-readable and machine-readable (2D data matrix barcode) product identifier on the smallest saleable unit (usually the carton) is not provided.	It is not clear what type of "Barcode" (i.e., linear barcode that contains the national drug code (NDC) and/or 2D data matrix barcode) is intended for your currently notated locations for "FPO 2D Barcode location." The drug package label must include the product identifier information (i.e., the NDC, serial number, lot number, and expiration date) in both the human-readable form and machine-readable, 2D data matrix barcode format.	We recommend you include the intended location of the machine-readable, 2D data matrix barcode product identifier, near the human-readable portion of the product identifier information. For more information, see draft guidance, Product Identifiers Under the Drug Supply Chain Security Act - Questions and Answers (September 2018).[b]

5 CONCLUSION

Our evaluation of the proposed Dapzura RT prescribing information (PI), container label, and carton labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Table 2 for the Applicant. We ask that the Division convey

[b] When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Table 2 in its entirety to Baxter Healthcare Corporation so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 3 presents relevant product information for Dapzura RT that Baxter Healthcare Corporation submitted on December 16, 2020, and the listed drug (LD).

<table>
<tr><th colspan="3">Table 3. Relevant Product Information for Dapzura RT and Listed Drug</th></tr>
<tr><td>Product Name</td><td>Dapzura RT</td><td>Cubicin RF (NDA 021572)</td></tr>
<tr><td>Initial Approval Date</td><td>N/A</td><td>09/12/2003</td></tr>
<tr><td>Active Ingredient</td><td colspan="2">daptomycin</td></tr>
<tr><td>Indication</td><td colspan="2">Treatment of:
Complicated skin and skin structure infections (cSSSI) in adult and pediatric patients (1 to 17 years of age)
Staphylococcus aureus bloodstream infections (bacteremia), in adult patients including those with right-sided infective endocarditis
Staphylococcus aureus bloodstream infections (bacteremia) in pediatric patients (1 to 17 years of age).</td></tr>
<tr><td>Route of Administration</td><td colspan="2">Adults: Intravenous injection over 2 minute period or by intravenous infusion over a 30-minute period
Pediatric patients 7 to 17 years of age: intravenous infusion over a 30-minute period
Pediatric patients 1 to 6 years of age: intravenous infusion over a 60-minute period</td></tr>
<tr><td>Dosage Form</td><td colspan="2">for Injection</td></tr>
<tr><td>Strength</td><td colspan="2">500 mg/vial</td></tr>
<tr><td>Dose and Frequency</td><td colspan="2">Recommended dosage regimen for adult patients:<table><tr><th rowspan="2">Creatinine Clearance (CL_{CR})</th><th colspan="2">Dosage Regimen</th></tr><tr><th>cSSSI
For 7 to 14 days</th><th>S. aureus
Bacteremia
For 2 to 6 weeks</th></tr><tr><td>≥30 mL/min</td><td>4 mg/kg once every 24 hours</td><td>6 mg/kg once every 24 hours</td></tr><tr><td><30 mL/min, including hemodialysis and CAPD</td><td>4 mg/kg once every 48 hours*</td><td>6 mg/kg once every 48 hours*</td></tr><tr><td colspan="3">*Administered following hemodialysis on hemodialysis days.</td></tr></table>Recommended dosage regimen for pediatric patients (1 to 17 years of age) with cSSSI, based on age:</td></tr>
</table>

<table>
<tr><td></td><td>
<table>
<tr><th>Age group</th><th>Dosage*</th><th>Duration of therapy</th></tr>
<tr><td>12 to 17 years</td><td>5 mg/kg once every 24 hours infused over 30 minutes</td><td rowspan="4">Up to 14 days</td></tr>
<tr><td>7 to 11 years</td><td>7 mg/kg once every 24 hours infused over 30 minutes</td></tr>
<tr><td>2 to 6 years</td><td>9 mg/kg once every 24 hours infused over 60 minutes</td></tr>
<tr><td>1 to less than 2 years</td><td>10 mg/kg once every 24 hours infused over 60 minutes</td></tr>
<tr><td colspan="3">* Recommended dosage is for pediatric patients (1 to 17 years of age) with normal renal function. Dosage adjustment for pediatric patients with renal impairment has not been established.</td></tr>
</table>
Recommended dosage regimen for pediatric patients (1 to 17 years of age) with S. aureus bacteremia, based on age:
<table>
<tr><th>Age group</th><th>Dosage*</th><th>Duration of therapy</th></tr>
<tr><td>12 to 17 years</td><td>7 mg/kg once every 24 hours infused over 30 minutes</td><td rowspan="3">Up to 42 days</td></tr>
<tr><td>7 to 11 years</td><td>9 mg/kg once every 24 hours infused over 30 minutes</td></tr>
<tr><td>1 to 6 years</td><td>12 mg/kg once every 24 hours infused over 60 minutes</td></tr>
<tr><td colspan="3">*Recommended dosage is for pediatric patients (1 to 17 years of age) with normal renal function. Dosage adjustment for pediatric patients with renal impairment has not been established.</td></tr>
</table>
</td></tr>
<tr><td>How Supplied</td><td>single-dose 10 mL vial: Package of 1</td></tr>
<tr><td>Storage</td><td>Store original packages at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature] [see Dosage and Administration].</td></tr>
</table>

APPENDIX B. PREVIOUS DMEPA REVIEWS

On February 5, 2021, we searched for previous DMEPA reviews relevant to this current review using the terms, "daptomycin" and "NDA 213645." Our search identified 15 previous reviews[c,d,e,f,g,h,i,j,k,l,m,n,o,p,q], and we considered our previous recommendations to see if they are applicable for this current review.

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[c] Myers, D. Proprietary Name Review for Dapzura RT (NDA 213645). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 DEC 09. RCM No.: 2020-42743080.

[d] Myers, D. Label and Labeling Review for Daptomycin (NDA 209949/S-007). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 10. RCM No.: 2020-2137.

[e] Myers, D. Label and Labeling Review Memo for Daptomycin (NDA 209949/S-006). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 JUN 22. RCM No.: 2020-866-1.

[f] Myers, D. Label and Labeling Review for Daptomycin (NA 209949/S-006). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 MAY 28. RCM No.: 2020-866.

[g] Kolejian, S. Label and Labeling Review Memo for Daptomycin for Injection (NDA 210282). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 FEB 27. RCM No.: 2017-983-2.

[h] Kolejian, S. Label and Labeling Review Memo for Daptomycin for Injection (NDA 210282). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 FEB 06. RCM No.: 2017-983-1.

[i] Kolejian, S. Label and Labeling Review for Daptomycin for Injection (NDA 210282). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JAN 30. RCM No.: 2017-983.

[j] Kolejian, S. Label and Labeling Review for Cubicin (NDA 021572/S-057). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 AUG 24. RCM No.: 2017-1225.

[k] Kolejian, S. Label and Labeling Review Memo for Daptomycin for Injection (NDA 208385). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 JUL 26. RCM No.: 2015-2300-3.

[l] Kolejian, S. Label and Labeling Review for Daptomycin for Injection (NDA 209949). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 JUL 17. RCM No.: 2016-2913.

[m] Kolejian, S. Label and Labeling Review Memo for Cubicin RF (NDA 021572/S-052). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 MAY 19. RCM No.: 2016-435-1.

[n] Kolejian, S. Label and Labeling Review for Daptomycin for Injection (NDA 208385). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 25. RCM No.: 2015-2300.

[o] Kolejian, S. Label and Labeling Review for Cubicin RF (NDA 021572/S-052). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 APR 07. RCM No.: 2016-435.

[p] Kolejian, S. Label and Labeling Review Memo for Cubicin (NDA 021572/S-048). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 FEB 05. RCM No.: 2014-2635.

[q] Winiarski, A. Label and Labeling Review for Daptomycin for Injection (NDA 203797). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 FEB 21. RCM No.: 2012-1561.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[r] along with postmarket medication error data, we reviewed the following Dapzura RT labels and labeling submitted by Baxter Healthcare Corporation.

- Container label received on September 11, 2020
- Carton labeling received on September 11, 2020
- Prescribing Information (PI):
    - Annotated comparison with listed drug PI received on December 16, 2020 available at the following link: \\CDSESUB1\evsprod\nda213645\0009\m1\us\pi-draft-labeling-text-original-draft-v2-c-redlined.docx
    - Clean proposed (Draft) PI received on September 18, 2020 available at the following link: \\CDSESUB1\evsprod\nda213645\0003\m1\us\pi-draft-labeling-text-original-draft-v3-c.docx
    - Labeling text for the Listed Drug received on September 18, 2020 available at the following link: \\CDSESUB1\evsprod\nda213645\0003\m1\us\labeling-text-reference-pi-merck-cubicin-rf.pdf

F.2 Label and Labeling Images

Container label

[r] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

Carton labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DEBORAH E MYERS
02/10/2021 12:27:45 PM

IRENE Z CHAN
02/10/2021 05:44:04 PM