Summary of risk management plan for Trexan 2.5 mg and 10 mg tablets (methotrexate disodium) Orion Corporation

Date: 29-06-2020, Version 3.2

The RMP details important risks of this product, how these risks can be minimised, and how more information will be obtained about Trexan's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Trexan is authorised as:

- *Antirheumatic:* Active rheumatoid arthritis in adult patients
- *Antipsoriatic:* Severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, psoralene-ultraviolet A (PUVA), and retinoids. Severe psoriatic arthritis in adult patients.
- *Cytostatic:* Maintenance therapy in acute lymphoblastic leukemia (ALL)

It contains methotrexate as the active substance and it is taken by mouth.

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

Important risks, together with measures to minimise such risks and the proposed studies for learning more about Trexan'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 Trexan these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

If important information that may affect the safe use of Trexan is not yet available, it is listed under 'missing information' 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*.

If important information that may affect the safe use of the product is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Trexan 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 the product. 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	• Haematological toxicity • Hepatotoxicity • Pulmonary toxicity • Renal toxicity • Administration during pregnancy and lactation • Risk of medication errors due to inadvertent daily instead of once weekly dosing
Important potential risks	None
Missing information	None

II.B Summary of important risks

Safety concerns are adequately addressed in product information.

Important identified risk: Risk of medication errors due to inadvertent daily instead of once weekly dosing	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC sections 4.2, 4.4 and 4.9 PL section 2 and 3. Package label Warnings regarding wrong daily administration and advice/measures how to ensure that medicine is taken only once a week (for psoriasis and rheumatoid arthritis) is given in product

Important identified risk: Risk of medication errors due to inadvertent daily instead of once weekly dosing	
	information. Place where the day of intake can be written is included in the outer carton. Bottle packages will be replaced with blisters. <u>Additional risk minimisation measures:</u> Educational material for Healthcare Professionals including Direct Healthcare Professional Communication Patient card
Routine pharmacovigilance activities	<u>Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:</u> Specific targeted adverse reaction follow-up questionnaire form to be used for all medication errors reported with methotrexate and resulting in overdose.

II.C Post-authorisation development plan

There are no studies required for this product.