Daptomycin

Product:
DAPTOMYCIN (Cubicin®)
500mg/10mL vial

Class of drugs:
Antimicrobial agent

Indication:
Treatment of complicated skin and skin structure infections and *Staphylococcus aureus* bloodstream infections

Manufacturer:
Oryx Pharmaceuticals Inc.

CED Recommendation

The CED recommended that daptomycin (Cubicin) not be funded, on the basis that there is no evidence that this drug provides added value over available alternatives in terms of efficacy, safety or cost-effectiveness.

Executive Officer Decision

Based on the CED's recommendation, the Executive Office decided not to fund daptomycin (Cubicin).

Status

Funding not available through the Ontario Public Drug Programs.

Highlights of Recommendation:

♦ Daptomycin (Cubicin) is an antibiotic indicated for the treatment of bloodstream infections (bacteremia) caused by *S. aureus* and complicated skin and skin structure infections (cSSSI). *(See Background section for details.)*

♦ Although there were clinical studies that evaluated the efficacy and safety of daptomycin (Cubicin) against alternative antibiotics, these studies were not well designed and had many potential biases, making the results difficult to interpret. On the whole, daptomycin (Cubicin) has not been shown to provide any clinical advantage over other antimicrobial drugs in the treatment of *S. aureus* bacteremia or cSSSI.

♦ Safety concerns with daptomycin (Cubicin) include muscle-related adverse events.

♦ Daptomycin (Cubicin) costs $165 per day, which is higher than comparator agents.

♦ **Overall, the Committee recommended that daptomycin (Cubicin) not be funded because this drug provides no efficacy, safety or cost advantage over existing alternatives.**

Background:

Daptomycin (Cubicin) is an antibiotic indicated for:

– *Staphylococcus aureus* (*S. aureus*) bloodstream infections (bacteremia), including those with right-sided infective endocarditis; and

– Complicated skin and skin structure infections (cSSSI) caused by susceptible bacteria.

S. aureus is a common type of bacteria that can colonize the skin and nose of humans. The bacteria can cause infection when it enters the body through a cut, sore, catheter, or breathing tube. The infection can be minor and local, or more serious (involving the heart, blood, or bone). When the bacteria infect the bloodstream, the condition is called S. *aureus* bacteremia, a serious and potentially fatal infection. Endocarditis, an infection of the heart valves, is a common complication of S. *aureus* bacteremia.

Complicated skin and skin structure infections (cSSSI) refer to various infections that involve soft tissues (e.g. the skin, subcutaneous tissues, lymphatics, fascia and muscles) that may or may not require surgical intervention in additon to antibiotic therapy. The term is also used to describe infections in patients who are hospitalized or who have underlying illnesses (such as diabetes or HIV infection). cSSSI are often caused by Gram-positive bacteria, such as S. *aureus* and Streptococci. Other types of bacteria have also been identified as causes of cSSSI particularly in patients with underlying conditions such as diabetes or peripheral vascular disease.

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Detailed Discussion:

♦ The Committee considered three randomized controlled studies evaluating the efficacy and safety of daptomycin (Cubicin) versus alternative antimicrobial agents.

♦ One study was conducted in 235 patients with *S. aureus* bacteremia and endocarditis. Patients treated with daptomycin (Cubicin) were compared against a mixed comparator group, in which patients were treated with either vancomycin or one of four semi-synthetic penicillins.

♦ Two of the three studies evaluated cSSSI in a total of 899 patients and also compared daptomycin (Cubicin) against a mixed comparator group of either vancomycin or one of four semi-synthetic penicillins.

♦ All three studies had a non-inferiority design, i.e., can only determine whether daptomycin (Cubicin) is not worse than the comparator treatment by a specified margin. *(Please see Glossary for details: http:// www.health.gov.on.ca/english/ providers/program/drugs/dr_glossary/ glossary_mn.html.)*

♦ There were concerns with the design, conduct and reporting of the studies. The three open-label, non-inferiority trials showed that there was no therapeutic advantage of daptomycin over other antibiotics .

♦ The manufacturer requested that funding for daptomycin (Cubicin) be considered for patients with vancomycin-resistant *S. aureus* infections or patients with intolerance to vancomycin. However, there is inadequate clinical evidence evaluating the use of daptomycin (Cubicin) in these patient subgroups.

♦ Frequent side effects with daptomycin (Cubicin) include constipation, nausea, vomiting, injection site reactions, headache and diarrhea. There have also been case reports of rhabdomyolysis (breakdown of muscle fibers).

♦ Data on dosing and safety are lacking in patients with kidney impairment.

♦ The drug cost for daptomycin (Cubicin) is $165 per day. This is more expensive than other alternative treatments such as vancomycin ($92.54), cloxacillin ($0.70-$14.40) and linezolid ($141.28). The cost-effectiveness of daptomycin (Cubicin) could not be determined, largely due to uncertainties regarding its relative efficacy and safety versus other treatments.

♦ Overall, the Committee recommended that daptomycin (Cubicin) not be funded because there is no evidence that this drug provides added value over available alternatives in terms of efficacy, safety or cost-effectiveness.

(http://www.cadth.ca/index.php/en/cdr/ recommendations)

CEDAC Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that daptomycin (Cubicin) not be listed.

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