Curatis AG	Gebro Pharma AG	Orion Pharma AG
Pfizer AG	Sandoz Pharmaceuticals AG	Teva Pharma AG

IMPORTANT COMMUNICATION

Low-dose methotrexate in rheumatoid arthritis and psoriasis:
ADMINISTRATION ONLY ONCE A WEEK
Measures for preventing accidental overdoses resulting from daily administration

Methotrexate preparations authorised for use in rheumatoid arthritis and psoriasis

Methotrexat Farmos tablets: 2.5 mg and 10 mg (pack of 100 tablets)
Methotrexat Pfizer tablets: 2.5 mg (pack of 100 tablets)
Methotrexat Sandoz tablets: 5 mg (pack of 20 tablets) and 10 mg (pack of 10 tablets)
Metoject prefilled syringes
Methrexx prefilled syringes
Methotrexat Farmos, solution for parenteral administration
Methotrexat Pfizer, solution for parenteral administration
Methotrexat Sandoz, concentrate for solution for infusion
Methotrexat Teva, solution for parenteral administration
Methotrexat Proreo, solution for parenteral administration (only for the indication of psoriasis)

Dear Sir/Madam,

In consultation with Swissmedic we would like to inform you about jointly devised measures for preventing accidental overdoses as a result of daily instead of once weekly administration of low-dose methotrexate in patients with rheumatoid arthritis or psoriasis.

Summary

- Despite warnings in the medicinal product information texts and repeatedly in professional publications, cases of serious accidental overdosage with low-dose methotrexate continue to occur as a result of incorrect daily administration in patients with rheumatoid arthritis or psoriasis.
- The specified weekly interval conflicts with the normal habit of taking medicines, particularly tablets, on a daily basis.
- Together with Swissmedic, the Patient Safety Switzerland foundation and the relevant patient organisations, further measures have now been devised for ensuring that all those concerned are aware of, and observe in daily practice, the correct once weekly administration of low-dose methotrexate. **The success of these measures depends on their consistent implementation by all those concerned in daily practice. We would welcome your support.**

Risk

- From January 1997 to July 2015, 18 incidents involving the incorrect daily administration of low-dose methotrexate, primarily via the oral route but in isolated cases after subcutaneous administration, were reported to Swissmedic.

- Four of these intoxications had a fatal outcome (2000, 2009 (2) and 2014). The daily administration was continued for 10 days or more in these cases, while three of the four patients also had renal insufficiency.
- Mucositis, stomatitis, diarrhoea, vomiting, skin lesions, fever, bleeding episodes, unusual weakness or fatigue (as a result of myelosuppression) raise suspicions of intoxication, which requires urgent hospitalisation.
- The mistakes can occur both at the start of treatment or at any time when therapy is well established. Any change is critical, e.g. from s.c. prefilled syringes to tablets, or a change in institution or caregiver.
- The mistakes occur at all levels, including errors at medical prescribing, wrong administration by caregivers or relatives mistakes at dispensing in the pharmacy as well as wrongadministration by the patients themselves. A lack of, or poor, communication plays a crucial role.

New measures

1. Patient Card

Please find enclosed the Patient Card(s). The card is intended to be issued to the patient by the doctor/pharmacist, who enters the specified day of the week for administration and the methotrexate preparation. The card provides information on correct administration, possible symptoms of an overdose and the steps to be taken in this situation. The patients should carry the card with them and present it to doctors and medical personnel, particularly on admission to a hospital department or care institution or in the event of a change in the caregivers.

2. Sticker/fixed overprint on the pack (German and French)

The following “Boxed Warning” has been affixed to the outer packages as a sticker or fixed overprint: For rheumatoid arthritis and psoriasis, take/administer only once a week. The pack also has space for the dispensing outlet to enter the specified day of the week for administration.

3. Boxed warning on the SPC and patient information leaflets

Notice highlighted prominently in colour and framed in a box in the “Dosage and administration” section stating that the medicinal product may be taken/administered only once a week for non-oncological indications and requesting the prescriber to note the day of the week for administration on the prescription.

Recommendation: Two-person checking

Hospitals and care institutions are advised to appoint a professional who will be responsible for checking all prescriptions of low-dose methotrexate before they are released. Two-person checking should be employed in practice if possible.

Reporting adverse reactions

For reports of adverse drug reactions (ADRs), Swissmedic recommends the use of the reporting portal developed for this purpose. ADRs can be recorded and submitted using the Electronic Vigilance System (EIViS). (All the necessary information can be found at www.swissmedic.ch > Market surveillance > Pharmacovigilance).

Ordering and downloading the Patient Card

The Patient Card is available in credit card format in German, French or Italian. It can be ordered from the company contacts listed below. The content can also be downloaded in a larger font and format from the websites of the companies and Swissmedic.

Company contacts

To order the Patient Cards in credit card format, or if you have any questions, please contact the authorisation holders listed below:

Company	Preparation	Tel.: Fax:	e-mail
Curatis AG	Methotrexate Proreo	Tel.: 061 927 8777 Fax 061 927 8775	info@curatis.com
Gebro Pharma AG	Metoject	Tel.: 061 926 88 33 Fax: 061 926 88 44	info@gebro.ch
Orion Pharma AG	Methotrexate Farmos	Tel.: 041 767 40 90 Fax: 041 767 40 99	info.switzerland@orionpharma.com
Pfizer AG	Methotrexate Pfizer	Tel.: 043 495 71 11 Fax: 043 495 72 80	info.ch@pfizer.com
Sandoz Pharmaceuticals AG	Methotrexate Sandoz Methrexx	Tel.: 041 763 74 11 Fax: 041 763 74 00	info.switzerland@sandoz.com
Teva Pharma AG	Methotrexate-Teva®	Tel.: 061 705 43 43 Fax:061 705 46 27	kundendienst@mepha.ch

Yours sincerely,

The authorisation holders

Curatis AG	Gebro Pharma AG	Orion Pharma AG
Pfizer AG	Sandoz Pharmaceuticals AG	Teva Pharma AG

Encl.: Patient Card