Summary of risk management plan for Methotrexate Orion 25 mg/ml Solution for Injection in Pre-Filled Syringe (Methotrexate) Orion Corporation

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This is a summary of the risk management plan (RMP) for Methotrexate Orion. The RMP details important risks of this product, how these risks can be minimised, and how more information will be obtained about Methotrexate Orion's risks and uncertainties (missing information).

Methotrexate Orion'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

Methotrexate Orion is authorised for

- Active rheumatoid arthritis in adult patients where treatment with disease modifying antirheumatic drugs (DMARD) is indicated.
- Polyarthritic forms of severe, active juvenile idiopathic arthritis (JIA), when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- Severe forms of psoriasis vulgaris, particularly of the plaque type, which cannot be sufficiently treated with conventional therapy such as phototherapy, PUVA, and retinoids, and severe psoriatic arthritis

It contains methotrexate as the active substance and it is given as injection under the skin (subcutaneously) or in the muscle (intramuscularly).

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 Methotrexate Orion'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed 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 Methotrexate Orion 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 sections 2, 3 and instructions for use.

Important identified risk: Risk of medication errors due to inadvertent daily instead of once weekly dosing	
	Package label Patients must be clearly informed, that Methotrexate Orion must be administered once a week, not every day. Patients should be aware of importance of adhering to the once weekly intakes and that incorrect use of methotrexate can result in severe and even fatal adverse reactions. Package label Box with red frames in the outer carton to remind that medicine should be used only once a week. The framed box includes space where the day of administration should be written. “Use only once a week” reminder in the intermediate package. Similar reminder in the inner package if space allows. <u>Additional risk minimisation measures:</u> Direct Healthcare Professional Communication (DHPC)
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 which are conditions of the marketing authorisation or specific obligation of this product.

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

There are no studies required for this product.