Summary of risk management plan for Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion (Daptomycin)

This is a summary of the risk management plan (RMP) for Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion. The RMP details important risks of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion, how these risks can be minimised, and how more information will be obtained about Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion's risks and uncertainties (missing information).

Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion should be used.

Important new concerns or changes to the current ones will be included in updates of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion's RMP.

I. The medicine and what it is used for

Daptomycin is authorised for treatment of the following infections:

Adults and paediatric (2 to 17 years of age) patients with complicated skin and soft-tissue infections (cSSTI).

Adults patients with right-sided infective endocarditis (RIE) due to *Staphylococcus aureus*. It is recommended that the decision to use daptomycin should take into account the antibacterial susceptibility of the organism and should be based on expert advice.

Adult and paediatric (1 to 17 years of age) patients with *Staphylococcus aureus* bacteraemia (SAB) In adults, use in bacteraemia should be associated with RIE or with cSSTI, while in paediatric patients, use in bacteraemia should be associated with cSSTI.
Daptomycin is active against Gram positive bacteria only.

In mixed infections where Gram negative and/or certain types of anaerobic bacteria are suspected, daptomycin should be coadministered with appropriate antibacterial agent(s).

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion, together with measures to minimise such risks and the proposed studies for learning more about Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status - the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.
In the case of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below under section II.B.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment and signal management activity, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential.

Identified risks are concerns for which there is sufficient proof of a link with the use of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Severe skeletal muscle toxicity • Reduced susceptibility to daptomycin in S. aureus • Peripheral neuropathy • Severe hypersensitivity reactions (including pulmonary eosinophilia) • Eosinophilic pneumonia
Important potential risks	• Bone marrow toxicity • Severe hepatotoxicity • Dysregulation of in vivo coagulation
Missing information	• Patients with underlying renal impairment • Patients with hepatic impairment • Pregnant or lactating women

II.B Summary of important risks with additional risk minimisation measures	
Important identified risks: Severe skeletal muscle toxicity	
Risk minimisation measures	Routine risk minimisation measures: In SmPC: Section 4.4 and 4.8 of Daptomycin SmPC and Section 4 of PIL has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. AE follow-up form for adverse reaction. Additional risk minimisation measures: Daptomycin dosage card for physicians.
Important identified risks: Reduced susceptibility to daptomycin in S. aureus	
Risk minimisation measures	Routine risk minimisation measures: Section 4.4 and 5.1 of Daptomycin SmPC has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. AE follow-up form for adverse reaction. Additional risk minimisation measures: The laboratory susceptibility testing leaflet.
Important potential risks: Dysregulation of in vivo coagulation	
Risk minimisation measures	Routine risk minimisation measures: Routine pharmacovigilance activities including close monitoring in the PSUR. AE follow-up form for adverse reaction. Additional risk minimisation measures: Daptomycin dosage card for physician

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Daptomycin 350 mg & 500 mg Powder for solution for injection or infusion.