SUMMARY OF RISK MANAGEMENT PLAN FOR TENKASI (ORITAVANCIN)

This is a summary of the risk management plan (RMP) for Tenkasi. The RMP details important risks of Tenkasi, how these risks can be minimised, and how more information will be obtained about Tenkasi's risks and uncertainties (missing information).
Tenkasi's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tenkasi should be used.

This summary of the RMP for Tenkasi should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).
Important new concerns or changes to the current ones will be included in updates of Tenkasi's RMP.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tenkasi is authorised for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults (see SmPCs for the full indication) and also for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in paediatric patients aged 3 months and older (only for 400 mg powder for concentrate for solution for infusion). It contains oritavancin as the active substance and it is given by intravenous infusion (400 mg powder for concentrate for solution for infusion, and 1200 mg powder for concentrate for solution for infusion as new formulation proposed) administration.

Further information about the evaluation of Tenkasi's benefits can be found in Tenkasi's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/tenkasi-previously-orbactiv

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tenkasi, together with measures to minimise such risks and the proposed studies for learning more about Tenkasi'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A. List of important risks and missing information

Important risks of Tenkasi are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Tenkasi. 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	Hypersensitivity and histamine-like infusion reactions
Important Potential Risks	Pseudomembranous colitis / *Clostridium difficile*-associated diarrhea (CDAD) Osteomyelitis
Missing Information	None

II.B. Summary of important risks

Important Identified Risk: Allergic reactions (Hypersensitivity and histamine-like infusion reactions)	
Evidence for linking the risk to the medicine	Serious allergic reactions (e.g., rash, itching, redness, problems with breathing) have been seen following treatment with oritavancin. In a clinical study, 7 out of 100 patients treated with oritavancin had an allergic reaction, compared with 14 out of 100 patients who took vancomycin. Patients who had an allergic reaction following a glycopeptide other than oritavancin are likely to also be allergic to oritavancin (this is referred to as cross-sensitivity).
Risk factors and risk groups	Known hypersensitivity to this class of antibiotics.
Risk minimisation measures	Routine risk minimisation measures: - SmPC section 4.3 Contraindications - SmPC section 4.4 Special warnings and precautions for use - SmPC section 4.8 Undesirable effects The PL of the concerned products is in line with the information contained in the SmPC previously described. Such information is given in the following sections of the PL: - PL Section 2 What you need to know before you take You must not be given Warnings and precautions - PL Section 4 Possible side effects Legal status: prescription only medicine Additional risk minimisation measures: No risk minimisation measures

Important Potential Risks: Antibiotic-associated diarrhea/infectious diarrhoea [**Pseudomembranous colitis / *Clostridium difficile*-associated diarrhea (CDAD)**]	
Evidence for linking the risk to the medicine	Antibiotic-associated diarrhoea refers to diarrhoea that develops in a person who is taking or recently took antibiotics. Some antibiotics can decrease the levels of protective bacteria normally found in the gut, and when this happens, harmful bacteria may be able to multiply and cause symptoms such as cramping pain, fever, and diarrhoea,

	sometimes occurring more than 2 months after receiving antibiotic treatment. One of the most serious causes of antibiotic associated diarrhoea is infection with a bacterium called *Clostridium difficile*. Antibiotic-associated diarrhoea has been reported with oritavancin. Patients who experience prolonged or severe diarrhoea following their treatment with oritavancin should contact their healthcare provider. Appropriate treatment should be considered.
Risk factors and risk groups	Patients with the following factors are at risk of antibiotic-associated diarrhea / infectious diarrhoea: 1) compromised immune system; 2) older age; 3) serious illness; 4) extended hospital stay; 5) extended course and / or multiple antibiotic treatment; 6) presence of a nasogastric tube; and 7) anti-ulcer medications.
Risk minimisation measures	Routine risk minimisation measures: - SmPC section 4.4 Special warnings and precautions for use - SmPC section 4.8 Undesirable effects The PL of the concerned products is in line with the information contained in the SmPC previously described. Such information is given in the following sections of the PL: - PL Section 2 What you need to know before you take Warnings and precautions - PL Section 4 Possible side effects Legal status: prescription only medicine Additional risk minimisation measures: No risk minimisation measures

Important Potential Risks: Infection or inflammation of the bone or bone marrow (Osteomyelitis)	
Evidence for linking the risk to the medicine	More cases of osteomyelitis (infection in the bone) were reported with oritavancin than with vancomycin. Patients should be monitored for signs and symptoms of osteomyelitis following treatment with oritavancin. If osteomyelitis is diagnosed or suspected, alternative antibiotic treatment should be started. Oritavancin is not approved for the treatment of bone or bone marrow infections. Patients suspected or confirmed to have underlying bone or bone marrow infections should receive appropriate treatment.
Risk factors and risk groups	During the clinical development, patients with diabetes mellitus at baseline had a higher rate of osteomyelitis than did non-diabetic patients; the incidence of osteomyelitis was higher in oritavancin-treated patients with baseline peripheral vascular disease vs patients without peripheral vascular disease.
Risk minimisation measures	Routine risk minimisation measures: - SmPC section 4.4 Special warnings and precautions for use - SmPC section 4.8 Undesirable effects The PL of the concerned products is in line with the information contained in the SmPC previously described. Such information is given in the following sections of the PL: - PL Section 2 What you need to know before you take - Warnings and precautions - PL Section 4 Possible side effects Legal status: prescription only medicine

	Additional risk minimisation measures: No risk minimisation measures

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 Tenkasi.

II.C.2. Other studies in post-authorisation development plan

There are no studies required for Tenkasi.