A New ICD-10-PCS Code For the Administration of Dalbavancin

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ICD-10-CM/PCS Coordination and Maintenance Committee Meeting
Centers for Medicare & Medicaid Services (CMS)
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Agenda

- Coding Issue
- Introduction to Durata Therapeutics
- ABSSSI: Unmet medical need for the treatment of acute bacterial skin and skin structure infections
- Overview of Dalbavancin
  - Dosing and Administration
  - Efficacy and Safety
- Dalbavancin therapy and its role in ABSSSI
- ABSSSI and ICD-10 Considerations

Coding Issue

Issue

- There is not a unique ICD-10-PCS code to describe the intravenous (IV) administration of dalbavancin to treat patients with acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive bacteria, such as *S. aureus*, including Methicillin-Resistant and multi-drug resistant strains, and certain streptococcal species.

New Technology Application

- Durata Therapeutics, Inc. submitted a New Technology Add-On Payment application for dalbavancin for fiscal year (FY) 2015.

Food and Drug Administration (FDA) Approval

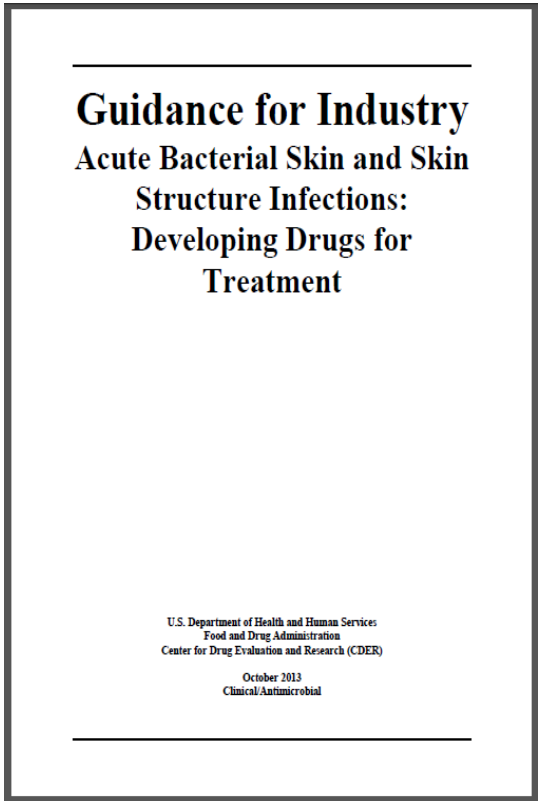
- The New Drug Application (NDA) for dalbavancin was submitted to the FDA on September 26, 2013. Based on PDUFA regulations, the target date of regulatory approval is May 26, 2014.

Durata Therapeutics: Introduction

- Durata Therapeutics, Inc., ("Durata") is a pharmaceutical company focused on the development and commercialization of therapeutic solutions to advance patient care in infectious disease
- Established in 2009, Durata became a publicly traded company (NASDQ: DRTX) in March 2012 and is headquartered in Chicago, IL
- Durata is initially developing dalbavancin, an IV antibiotic product candidate, for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and is investing in high-unmet need indications
- Dalbavancin received a Qualified Infectious Disease Product (QIDP) designation by FDA on Nov 5, 2012.
  - Dalbavancin is among the first anti-infective agents to receive QIDP designation through the new Generating Antibiotic Incentives (GAIN) statute
  - The QIDP designation provides dalbavancin priority review by the FDA and eligibility for fast-track status

ABSSSI Indication: FDA Criteria

- ABSSSI are serious, bacterial infections of the skin with a lesion size area of at least 75 cm^2
  - Infection types
    - Cellulitis/erysipelas
    - Wound infection (traumatic or surgical site)
    - Major cutaneous abscess
  - Accompanied by
    - Fever
    - Leukocytosis
    - And/or increased immature neutrophils
    - Each consistent with values defining the systemic inflammatory response syndrome [SIRS]
- Pathogens include Staphylococcus aureus and streptococci, mainly Streptococcus pyogenes
  - Over 50% of S. aureus involved in ABSSSI is methicillin-resistant (MRSA)


Guidance for Industry

Acute Bacterial Skin and Skin Structure Infections: Developing Drugs for Treatment

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

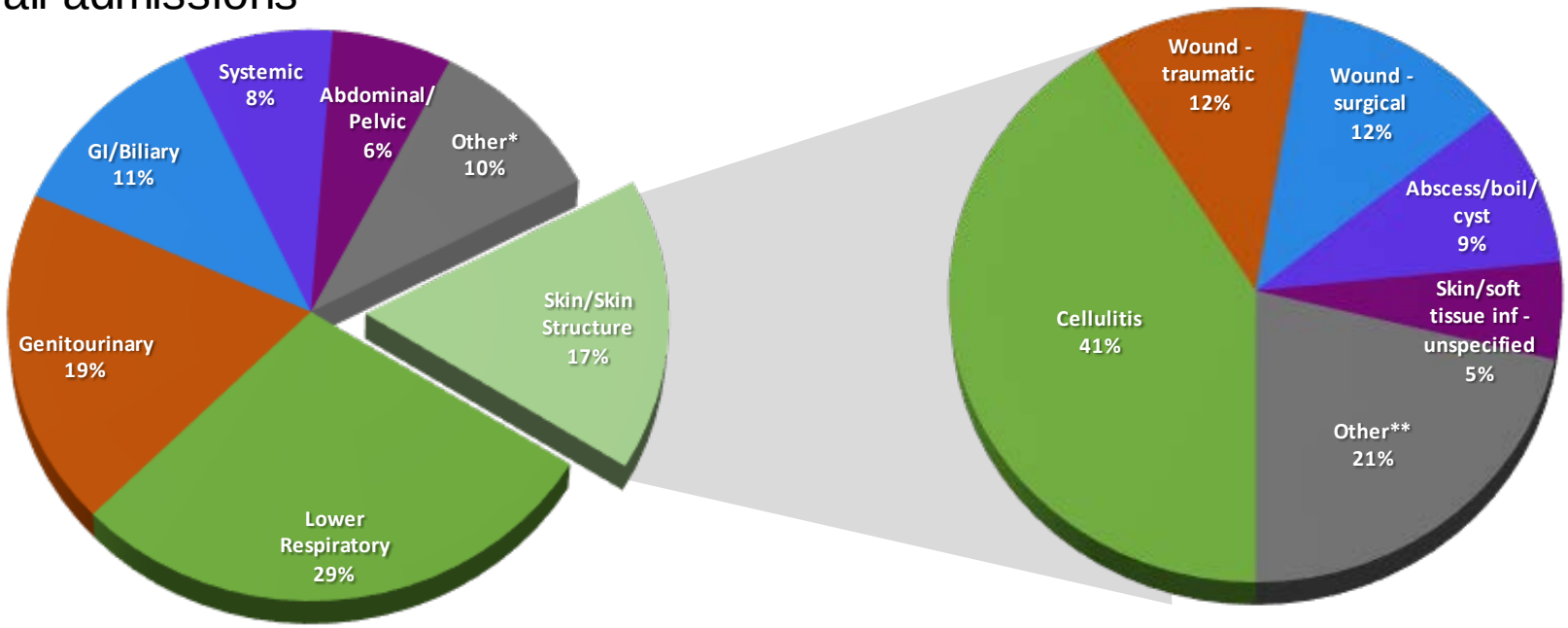
October 2013
Clinical/Antimicrobial

ABSSSI: The Unmet Medical Need

- Antimicrobial therapy practice patterns in ABSSSI:
  - IV vancomycin used in 75% patients
    - 80% is administered intravenously during an inpatient stay; 50% through peripherally inserted central catheter (PICC)
  - Total duration of therapy (inpatient and outpatient) ranges 10 - 17 days
  - At discharge, patients will continue with IV therapy or switch to oral treatment
- Issues with existing options include:
  - Daily dosing limits potential for outpatient treatment with existing IV therapies
  - **Vancomycin:** efficacy concerns at higher minimum inhibitory concentration (MIC); dose limiting toxicities require drug monitoring
  - **Daptomycin:** development of resistance on therapy; rhabdomyolysis
  - **Linezolid:** mitochondrial toxicity limits duration of treatment; serotonin syndrome liability
- Current challenges and unmet needs
  - Clinical failure (treatment failure, recurrence or readmission within 30 days) observed in 12% of ABSSSI patients
    - 63% of clinical failures with cellulitis cohort discharged on oral trimethoprim-sulfamethoxazole
  - PICC poses additional risks and complications
    - Increased risk of bloodstream infection and venous thrombus formation
    - Emergency department visit (2%), re-hospitalization (1%), PICC replacement and fluoroscopic confirmation (5%), physician visit (17%), declotting procedure (7%) and administration of tissue plasminogen activator (7%)

Hospital Incidence of Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

- U.S. hospitals treat ~18 million patients annually for infections
- ABSSSI accounts for ~17% of these infections, or 3.3M patients[1]
- ABSSSI represents ~3% of all admissions[2]
- ~1.3M (39%) of 3.3M ABSSSI patients are ≥ 65 years of age[1]
- Cellulitis and wound infections comprise the majority of clinical presentations



Sources: [1] AMR Hospital Antibiotic Market Guide - Book 2: Diagnosis and Surgery Reports, January 2010 – June 2010. [2] HCUP Data 2009. *Other categories include fevers of unknown origin, upper respiratory, bone/joint, non-surgical prophylaxis, CNS, cardiovascular and eye infections. **Other diagnoses include ulcer - diabetic foot/leg, ulcer - decubitus, gangrene, dental, burn, mastitis and lymphadenitis/lymphangitis.

Dalbavancin: Overview

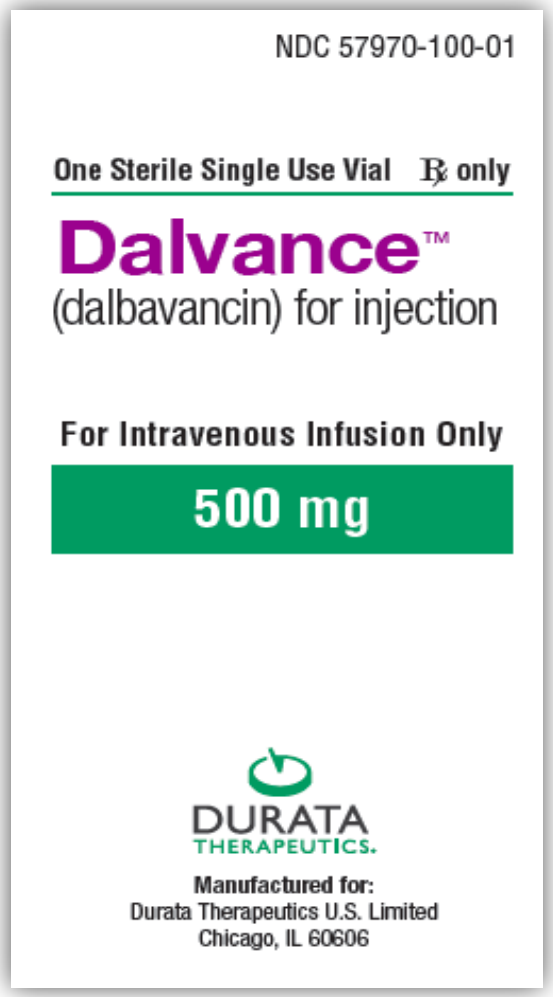
- Dalbavancin is a semisynthetic lipoglycopeptide intravenous (IV) antibiotic that interferes with cell wall synthesis which results in bacterial cell death
  - Administered as a once-weekly 30 minute IV infusion
- The pharmacokinetic profile of dalbavancin demonstrates rapid bactericidal activity that is potent and sustained against serious gram-positive infections including MRSA
- Dalbavancin's long half-life provides a once-weekly treatment regimen and bactericidal concentrations are sustained throughout the dosing interval
- Once-weekly dosing allows for the discontinuation of IV access with its attendant risks of line-related thrombosis and infection
- A complete course of therapy (14 days) consists of two doses of dalbavancin administered on Day 1 and Day 8

Dalbavancin will be administered in both inpatient and outpatient settings of care

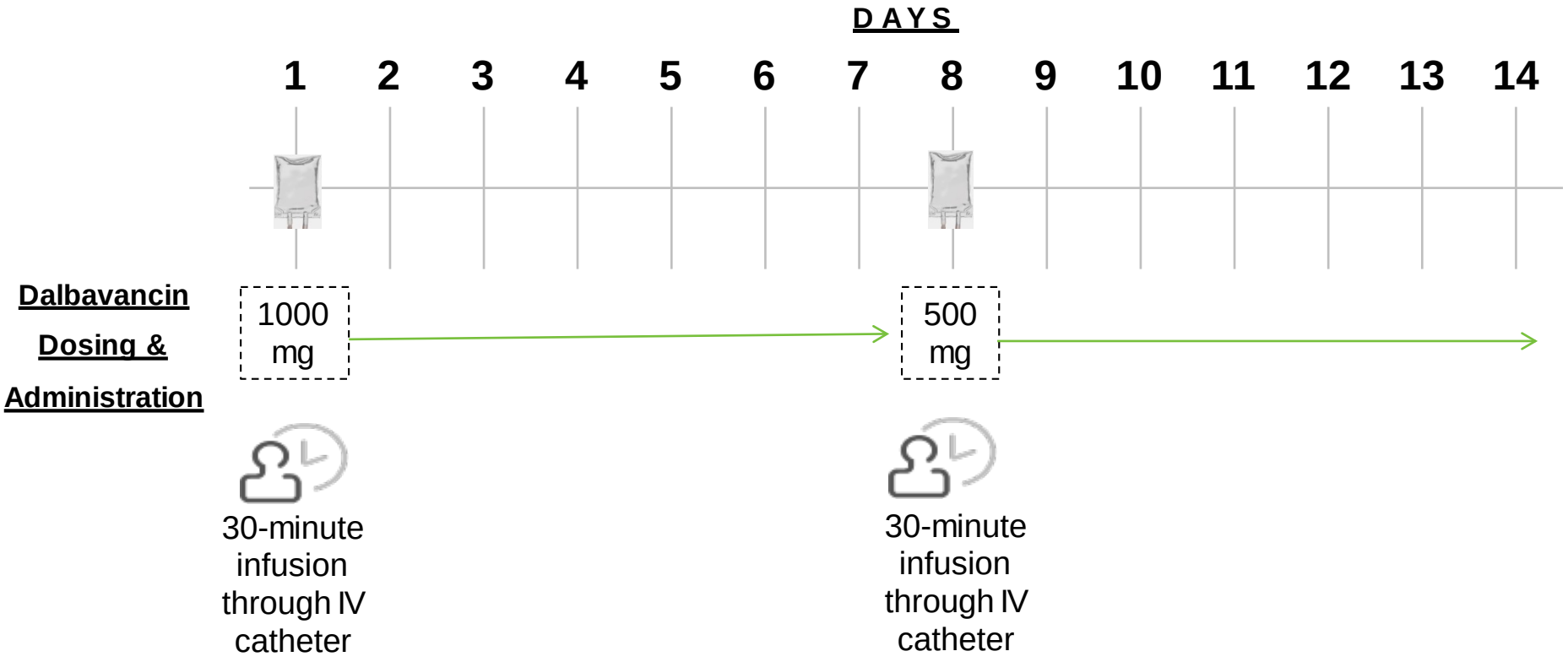
Proposed Indication and Usage

- DALVANCE™ (dalbavancin) for injection is indicated for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible strains of the following Gram-positive microorganisms:
  - Staphylococcus aureus (including MSSA and MRSA)
  - Streptococcus pyogenes
  - Streptococcus agalactiae
  - Streptococcus anginosus group (including S. anginosus, S. intermedius, S. constellatus)

Proposed Product Packaging



Dalbavancin is the First IV Antibiotic for ABSSSI with a Once-Weekly Dosage Regimen



- The recommended dosage regimen for dalbavancin in adult patients with ABSSSI is 1000 mg on Day 1 and 500 mg on Day 8, administered via an intravenous (IV) catheter over 30 minutes
- In clinical trials, dalbavancin was primarily delivered via peripheral line; however, administration via central line may be clinically appropriate under certain circumstances or preferred by the physician or patient

Use in Special Populations & Contraindications

- The dosage regimen for dalbavancin should be reduced to 750 mg on Day 1 and 375 mg on Day 8 in patients with chronic renal impairment whose creatinine clearance is <30 mL/min and who are not receiving regularly scheduled renal dialysis
- No dose adjustment for patients with mild hepatic impairment
- Pregnancy: Category C
- Of the adult patients (n=1778) treated with dalbavancin in Phase 2/3 clinical trials, efficacy & tolerability were similar to comparator regardless of age
- Safety and efficacy in pediatric patients have not been established
- Dalbavancin is contraindicated in patients with known hypersensitivity to dalbavancin or any of its components
- No data are available on cross-reactivity between dalbavancin and other glycopeptides, including vancomycin

Efficacy and Safety Overview

- Dalbavancin achieved the primary non-inferiority efficacy endpoints in multiple Phase 3 ABSSSI clinical trials when tested against presently approved and appropriate standard-of-care comparators in relevant indications and patient populations
- Efficacy was durable when patients were followed for as long as 70 days after initiation of treatment
- Safety and tolerability were acceptable relative to each of the comparators
- Adverse events occurred less frequently in the dalbavancin treated patients and no dose-limiting toxicity was observed
- The duration of adverse events was similar to that of comparators and late onset adverse events were not identified as a concern
- Demonstrated consistent safety and efficacy in relevant subpopulations, such as the elderly and diabetic patients

Safety Profile

PHASE 2/3 DATA IN DALBAVANCIN CLINICAL PROGRAM

Adverse Event*	Dalbavancin, n (%) (N=1778)	Comparator, n (%) (N=1224)	P value
Nausea	49 (2.8)	40 (3.3)	0.441
Diarrhoea	45 (2.5)	45 (3.7)	0.081
Pruritus	11 (0.6)	23 (1.9)	0.002

*Defined as treatment-related adverse events occurring in >2% of subjects in any dosing subgroup

Dalbavancin: Potential Impact On Current Standard Of Care in ABSSSI

- Compared to current standard of care administered once or twice per day, once-weekly dalbavancin has the potential to streamline process of care and lower total cost of care in both inpatient and outpatient treatment settings via:
  - Reduction in length of stay (emergency department and/or inpatient)
  - Avoidable admissions including skilled nursing facility stays for IV antibiotic dosing following a hospitalization
  - Reduced risk of readmission
  - Avoidance of potential complications (i.e., PICC)

- Individual patient experience of care will also be improved
  - No need for indwelling catheter (i.e., PICC)
  - Built-in adherence to therapeutic regimen
  - Less patient disruption, inconvenience and multiple site of care options
    - 2 doses of dalbavancin v. 28 doses of vancomycin

PICC Avoidance

Eliminates need for PICC line for post-acute setting IV antibiotic dministration

Avoids possible complications associated with PICC lines (i.e., venous thrombus, declotting procedures, readmissions)

ICD-10-PCS

- Create the following new ICD-10-PCS codes to capture the administration of dalbavancin by creating a new, separate qualifier in table 3E0 as is shown below. This option is limited to 3 Peripheral Vein and 4 Central Vein body part values and a percutaneous approach.

Administration	**3**	Administration
Body System	**E**	Physiological Systems and Anatomical Regions
Operation	**0**	Introduction: Putting in or on a therapeutic, diagnostic, nutritional, physiological, or prophylactic substance except blood or blood products

Body System / Region	*Approach*	*Substance*	*Qualifier*
3 Peripheral Vein **4** Central Vein	**3** Percutaneous	**2** Anti-infective	**8** Oxazolidinones **9** Other Anti-infective **ADD R Dalbavancin**

Durata recommends the creation of a new ICD-10-PCS qualifier in order to identify the administration of dalbavancin for NTAP purposes on inpatient claims