Part VI: Summary of the risk management plan

Summary of risk management plan for Zynrelef (bupivacaine/meloxicam)

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

Zynrelef's SmPC and its package leaflet give essential information to healthcare professionals and patients on how Zynrelef should be used.

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

I. The medicine and what it is used for

ZYNRELEF is authorised for treatment of somatic postoperative pain from small- to medium-sized surgical wounds in adults. It contains bupivacaine and meloxicam as the active ingredients.

Further information about the evaluation of Zynrelef's benefits can be found in Zynrelef'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/zynrelef.

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

Important risks of Zynrelef, together with measures to minimise such risks and the proposed studies for learning more about Zynrelef's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be the following:

- 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 (eg, 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 Zynrelef is not yet available, it is listed under "missing information" below.

II.A List of important risks and missing information

Important risks of Zynrelef 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 Zynrelef. 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 (eg, on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	None.
Important potential risks	Wound healing impairment.
Missing information	Use in breast feeding women.

II.B Summary of important risks

Important potential risk: Wound healing impairment	
Evidence for linking the risk to the medicine	Impaired wound healing was observed in the Phase 3 study of bunionectomy (Study 301) which is a model of surgery with a small, confined anatomic space available to instill Zynrelef. Given there is currently insufficient evidence to conclude that this is a causal association, wound healing impairment is included in the list of safety concerns as an important potential risk for Zynrelef.
Risk factors and risk groups	Patients undergoing bunionectomy (a model of surgery with a small, confined anatomic space available to instill Zynrelef) may potentially be at increased risk of impaired wound healing with Zynrelef treatment.
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2* *SmPC section 4.8* *PL section 2* *PL IFU* Additional risk minimisation measures: *None*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: *None*

Important missing information: Use in breast feeding women	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.6* *PL section 2* Additional risk minimisation measures: *None*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: *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 a specific obligation of Zynrelef.

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

There are no studies required for Zynrelef.