

Medication Therapy of High-Dose Methotrexate: An Evidence-Based Practice Guideline Division of Therapeutic Drug Monitoring, Chinese Pharmacological Society

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June 3, 2021

Abstract

Objectives: A lot of medication risks related to high-dose methotrexate (HDMTX) therapy still remain to be identified and standardized. This study aims to establish an evidence-based practice guideline for individualized medication of HDMTX. **Methods:** The practice guideline was launched by the Division of Therapeutic Drug Monitoring, Chinese Pharmacological Society. The guideline was developed following the WHO handbook for guideline development and the methodology of evidence-based medicine (EBM). The guideline was initially registered in the International Practice Guidelines Registry Platform (IPGRP-2017CN021). Systematic reviews were conducted to synthesis available evidence. A multicenter cross-sectional study was conducted by questionnaires to evaluate patients' perception and willingness on individualized medication of HDMTX. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to rate the quality of evidence and to grade the strength of recommendations. **Results:** Multidisciplinary working groups were included in this guideline, including clinicians, pharmacists, methodologists, pharmacologists and pharmacoeconomic specialists. A total of 124 patients were involved to integrate patient values and preferences. Finally, the guideline presents 28 recommendations, regarding evaluation prior to medication (renal function, liver function, pleural effusion, comedications, genetic testing), pre-treatment and routine dosing regimen, therapeutic drug monitoring (necessity, method, timing, target concentration), leucovorin rescue (initial timing, dosage regimen and optimization), management of toxicities. Of them, 12 are strong recommendations. **Conclusions:** We developed an evidence-based practice guideline with respect to HDMTX medication using a rigorous and multidisciplinary approach. This guideline provides comprehensive and practical recommendations involving the whole process of HDMTX medication to health care providers.

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Conflicts of interest disclosure statements for all authors:

All authors reported no potential conflicts of interest.

Statement of funding source:

This work was supported by the Division of Therapeutic Drug Monitoring, Chinese Pharmacological Society, and the National Natural Science Foundation of China (NSFC) (grant number 72074005).

Word count: 6366

Abstract word count : 248

Figure count: 2

Table count: 2

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