Part VI: Summary of the risk management plan

Summary of risk management plan for Everolimus ETHYPHARM Tablets

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

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

Important new concerns or changes to the current ones will be included in updates of Everolimus ETHYPHARM 's RMP.

I. The medicine and what it is used for

ETHYPHARM Everolimus is authorised in oncology for the following indications:

Hormone receptor-positive advanced breast cancer
Everolimus Ethypharm is indicated for the treatment of hormone receptor-positive, HER2/neu negative advanced breast cancer, in combination with exemestane, in postmenopausal women without symptomatic visceral disease after recurrence or progression following a non-steroidal aromatase inhibitor.

Neuroendocrine tumours of pancreatic origin
Everolimus Ethypharm is indicated for the treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease.

Neuroendocrine tumours of gastrointestinal or lung origin
Everolimus Ethypharm is indicated for the treatment of unresectable or metastatic, well-differentiated (Grade 1 or Grade 2) non-functional neuroendocrine tumours of gastrointestinal or lung origin in adults with progressive disease (see sections 4.4 and 5.1).

Renal cell carcinoma
Everolimus Ethypharm is indicated for the treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.

It contains Everolimus as the active substance and it is given by oral.

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

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

II.A List of important risks and missing information

Important risks of Everolimus ETHYPHARM 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 Everolimus ETHYPHARM. 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	Non-infectious pneumonitis Severe infections Hypersensitivity (anaphylactic reactions) Stomatitis Wound healing complications Increased creatinine / proteinuria / renal failure Hyperglycemia/ new onset diabetes mellitus Dyslipidemia Hypophosphatemia Cardiac failure Cytopenia Haemorrhages Thrombotic and embolic events Female fertility (including secondary amenorrhea) Pre-existing infection (reactivation, aggravation, or exacerbation) Safety in patients with hepatic impairment Drug-drug interactions: Strong CYP3A4 inhibitors and PgP inhibitors Moderate CYP3A4 inhibitors and PgP inhibitor Strong CYP3A4 inducers and PgP inducers CYP3A4 substrates and PgP substrates Increased risk for angioedema when combining mTOR inhibitors and ACE inhibitors
Important potential risks	Postnatal developmental toxicity Pregnant or breast-feeding women Male infertility Muscle-wasting / muscle-loss

	Drug-drug interactions: Everolimus with concomitant exemestane use
Missing information	Off-label use in pediatric and adolescent patients Patients with uncontrolled cardiac disease Long-term safety Onset of benign or malignant tumors Comparative safety of everolimus and exemestane therapy vs. everolimus monotherapy Safety in breast cancer patients pre-treated with cytotoxic therapies

II.B Summary of important risks

The safety information in the Product Information are aligned to the reference medicinal products.

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 Everolimus ETHYPHARM.

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

There are no studies required for Everolimus ETHYPHARM.