Part VI: Summary of the risk management plan

Summary of risk management plan for ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA (isotretinoin)

This is a summary of the risk management plan (RMP) for ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA. The RMP details important risks of ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA, how these risks can be minimised, and how more information will be obtained about ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA 's risks and uncertainties (missing information).
ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA 's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA, should be used.

I. The medicine and what it is used for

ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA are 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). They contain isotretinoin as the active substance and they are given by oral administration in soft capsules, containing 5, 10, 20 and 30 mg, 10 and 20 mg and 40 mg of isotretinoin respectively.

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

Important risks of ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA together with measures to minimise such risks and the proposed studies for learning more about ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA '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 ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, as 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 ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFAare 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 ISODIFA, ISOTRETINOIN DIFA COOPER, ISOTRETINOINA DIFA, ISOTRETINOIN DIFA. 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	• Teratogenicity • Psychiatric disorders- including depression suicidality and anxiety
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Important Identified Risk: Teratogenicity

Risk minimisation measures	Routine risk minimisation measures Current SmPC (PIL accordingly): Absolute contraindication in pregnant or childbearing women are included in SmPC sections 4.3, 4.4. and 4.6 and Special warning and precaution of use in 4.4. PIL section 2. Detailed advice on the Pregnancy Prevention Programme (PPP) in SmPC section 4.4 and PIL section 2. Warning on teratogenicity and embryotoxicity observed in animal experiments in SmPC section 5.3. Visual/text warning on the outer package informing of the teratogenic effect of Isotretinoin. Legal status: ○ Prescription by or under the supervision of physicians with expertise in the use of systemic retinoids and limitation of prescription to 30 days of treatment; continuation of treatment requires a new prescription. ○ Dispensing of isotretinoin by pharmacist within a maximum of 7 days after prescription. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: - follow-up form during pregnancy; - Annual review of the PPP, - PSURs: detailed and cumulative analysis of cases of pregnancies. Additional risk minimization measures: - Direct Healthcare Professional Communication (DHPC), - Physician's checklist/acknowledgement form, - Pharmacist's checklist,
	- Patient reminder card.

Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities</u> A qualitative study on HCPs and Patients' perceptions, behaviors, perspectives, and barriers on the implementation of the PPP.
Psychiatric disorders- including depression suicidality and anxiety	
Risk minimisation measures	<u>Routine risk minimisation measures</u> SmPC sections 4.4 and 4.8. PIL section 4. Recommendation to take particular care in patients with a history of depression in SmPC section 4.4. PIL section 2 advices the patient: • to consult a physician before starting the therapy with Isotretinoin if the patient has already experienced mental health problems; • to inform familiars and friends that Isotretinoin therapy is on-going so that their awareness may be useful to detect mental health deterioration. <u>Additional risk minimization measures:</u> - Direct Healthcare Professional Communication (DHPC).

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 containing medicinal products.

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.