Part VI: Summary of the risk management plan

Summary of risk management plan for [ISOTRETINOIN] soft capsules.

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

[ISOTRETINOIN] soft capsules summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how [ISOTRETINOIN] soft capsules should be used.

Important new concerns or changes to the current ones will be included in updates of [ISOTRETINOIN]'s RMP.

I. The medicine and what it is used for

[ISOTRETINOIN] soft capsules is authorised for Severe forms of acne (such as nodular or conglobate acne or acne at risk of permanent scarring) resistant to adequate courses of standard therapy with systemic anti-bacterials and topical therapy (see SmPC for the full indication). It contains isotretinoin as the active substance and it is given by oral route of administration.

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

Important risks of [ISOTRETINOIN] soft capsules, together with measures to minimise such risks and the proposed studies for learning more about [ISOTRETINOIN] soft capsules 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 the case of [ISOTRETINOIN] soft capsules these measures are supplemented with **additional risk minimisation 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.

II.A List of important risks and missing information

Important risks of [ISOTRETINOIN] soft capsules, 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 [ISOTRETINOIN] soft capsules. 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);

Summary of safety concerns	
Important identified risks	• Teratogenicity • Psychiatric disorders – including depression, suicidality and anxiety
Important potential risks	• None
Missing information	• None

The summary of safety concerns is in accordance with Isotretinoin-ratiopharm, RMP version 8.3, dated 12-11-2020 on the list of safety concerns from the CMDh-website (rev 36)).

II.B Summary of important risks

Important identified Risks: Teratogenicity	
Risk minimization measures	*Routine risk minimisation measures:* SmPC section 4.4, PIL section 4 Prescription only medicine Prescription should be limited to 30 days treatment. *Additional risk minimisation measures:* • educational PPP • Patient reminder card • Pharmacist material (optional) • Physician checklist/acknowledgement form • DHPC (2018); DHPC (2024, PL) • Information for Patients (2024, PL)
Additional pharmacovigilance activities	*Additional pharmacovigilance activities:* Qualitative Survey to investigate barriers and reasons why certain measures part of the PPP are not always followed in clinical practice.
Important potential risks: Psychiatric disorders – including depression, suicidality and anxiety	
Risk minimization measures	*Routine risk minimisation measures:* SmPC sections 4.4 and 4.8 PIL sections 2 and 4. Prescription only medicine Prescription should be limited to 30 days treatment. *Additional risk minimisation measures:* DHPC from 2018

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

Not applicable.

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

Qualitative Study

Purpose of the study:

In Europe, what are the barriers and reasons for low adherence to the oral retinoid therapy PPP measures from the perspectives of (i) healthcare professionals (HCPs) who prescribe or dispense oral retinoid therapy to women of childbearing potential (WCBP), (ii) WCBP who recently used or are currently using oral retinoid therapy, (iii) parents, guardians, or caregivers of adolescent WCBP who recently used or are currently using an oral retinoid therapy?

The overarching global objectives for all three populations of this study are the following:

P1. To describe the understanding of oral retinoid therapy PPP measures

P2. To describe the acceptability of oral retinoid therapy PPP measures

P3. To identify barriers and potential facilitators influencing adherence to oral retinoid therapy PPP