

VI.2 Elements for a Public Summary

[Invented Name] 350 mg Powder for solution for injection or infusion

[Invented Name] 500 mg Powder for solution for injection or infusion

VI.2.1 Overview of disease epidemiology

Skin and soft tissue (e.g. nose, sinuses) infections

Skin and soft tissues (e.g. nose, sinuses) are a natural host for many bacterial species. Normally, these species do not cause any problems but in times of lower immunity and /or low standard of hygiene, these organisms can lead to infections. Numerous skin and soft tissue infections are known and include, for instance, erysipelas and cellulitis. Erysipelas is characterised by large raised red patches on the skin (mostly affects legs or face), which typically resolve after treatment. Cellulitis is similar to erysipelas but it involves deeper layers of the skin and hence manifests itself as swelling. It usually affects lower legs. If left untreated, cellulitis can be life-threatening.

Heart infections

Daptomycin is commonly used for endocarditis (a rare and potentially fatal heart infection). Endocarditis is most commonly caused by bacteria in the blood (such as *Staphylococcus aureus*). Symptoms include fever, headache, joint and muscle pain. Endocarditis is typically treated with antibiotics but some patients may require surgery. Endocarditis is a serious condition which, even if treated, could be life-threatening or lead to complications.

Staphylococcus aureus bacteraemia

Bacteraemia is an infection of the blood. If not treated on time, bacteremia can spread to other areas, such as heart, or even lead to sepsis (known as 'blood poisoning'), which may be life-threatening. Bacteraemia symptoms include fever, chills vomiting and diarrhoea; dizziness, confusion and disorientation may also appear. Patients with a weakened immune system, elderly or patients who have recently had an open wound or a surgery may be at a higher risk of developing bacteraemia.

VI.2.2 Summary of treatment benefits

The active substance in [Invented Name] is daptomycin. Daptomycin is an antibiotic that can stop the growth of certain bacteria. [Invented Name] is used in adults and in children and adolescents (age from 1 to 17 years) to treat infections of the skin and the tissues below the skin. It is also used in adults to treat infections in the tissues that line the inside of the heart (including heart valves) which are caused by a bacterium called *Staphylococcus aureus* and to treat infections in the blood caused by the same bacterium when associated with skin or heart infection. Depending on the type of infection(s) that you have, your doctor may also prescribe other antibiotics while you are receiving treatment with [Invented Name].

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of daptomycin in children and adolescents aged below 18 years with right-sided infective endocarditis due to *Staphylococcus aureus* or with *Staphylococcus aureus* bacteraemia when associated with right-sided infective endocarditis or with complicated skin and soft-tissue infections have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
------	---------------	----------------

<p>Severe skeletal muscle toxicity</p>	<p>Occasionally, patients receiving daptomycin may develop tender or aching muscles or muscle weakness. The symptoms generally go away within a few days of stopping</p>	<p>Your doctor will perform blood tests to monitor the health of your muscles both before you start treatment and frequently during treatment with daptomycin.</p>
<p>Reduced susceptibility to daptomycin in a bacterium called <i>S. aureus</i></p> <p>(Reduced susceptibility to daptomycin in <i>S. aureus</i>)</p>	<p>Susceptibility to daptomycin in a bacterium called <i>S. aureus</i> may be reduced in some patients. This means that the infection may worsen or may simply not get better with treatment. This has been reported especially during the treatment of difficult-to-treat infections and/or following administration for prolonged periods.</p>	<p>Tell your doctor if you feel that daptomycin is not working. Your doctor may be able to switch you to another antibiotic to aid your symptoms.</p>
<p>Condition resulting from damaged nerves</p> <p>(Peripheral neuropathy)</p>	<p>Peripheral neuropathy, condition resulting from damaged nerves and which typically manifests as weakness, numbness and pain, usually in hands and feet, may occur with daptomycin treatment.</p>	<p>Inform your doctor if you have ever had any conditions which were due to damaged nerves.</p>
<p>Severe allergic reactions (including accumulation of white blood cells in the lungs)</p> <p>(Severe hypersensitivity reactions (including pulmonary eosinophilia))</p>	<p>Serious allergic reaction including anaphylaxis, have been reported in some cases during administration of daptomycin. These serious allergic reactions need immediate medical attention.</p>	<p>Inform your doctor about any allergies which you may have.</p> <p>Tell your doctor or nurse straight away if you experience any of the following symptoms:</p> <ul style="list-style-type: none"> • chest pain or tightness • rash with blistering, sometimes affecting the mouth and genitals • swelling around throat • rapid or weak pulse • wheezing • fever • shivering or trembling • hot flushes • dizziness • fainting • metallic taste

Disease where a type of white blood cells accumulate in the lungs (Eosinophilic pneumonia)	New or worsening fever, cough or difficulty breathing may be signs of a rare but serious lung disorder called eosinophilic pneumonia which may occur with daptomycin therapy.	Your doctor will check the condition of your lungs and decide whether or not you should continue with daptomycin therapy.
---	---	---

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Bone marrow toxicity	Patients treated with daptomycin may be at an increased risk of developing bone marrow toxicity. Causality has not been established.
Severe hepatotoxicity	Patients treated with daptomycin may be at an increased risk of developing severe liver adverse events. Causality has not been established.
Dysregulation of in vivo coagulation	Cases of interference between daptomycin and particular reagents used in some coagulation tests (prothrombin time [PT]; international normalized ratio [INR]) have been reported. The interference leads to false results, with an apparent prolongation of PT and elevation of INR.

Missing information

Risk	What is known
Patients with underlying renal impairment	Due to limited clinical experience, daptomycin should only be used in patients with any degree of kidney impairment when it is considered that the expected clinical benefit outweighs the potential risk.
Patients with hepatic impairment	The way daptomycin is processed in the body is not altered in subjects with moderate liver impairment compared with healthy volunteers matched for gender, age and weight following a single 4 mg/kg dose. No dosage adjustment is necessary when administering daptomycin in patients with moderate liver impairment. The way daptomycin is processed in the body of patients with severe liver impairment is unknown.
Pregnant or lactating women	No clinical data on pregnancies are available for daptomycin. Daptomycin should not be used during pregnancy unless clearly necessary i.e., only if the expected benefit outweighs the possible risk. Until more experience is gained, breast-feeding should be discontinued when daptomycin is administered to nursing women.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

Severe skeletal muscle toxicity, Dysregulation of in vivo coagulation, Patients with underlying renal impairment

Risk minimisation measure(s): Dosage card for healthcare professionals
<u>Objective and rationale:</u> Additional educational materials for prescribers to highlight the risks of severe skeletal muscle toxicity and dysregulation of in vivo coagulation, as well as to address dosing in patients with underlying renal impairment.
<u>Summary description of main additional risk minimisation measures:</u> <ul style="list-style-type: none"> • Dosage card for healthcare professionals Details of educational material can be found in Annex 10.

Reduced susceptibility to daptomycin in S. aureus

Risk minimisation measure(s): Laboratory susceptibility testing leaflet
<u>Objective and rationale:</u> Additional educational materials for all laboratories expected to perform daptomycin susceptibility testing in order to highlight that susceptibility testing minimises the risk of treatment failure and that daptomycin susceptibility testing needs Ca in the testing medium.
<u>Summary description of main additional risk minimisation measures:</u> <ul style="list-style-type: none"> • Educational materials for all laboratories expected to perform daptomycin susceptibility testing Details of educational material can be found in Annex 10.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.