



Project to Collect Medical Near-Miss/
Adverse Event Information

Medical Safety Information

No.167, October 2020

Bone Marrow Suppression Due to Antirheumatic (Methotrexate) Overdose (2nd Follow-up Report)

Events in which bone marrow suppression resulted from an overdose of an antirheumatic (methotrexate) were highlighted in Medical Safety Information No.2 (January 2007) and Medical Safety Information No.45 (August 2010). As seven similar cases have subsequently been reported, information about this issue is hereby provided once again (information collection period: from January 1, 2015 to August 31, 2020). This information was compiled on the basis of the content featured in the Recurrence of Events and Occurrence of Similar Events section of the 61st Quarterly Report.

Cases have again been reported in which a patient was affected by the administration on consecutive days of a methotrexate preparation requiring a drug holiday.

Drug Name	Intended Administration Regime	Number of Days of Consecutive Administration	Main Background Factors Concerning Information about Administration Days			
Methotrexate Capsules 2 mg	1 day of administration 6 days of drug holiday per week	28 days	Prescription	<ul style="list-style-type: none"> The quantity prescribed was correct, but the physician forgot to write "Take once a week on a ● day" in the comments field After erroneously prescribing 30 days' supply, the physician changed the prescription to once a week following an inquiry about the prescription, but did not write "Take once a week on a ● day" in the comments field The pharmacist made an inquiry about the prescription, because the drug was prescribed for consecutive days, but the physician replied, "It's fine as it is, because we'll adjust it on the ward," so the pharmacist dispensed the drug. The physician did not tell the nurse about the adjustment to be made 		
		10 days				
Rheumatex Capsules 2 mg		7 days				
		7 days				
Methotrexate tablets 2 mg		6 days			Dispensing	<ul style="list-style-type: none"> Although the comment on the prescription stated "once a week" and "Take on a ● day," the pharmacist did not write the comment on the drug bag, because they deemed the patient to be capable of self-administration
		6 days				
Metolate tablets 2 mg	5 days					

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Case 1

Rheumatrex Capsules were prescribed for the first time to a patient (aged in their 70s) with rheumatoid arthritis. The physician explained to the patient that it was a drug to be taken once a week, but forgot to write "Take once a week on a ● day" in the comments field when entering the prescription. Having been told by the patient that the physician had explained how to take the drugs, the pharmacist at the pharmacy just explained the dosage written on the prescription before handing the drugs over. The day on which the drug should be taken was not written on the drug packaging sheet. The patient took the drug on seven consecutive days and was admitted to hospital as an emergency two weeks later, due to mild liver damage and pancytopenia.

Case 2

The patient (aged in their 70s) had been taking a methotrexate preparation for rheumatoid arthritis for the past 12 years. The physician issued an internal prescription for eight weeks' supply of Methotrexate Capsules 2 mg to be taken once a week and wrote "Take every Sunday after breakfast" in the comments field on the prescription. The pharmacist was supposed to write "Sunday morning" in red on the drug bag, but forgot to do so. As the patient had dementia, a family member was managing their drugs and assumed that the drug was to be taken daily, because the day was not written on the drug bag, so the family member made the patient take the drug on consecutive days. The patient subsequently suffered bone marrow suppression and was admitted to hospital.

Preventive measures taken at the medical institutions in which the events occurred

- When prescribing and dispensing methotrexate preparations:
 - Physicians enter "● times/week on a ● day."
 - Pharmacists check the physician's order and write "● times/week on a ● day" on the drug bag.
- Inform patients that a drug holiday is required and clearly communicate the day on which the drug should be taken.

The measures above are examples. Please consider initiatives suitable for your own facility.

Key Preventive Measures

- As methotrexate preparations are highly dangerous drugs if taken on consecutive days, pharmacists should explain to the patient how to take them every time, without fail.
- When providing explanations to patients, pharmacists should use an instruction sheet or similar to explain how to take the drugs.

(Comprehensive Evaluation Panel)

* As part of the Project to Collect Medical Near-Miss/Adverse Event Information (a Ministry of Health, Labour and Welfare grant project), this medical safety information was prepared based on the cases collected in the Project as well as on opinions of the "Comprehensive Evaluation Panel" to prevent the occurrence and recurrence of medical adverse events. See the Project website for details.

<http://www.med-safe.jp/>

* Accuracy of information was ensured at the time of preparation but cannot be guaranteed in the future.

* This information is intended neither to limit the discretion of healthcare providers nor to impose certain obligations or responsibilities on them.

