



Direct Healthcare Professional Communication

20/11/2019

Recommendations to avoid potentially fatal dosing errors when using methotrexate for inflammatory diseases

Dear Healthcare Professional,

In agreement with the European Medicines Agency and the Health Products Regulatory Authority (HPRA), we would like to inform you of the following:

Summary

- Dosing errors with serious consequences, including fatalities, have been reported when methotrexate intended for once-weekly use in inflammatory diseases was taken daily.
- Only physicians with expertise in using methotrexate-containing medicines should prescribe them.
- Healthcare professionals who prescribe or dispense methotrexate for inflammatory diseases should
 - provide to the patient/carer complete and clear dosing instructions on the once-weekly dosing;
 - check carefully at every new prescription /dispensing that the patient/carer understands that the medicine must be used once weekly;
 - decide together with the patient/carer on which day of the week the patient uses methotrexate;
 - inform the patient/carer of signs of overdose and instruct them to promptly seek medical advice in case of suspected overdose.

Background on the safety concern

Methotrexate is authorised in the EU for two different groups of indications, each of them with a different dosing schedule:

- For the treatment of cancer in which frequency depends on the regimen and can require daily administration of methotrexate.
- For the treatment of inflammatory diseases including rheumatoid arthritis, psoriasis and Crohn's disease, which require once-weekly use.

Despite measures already taken to prevent dosing errors, serious, sometimes fatal, cases continue to be reported, in which patients being treated for inflammatory diseases have taken methotrexate daily instead of once weekly. A safety review performed at EU level found that these errors can occur at all stages of the medication process.

Therefore, further measures to prevent dosing errors will be introduced, including prominent warnings on outer and inner packaging and updates to the Summary of Product Characteristics and package leaflet. For oral formulations, there will be educational materials for healthcare professionals and a patient card will be provided with each package. In addition, tablets will only be available in blister packs.

Further information

For more information, please refer to EMA review at:

<https://www.ema.europa.eu/en/medicines/human/referrals/methotrexate-containing-medicinal-products>.

Call for reporting

Suspected adverse reactions and **any medication error** should be reported to the to the Health Products Regulatory Authority (HPRA):

- Online Reporting via the HPRA Website: www.hpra.ie.
- Using downloadable form from the HPRA website. An adverse reaction report form can be downloaded from the HPRA Website. This can be sent by Freepost to the HPRA or by email to medsafety@hpra.ie.
- By telephoning the Pharmacovigilance Section of the HPRA, (01) 676 4971.

Company contacts

This information is being provided jointly by the below listed Marketing Authorisation Holders (MAHs). Suspected adverse reactions should also be reported to the relevant MAHs (see contact details below).

Marketing Authorisation Holder	Medicinal Product Full Name	Marketing Authorisation Number	Email contact	Phone
Amdipharm Limited, Ireland	Methotrexate 2.5 mg Tablets	PA1142/030/001	medicalinformation@advanzpharma.com	+44 (0) 8700 7030 33
medac GmbH (Wedel, DE)	Metoject 50 mg/ml Solution for injection, pre-filled syringe	PA0623/014/001	medical@dccvital.com	086-8394447 or 09066-61109
	Metoject 7.5 mg solution for injection in pre-filled pen	PA0623/014/002		
	Metoject 10 mg solution for injection in pre-filled pen	PA0623/014/003		
	Metoject 15 mg solution for injection in pre-filled pen	PA0623/014/004		
	Metoject 20 mg solution for injection in pre-filled pen	PA0623/014/005		
	Metoject 25 mg solution for	PA0623/014/006		

	injection in pre-filled pen			
Pfizer Healthcare Ireland	Methotrexate 2.5mg tablets	PA0822/206/004	GBR.AEReporting@Pfizer.com	1800 633363
	Methotrexate 10mg tablets	PA0822/206/005		
	Methotrexate 5g/50ml Solution for injection	PA0822/206/007		
	Methotrexate 5mg/2ml Solution for injection	PA0822/206/001		
	Methotrexate 500mg/20ml Solution for injection	PA0822/206/003		
	Methotrexate 50mg/2ml Solution for injection	PA0822/206/002		
Accord Healthcare Ireland Ltd	Methofill 10mg solution for injection in pre-filled injector	PA2315/060/003	MedInfo@accord-healthcare.com	0044 1271 385 257
	Methofill 12.5 mg solution for injection in pre-filled injector	PA2315/060/004		
	Methofill 15mg solution for injection in pre-filled injector	PA2315/060/005		
	Methofill 17.5 mg solution for injection in pre-filled injector	PA2315/060/006		
	Methofill 20 mg solution for injection in pre-filled injector	PA2315/060/007		
	Methofill 22.5 mg solution for injection in pre-filled injector	PA2315/060/008		
	Methofill 25 mg solution for injection in pre-filled injector	PA2315/060/009		
	Methofill 27.5 mg solution for injection in pre-filled injector	PA2315/060/010		
	Methofill 30 mg solution for	PA2315/060/011		

	injection in pre-filled injector			
	Methofill 50 mg/mL solution for injection in pre-filled syringe	PA2315/060/001		
	Methofill 7.5 mg solution for injection in pre-filled injector	PA2315/060/002		
	Methotrexate 10 mg tablets	PA2315/062/002		
	Methotrexate 100 mg/ml concentrate for solution for infusion	PA2315/061/002		
	Methotrexate 2.5 mg tablets	PA2315/062/001		
	Methotrexate 25mg/ml Solution for Injection	PA2315/061/001		
Morningside Healthcare Ltd	Methotrexate 10 mg tablets	PA1333/009/001	medicalenquiry@morningsidehealthcare.com	+44 (0) 345 4592137
	Methotrexate 2.5mg tablets	PA1333/009/002		
Orion Corporation	Methotrexate 10 mg tablets	PA1327/009/002		
	Methotrexate 2.5mg Tablets	PA1327/009/001		
	Methotrexate Orion 10 mg tablets	PA1327/019/002	ie.medicalinformation@orionpharma.com	+353 1 428 7777
	Methotrexate Orion 2.5 mg Tablets	PA1327/019/001		

Yours sincerely,



Dr Declan O'Callaghan
Medical Director (Pfizer Healthcare Ireland)

And on behalf of:
Accord Healthcare Ireland Ltd
Amdipharm Limited, Ireland
medac GmbH (Wedel, DE)
Morningside Healthcare Ltd
Orion Corporation