Verzenios®

abemaciclib

film-coated tablets

Summary of Risk Management Plan (RMP)

Summary of the risk management plan (RMP) for Verzenios (abemaciclib)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Verzenios is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the „Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Verzenios in Switzerland is the „Arzneimittelinformation/ Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Eli Lilly is fully responsible for the accuracy and correctness of the content of this published summary RMP of Verzenios.

I. The Medicine and What It Is Used for

VERZENIOS is authorised for locally advanced and metastatic breast cancer. It contains abemaciclib as the active substance and it is given orally as immediate release film-coated tablets: 50, 100, 150 and 200 mg.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of VERZENIOS, together with measures to minimise such risks and the proposed studies for learning more about VERZENIOS'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 product information addressed to patients and healthcare professionals
- 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.

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

II.A. List of Important Risks and Missing Information

Important risks of VERZENIOS 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 VERZENIOS. 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	None
Important potential risks	Serious Infection Secondary to Neutropenia Liver Injury Reproductive and Developmental Toxicity Severe Clinical Outcomes of Venous Thromboembolic Events
Missing information	Exposure and Safety in Patients with Severe Renal Impairment

II.B. Summary of Important Risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important Potential Risk: Serious Infection Secondary to Neutropenia (Low White Blood Cell Count)	
Evidence for linking the risk to the medicine	Neutropenia is a potential risk for patients who are being treated with abemaciclib. A patient with neutropenia is more susceptible to infections, which can be severe if the neutropenia is not managed.
Risk factors and risk groups	Neutropenia places patients at a higher risk of life-threatening infections. Some risk factors include type of cancer, stage of cancer, if the patient is female, advanced age and other conditions the patient may have in addition to cancer. Some types of chemotherapy are more likely to cause neutropenia than others. Patients who are in hospital are at increased risk of infections associated with neutropenia.
Risk minimisation measures	Complete blood counts should be monitored before starting abemaciclib therapy and every 2 weeks for the first 2 months of therapy. Dose modification is recommended for patients who develop severe neutropenia.

Important Potential Risk: Liver Injury	
Evidence for linking the risk to the medicine	In the clinical development programme, some patients who were treated with abemaciclib in combination with endocrine therapy showed an increase in some laboratory values (blood tests) that could indicate liver injury. Generally, these increases were of low severity. Based on the frequency of these events, liver injury is considered an important potential risk.
Risk factors and risk groups	Patients who receive abemaciclib in combination with endocrine therapy may be at risk of liver injury. Risk factors associated with liver injury include advancing age, female gender, poor nutrition, drinking alcohol, chronic hepatitis B and C and genetic risk factors.
Risk minimisation measures	Aminotransferases should be monitored before starting abemaciclib therapy and every 2 weeks for the first 2 months of therapy. If the patient shows evidence of ALT or AST increased, dose adjustments or drug discontinuation could be done per SmPC guidelines based on the severity of the event.

Important Potential Risk: Reproductive and Developmental Toxicity	
Evidence for linking the risk to the medicine	Abemaciclib works by interfering with a certain step in cell division. Because foetal development requires cell division, it is likely that abemaciclib inhibits foetal development. In rats, lower foetal weight and other effects were observed, which is consistent with the classification of this risk as a potential risk. No human data are available.
Risk factors and risk groups	Chemotherapy exposure during pregnancy carries a higher risk of spontaneous abortion and major birth defects. Older patients (over age 40 years) are more likely to develop early menopause after chemotherapy. Additional risk factors include smoking, drinking alcohol, diabetes and obesity.
Risk minimisation measures	Abemaciclib is not recommended during pregnancy and in women of child-bearing potential who are not using birth control. Women of child-bearing potential should use a highly effective birth control method during treatment and for 3 weeks following treatment.

Important Potential Risk: Severe Clinical Outcomes of Venous Thromboembolic Events (VTEs)	
Evidence for linking the risk to the medicine	

In the clinical development programme, patients who were treated with abemaciclib in combination with endocrine therapy showed a higher number of VTEs than patients who received endocrine therapy alone. Per reported Common Terminology Criteria for Adverse Events (CTCAE) assessment, the majority of VTEs were uncomplicated; there were isolated cases with severe outcome (including fatal cases). Generally, treatment consisted of standard anti-coagulation therapy. In few cases only, treatment with abemaciclib was discontinued due to VTE.

Risk factors and risk groups	Risk factors for cancer-associated VTE include the type of cancer, presence of metastatic disease, use of anti-cancer medication including chemotherapy, hormonal therapy and surgery. Cancer patients on active therapy are at greatest risk of development of VTE.
Risk minimisation measures	As abemaciclib treatment, when combined with endocrine therapy, conveys an increased risk of VTEs, monitoring patients for signs and symptoms of VTEs could be done per guidelines based on the severity of the event.

Missing Information: Exposure and Safety in Patients with Severe Renal Impairment	
Risk minimisation measures	Use of abemaciclib in patients with severe renal impairment is not contraindicated. Abemaciclib should be administered with caution in patients with severe renal impairment. Complete blood counts should be monitored before starting abemaciclib therapy and every 2 weeks for the first 2 months of therapy.

VI.1.1. II.C. Post-authorisation development plan

VI.1.1.1. II.C.1. Studies that are conditions of the marketing authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of VERZENIOS.

VI.1.1.2. II.C.2. Other studies in the post-authorisation development plan

Not applicable