Summary of risk management plan for Vazkepa (icosapent ethyl)

This is a summary of the risk management plan (RMP) for Vazkepa. The RMP details important risks of Vazkepa, how these risks can be minimised, and how more information will be obtained about Vazkepa 's risks and uncertainties (missing information).

Vazkepa's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Vazkepa should be used.

This summary of the RMP for Vazkepa 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 Vazkepa's RMP.

I. The medicine and what it is used for

Vazkepa is authorised to reduce the risk of cardiovascular events in adult statin-treated patients at high cardiovascular risk with elevated triglycerides (≥150 mg/dL) and established cardiovascular disease, or diabetes, and at least one other cardiovascular risk factor (see SmPC for the full indication). It contains icosapent ethyl as the active substance and it is given orally.

Further information about the evaluation of Vazkepa's benefits can be found in Vazkepa'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/vazkepa

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

Important risks of Vazkepa, together with measures to minimise such risks and the proposed studies for learning more about Vazkepa '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***.

If important information that may affect the safe use of Vazkepa is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Vazkepa 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 Vazkepa. 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	Bleeding in patients on anti-thrombotic therapy
	Atrial fibrillation/flutter
Important potential risks	None
Missing information	Use in pregnant and breast-feeding women

II.B Summary of important risks

Important identified risk: Bleeding in patients on anti-thrombotic therapy	
Evidence for linking the risk to the medicine	In a clinical study of 8,179 patients with established cardiovascular disease (CVD) or at high risk of CVD, 482 (12%) of 4089 patients receiving Vazkepa experienced a bleeding event compared to 404 (10%) of 4090 patients receiving placebo. The incidence of bleeding was greater in patients receiving Vazkepa together with medications to prevent clot formation, such as acetylsalicylic acid, clopidogrel, or warfarin. Serious bleeding events occurred in 122 (3.4%) of 3640 patients receiving Vazkepa compared with 94 (2.6%) of 3635 patients receiving placebo, when administered together with medications to prevent clot formation. However, the frequency of serious bleeding was the same (0.2%) in those receiving Vazkepa and placebo, when administered to patients who were not taking medications to prevent clot formation.
Risk factors and risk groups	Risk factors for bleeding include older age, female sex, history of bleeding or anaemia, heart failure, cerebrovascular disease (e.g. stroke), liver or kidney disease, hypertension, cancer, trauma or surgery, genetic variations affecting clotting or metabolism and concomitant medications e.g. acetylsalicylic acid, warfarin, clopidogrel.
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4 where advice is given on periodic monitoring of patients receiving Vazkepa together with anti-thrombotic agents* *SmPC section 4.8* *PL section 2 and 4* *Prescription only medicine* Additional risk minimisation measures: *None*

Important identified risk: Atrial fibrillation/flutter	
Evidence for linking the risk to the medicine	In a clinical study of 8,179 patients with established CVD or at high risk of CVD, patients receiving Vazkepa had a significantly higher rate of abnormal heart rhythms called atrial fibrillation/flutter (236 patients (5.8%) of 4089 patients receiving Vazkepa) compared with those receiving placebo (183 patients (4.5%) of 4090 patients). The percentage of patients requiring more than 24 hours hospitalisation for atrial fibrillation/flutter was also significantly higher in those receiving Vazkepa (127 patients (3.1%) of 4089 patients) than in those receiving placebo (84 patients (2.1%) of 4090 patients). Atrial fibrillation is more common in patients with cardiovascular conditions. Therefore, some of the patients included in the clinical study will have had underlying health conditions (e.g. hypertension, atherosclerosis) putting them at greater risk for atrial fibrillation. Atrial fibrillation/flutter events assessed to be drug related were reported rarely 0.07% (3 of 4089 patients) and 0.02% (1 of 4090 patients) for Vazkepa and placebo, respectively.
Risk factors and risk groups	Risk factors for atrial fibrillation include coronary heart disease, hypertension (>140/90 mmHg), heart failure, diabetes, hyperthyroidism, obesity, and valvular heart disease
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4 where advice is given on monitoring for clinical evidence of atrial fibrillation or atrial flutter and performing electrocardiographic evaluation when clinically indicated.* *SmPC section 4.8* *PL section 2 and 4* *Prescription only medicine* Additional risk minimisation measures: *None*

Missing information: Use in pregnant and breast-feeding women	
Risk minimisation measures	Routine risk minimisation measures *SmPC section 4.6 and 5.3* *PL section 2* *Prescription only medicine* Additional risk minimisation measures: *None*

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 Vazkepa.

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

There are no studies required for Vazkepa.