Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for Isotretinoin Actavis/Isotretinoin Teva/Isomacne/Acnenor

This is a summary of the risk management plan (RMP) for Isotretinoin Actavis/Isotretinoin Teva/Isomacne/Acnenor (hereinafter also referred to as Isotretinoin). The RMP details important risks of Isotretinoin, how these risks can be minimised, and how more information will be obtained about Isotretinoin's risks and uncertainties (missing information).

Isotretinoin's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Isotretinoin 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 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 antibacterials and topical therapy (see SmPC for the full indication). It contains Isotretinoin as the active substance and it is given orally.

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

Important risks of Isotretinoin, together with measures to minimise such risks and the proposed studies for learning more about Isotretinoin’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.

In the case of Isotretinoin, 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 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 Isotretinoin. 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 Part VI.II.A: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Teratogenicity • Psychiatric disorders - including depression, suicidality and anxiety
Important potential risks	• None
Missing information	• None

II.B Summary of Important Risks

Table Part VI.II.B: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Teratogenicity	
Evidence for linking the risk to the medicine	Justification of safety concern with a submission of this RMP: A requirement to present the important identified risk linked to additional pharmacovigilance activities and additional risk minimization measures, updated following Article-31 referral (EMEA/H/A-31/1446).
Risk factors and risk groups	The risk of giving birth to a deformed child is exceptionally high if isotretinoin is taken before or during pregnancy, no matter for how long or at what dosage. This risk applies during treatment with isotretinoin and one month after treatment.
Risk minimisation measures	<u>Routine risk minimisation measures</u> SmPC sections 4.3, 4.4, 4.5, and 4.6. PL section 2. *Key messages:* For SmPC/PL: • Causes severe and life-threatening birth defects in the unborn child • Strictly contraindicated in pregnant women and women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met. For outer packaging: CAN SERIOUSLY HARM AN UNBORN BABY • Women must use effective contraception • Do not use if you are pregnant or think you may be pregnant. Prescription only medicine. <u>Additional risk minimisation measures</u> PPP. Reminder DHPC (to be agreed on the national level).

Additional pharmacovigilance activities	Additional pharmacovigilance activities A qualitative study on HCPs and Patients' perceptions, behaviors, perspectives, and barriers on the implementation of the PPP.
Important identified risk: Psychiatric disorders - including depression, suicidality and anxiety	
Evidence for linking the risk to the medicine	Justification of safety concern with a submission of this RMP: A requirement to present the important identified risk linked to additional risk minimization measure, updated following Article-31 referral (EMEA/H/A-31/1446).
Risk factors and risk groups	There is no evidence to suggest that any particular patient groups are at special risk.
Risk minimisation measures	Routine risk minimisation measures SmPC section 4.4. PL section 2. Prescription only medicine. Additional risk minimisation measures 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 specific obligation of Isotretinoin.

II.C.2 Other Studies in Post-Authorisation Development Plan

The following study is a required additional pharmacovigilance activity:

Study short name

A qualitative study on Health Care Professionals and Patients' perceptions, behaviors, perspectives, and barriers on the implementation of the PPP

Rationale and study objectives: Study will identify, qualify and describe the barriers and reasons for insufficient adherence with the oral retinoid therapy PPP by HCPs who prescribe or dispense oral retinoid therapy and WCBP treated with oral retinoid therapy in Europe and the preferred ways of HCPs and patients to receive information on the PPP.