Part VI: Summary of the risk management plan: Farydak (panobinostat)

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

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

This summary of the RMP for panobinostat 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 panobinostat RMP.

Part VI: I. The medicine and what it is used for

Panobinostat in combination with bortezomib and dexamethasone, is indicated for the treatment of adult patients with relapsed and/or refractory multiple myeloma who have received at least two prior regimens including bortezomib and an immunomodulatory agent.

Further information about the evaluation of panobinostat benefits can be found in panobinostat EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage link to the EPAR summary landing page on the EMA webpage.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/003725/WC500193301.pdf. (last accessed 21-May-2018).

Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of panobinostat, together with measures to minimize such risks and the proposed studies for learning more about panobinostat risks, are outlined below.

Measures to minimize 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

In the case of panobinostat, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

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.

Part VI – II.A: List of important risks and missing information

Important risks of panobinostat are risks that need special risk management activities to further investigate or minimize 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 panobinostat. 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);

Table 1 List of important risks and missing information

Important identified risks	Severe hemorrhage Severe infections (including sepsis/ pneumonia/reactivation of hepatitis B infection)
Important potential risks	Developmental toxicity Carcinogenicity/Second primary malignancy Medication errors
Missing information	None

Part VI - II B: Summary of important risks

Table 2 Important identified risk: Severe hemorrhage

Evidence for linking the risk to the medicine	The risk has been observed in preclinical and clinical studies, along with post-marketing reports.
Risk factors and risk groups	Patients with thrombocytopenia as well as those with renal disease, nephrosis, disseminated intravascular coagulation, von Willebrand syndrome, amyloidosis, platelet function defects, fibrin generation and aggregation defects, circulating anticoagulants and heparin anticoagulants.
Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.2, Section 4.4, Section 4.8 and Section 4.9 **Additional risk minimization measures** None

Table 3 Important identified risk: Severe infections (including sepsis/pneumonia/reactivation of hepatitis B infection)

Evidence for linking the risk to the medicine	The risk has been observed in preclinical and clinical studies, along with post-marketing reports.
Risk factors and risk groups	Patients with myelosuppression or immune dysfunction. Patients from the areas with high incidence/prevalence of hepatitis B infection, without appropriate vaccination, with blood transfusion or treated with immunosuppressants.
Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.2, Section 4.4 and Section 4.8 **Additional risk minimization measures** None

Table 14 Important potential risk: Developmental toxicity

Evidence for linking the risk to the medicine	The risk has been observed in preclinical studies.
Risk factors and risk groups	Childbearing women, pregnant women and breastfeeding women. It is not known whether panobinostat is excreted in human milk. The risks to the fetus of inadvertent exposure may be considered to be greatest during the early gestation period.
Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.3, Section 4.4, Section 4.5, Section 4.6 and Section 5.3 **Additional risk minimization measures** None

Table 15 Carcinogenicity/Second primary malignancy

Evidence for linking the risk to the medicine	The risk has been observed in preclinical studies.
Risk factors and risk groups	None
Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.3, Section 4.4, Section 4.5, Section 4.6 and Section 5.3 **Additional risk minimization measures** None

Table 16 Important potential risk: Medication error

Evidence for linking the risk to the medicine	Not known
Risk factors and risk groups	None
Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.2 **Additional risk minimization measures** Compliance cards for patients

Part VI – II C: Post-authorization development plan

II.C.1 Studies which are conditions of the marketing authorization There are no studies which are conditions of the marketing authorization or specific obligation of panobinostat.

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

None.