Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for Acitretin (Neotigason) 10 mg and 25 mg hard capsules

This is a summary of the risk management plan (RMP) for acitretin (Neotigason) 10 mg and 25 mg hard-capsules (herein after also referred to as Neotigason). The RMP details important risks of Neotigason, how these risks can be minimised, and how more information will be obtained about Neotigason's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Neotigason is authorised for for severe forms of psoriasis including: erythrodermic psoriasis, localized or generalized pustular psoriasis, and serious keratinization disorders such as: congenital ichthyosis, pityriasis rubra pilaris, Darier's disease, other keratinization disorders resistant to other therapies (see SmPC for the full indication). It contains acitretin 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 Neotigason, together with measures to minimise such risks and the proposed studies for learning more about Neotigason’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 Neotigason, 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 Neotigason 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 Neotigason. 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 25: Summary of Safety Concerns

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

II.B Summary of Important Risks

Table 26: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Teratogenicity	
Evidence for linking the risk to the medicine	Non-clinical data. Clinical experience.
Risk factors and risk groups	The risk of giving birth to a deformed child is exceptionally high if acitretin is taken before or during pregnancy, no matter for how long or at what dosage. The risk applies during the treatment with Acitretin and for up to 3 years after acitretin discontinuation (particularly in women who have consumed alcohol due to possible formation of etretinate).
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 potential risk: Psychiatric disorders – including depression, suicidality and anxiety	
Evidence for linking the risk to the medicine	Clinical experience.
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 acitetin (Neotigason).

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.