



Prior Authorization Approval Criteria

Cubicin (daptomycin)

Generic name:	Daptomycin
Brand name:	Cubicin
Medication class:	Cyclic lipopeptide antibiotic
FDA-approved uses:	<p>Treatment of complicated skin and skin structure infections (cSSSI) caused by susceptible isolates of the following Gram-positive microorganisms:</p> <p style="padding-left: 40px;">S. aureus (including MRSA); Strep. pyogenes; Strep. agalactiae; Strep. dysgalactiae, subspecies equisimilis; and E. faecalis (vancomycin-susceptible isolates only)</p> <p>Staphylococcus aureus bloodstream infections (bacteremia), including those with right-sided endocarditis, caused by methicillin-susceptible or methicillin-resistant isolates.</p>

Combination therapy may be clinically indicated if the documented or presumed pathogens include Gram-negative or anaerobic organisms.

Available dosage forms:	500mg/vial, single-use 10ml capacity vial of lyophilized cake for reconstitution for intravenous infusion. Cubicin is compatible with 0.9% sodium chloride injection (Normal Saline) and lactated Ringer's injection.
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NOTE: Cubicin is incompatible with dextrose-containing diluents.

Usual dose:	(cSSSI) 4 mg/kg IV every 24 hours (S.aureus) 6 mg/kg IV every 24 hours
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Approximate monthly cost: (based on AWP 2008):	cSSSI---\$1,400.00 (for a 70kg pt for 10 days) S. aureus---\$6,300.00 (for a 70kg pt for 30 days)
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Duration of therapy:	<p>Complicated skin and skin structure infections (<u>cSSSI</u>)—7 to 14 days <u>S. aureus bacteremia</u>, including those with right-sided endocarditis caused by methicillin- susceptible and methicillin-resistant isolates—<u>minimum of 2 to 6 weeks</u>.</p> <p>Duration should be based on treating physician's working diagnosis. There is limited safety data for more than 28 days, however there have been study patients treated for ≥ 6 weeks.</p>
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Criteria for use (bullet points below are all inclusive unless otherwise noted):

- ≥ 18 years of age
- Diagnosis of complicated skin or skin structure infection caused by a susceptible organism as proven by culture and sensitivity, or a strongly suspected organism
- Staph. aureus bacteremia caused by methicillin-susceptible or methicillin-resistant isolates

Criteria for continuation of therapy:

- Positive response to therapy
- CPK levels within acceptable range
- Minimal adverse effects
- Staph. aureus caused bacteremia with susceptibility demonstrated by repeated culture and sensitivity tests

Caution:

In the absence of proven or strongly suspected infection, the use of daptomycin can increase the chance of bacteria developing drug-resistance

- The concomitant use of HMG-CoA reductase inhibitors (i.e. "statins") increases the risk of developing myopathies
- Diarrhea following the administration of daptomycin may be indicative of pseudomembranous colitis caused by the antibiotic
- Dosage adjustments are required in those patients who are renally impaired
- Use of Cubicin in patients with creatinine clearance $<30\text{mL}/\text{min}$ (including hemodialysis or CAPD) require more frequent monitoring of CPK levels and creatinine clearance, as well as a dosage adjustment of every 48-hour dosing rather than every 24 hours. Cubicin should be dosed after hemodialysis on dialysis days.
- C. difficile-associated diarrhea (CDAD) has been reported with the use of nearly all antibacterial agents, including Cubicin. If CDAD is suspected or confirmed antibiotic use not directed against C. difficile may need to be discontinued.
- Patients with persistent or relapsing S. aureus infection, or poor clinical response should have repeated blood cultures and diagnostic evaluation to rule out sequestered foci of infection.

Monitoring:

- Fever
- CBC
- Symptomatic improvement
- Liver function tests
- Weekly CPK levels
- Signs and symptoms of neuropathy
- Symptoms of muscle pain/weakness (particularly in the distal extremities)
- Blood cultures for patients with *S. aureus* or who exhibit a poor clinical response
- Common adverse effects: injection site reactions, rash, GI discomfort (nausea, vomiting, diarrhea, constipation), muscle aches, dyspnea

- Serious but rare adverse effects: jaundice, abnormal liver function tests, immune hypersensitivity reaction, rhabdomyolysis, renal failure, peripheral neuropathies

Drug and laboratory interactions:

- Falsely elevated INRs and prolonged PT times have been observed with Cubicin when certain recombinant thromboplastin reagents are used in the assays. The possibility of this interaction may be minimized by drawing specimens near the times of trough plasma concentrations of daptomycin, however there may still be sufficient daptomycin levels at trough to cause interaction.
- As both Cubicin and HMG-CoA reductase inhibitors often increase CPK levels, it is advisable to temporarily suspend the use of "statins" during Cubicin use.

Contraindication:

- Hypersensitivity to daptomycin
- CPK > 10x the upper limit of normal (ULN)
 - Normal range (male): 60-400 units/L
 - Normal range (female): 40-150 units/L
- CPK > 5x ULN with co-existing myopathies

Not approved if:

- Patient does not meet criteria matching with FDA-approved indications (see above)
- Patient presents with any contraindications (see above)
- Infection is not proven to be caused by susceptible organisms by culture and sensitivity test, or very strongly suspected.

Not approved for continued therapy if:

- Repeat cultures have not been done

Special considerations:

- Pregnancy Category B: no adequate controlled studies in pregnant women; should only be used in this population if absolutely necessary
- Breast feeding: infant risk cannot be ruled out
- Pediatrics: daptomycin has no safety and efficacy data for patients under the age of 18

FCHP Pharmacy and Therapeutics Committee approval: _____

Date: _____

Adopted: 10/08/2008