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## ARK™ Methotrexate II Assay – Clinical context

September 2025

# What is high dose Methotrexate (HD-MTX) treatment in Oncology?

- HD-MTX is used to treat several conditions including types of Lymphoma, Osteosarcoma and Leukaemia.
- Because MTX has dose-dependent renal clearance and a narrow safety window, as part of the treatment, patients receive aggressive intra-venous (IV) hydration and urine alkalinisation. **Folinic acid (leucovorin) rescue** then starts ~24–36 h after the MTX infusion begins and is **titrated using serial plasma MTX levels**—usually at 24, 48, and 72 h, then daily until cleared.
- Common decision points are **<10 µmol/L at 24 h, <1 µmol/L at 48 h, and <0.1 µmol/L at 72 h**. If levels remain high due to delayed clearance, especially with rising creatinine, clinicians consider **Glucarpidase treatment, which quickly breaks down MTX**. Additionally, drug interactions and any reduction in renal performance also risk delayed clearance.

# Why do fast, precise and accurate MTX lab results matter in clinical practice?

- **Time-critical rescue:** Rapid TAT (turn-around time) enables clinicians to **escalate or de-escalate leucovorin rescue treatment quickly**, preventing under-rescue (toxicity/complications/ICU admission) or over-rescue (unnecessary cost/length of stay (LOS))
- **Safe discharge:** Low-end precision and accuracy **below 0.1 µmol/L** supports confident end of therapy, discharge and avoids extra bed-days, again reducing cost and improving patient care
- **Avoid falsely elevated results:** Negligible cross-reactivity to **7-OH-MTX**, the primary metabolite of MTX, prevents over-treatment, improves patient care, saving time and cost
- **24/7 decisions:** Random-access immunoassay format offers fast TAT and accessibility, keeping oncology pathways moving.
- **System impact:** Fewer blood redraws, and faster decisions reduce ICU transfers, pharmacy spend (leucovorin/fluids), and LOS.

**Bottom line:** In HD-MTX, the MTX lab result **is the therapy 'compass'**, guiding clinicians in leucovorin rescue treatment. The faster and more reliable the result, the safer the patient and the more efficient oncology decision making and the treatment pathway.

# Next generation ARK™ Methotrexate II Assay

Make clinical decisions **faster** with **full-confidence** in HD-MTX treatment



**'Ask-For-ARK™'**



Most precise **and** accurate at low clinical decision-making levels for monitoring MTX clearance (LOQ 0.03  $\mu$ mol/L)



**Highly specific**, with negligible interference from 7-OH-MTX metabolite = **Confidence** ( $\leq 0.01\%$  cross-reactivity)



Shorter turn-around-time for **faster, safer decisions**. Supports 24/7 oncology rescue workflow



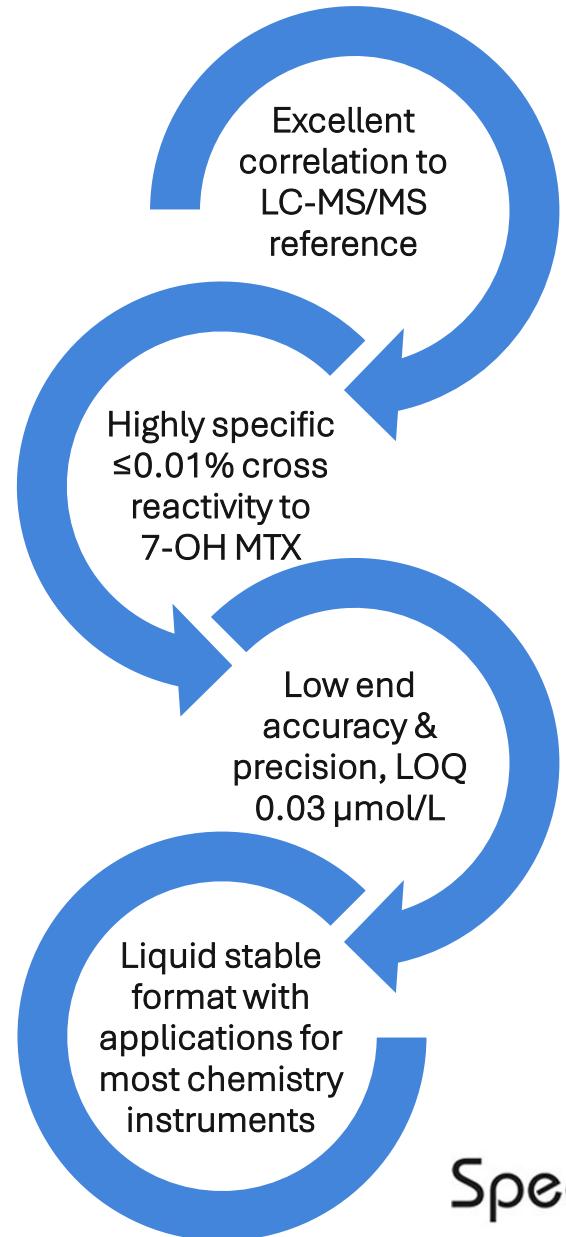
End leucovorin rescue & hydration therapy sooner. **Reduce length of stay and overall costs.**

For In Vitro Diagnostic use. Refer to instructions for use for full details. CE IVDR and FDA cleared.

Specialty  Diagnostix

‘Laboratories can support **faster** and **safer** clinical decision making, **improving patient care** and **reducing overall costs** by implementing the next generation ARK™ MTX II Assay’

**‘Ask-For-ARK™’**



Specialty  Diagnostix

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# But isn't LC/MS the reference method for MTX?

- LC-MS remains the reference method, but often isn't widely accessible within hospital departments to offer fast enough TAT for the safest and most efficient HD-MTX and leucovorin rescue treatment pathways
- LC-MS generally remains labour intensive, complex and requires highly skilled operatives and is best reserved for complex cases and reflex testing (i.e. rare cases where Glucarpidase\* is administered)
- When a high quality, clinically suitable immunoassay is readily available, on routine 24/7 chemistry instruments, overall workflow, clinical decision making and therefore patient care is improved

\*It's important to note that after Glucarpidase treatment in complex and rare cases, labs should reflex to LC-MS/MS (DAMPA interferes with all immunoassays and gives elevated results for at least 48 hours). A note for labs and clinicians should be included in the Lab information system (LIS). This shouldn't be a barrier to ARK MTXII implementation, since cases involving glucarpidase are rare (1- 4% of all cases)

# Not all Methotrexate lab results are equal – are you still relying on quality MTX results?

## **‘Ask-For-ARK™’**

- ARK Diagnostics Assays are recognised by clinical labs and the IVD industry as market leading for quality and technical performance
- The original ARK MTX Assay was, and still is, recommended by several major IVD companies for application on their Immuno-chemistry instruments (e.g. Roche Diagnostics and Siemens Healthineers)
- A recently launched MTX assay by a major IVD company was described as ‘adequate’ for MTX TDM in a publication presented at the 2025 ADLM (Association for Diagnostics & Laboratory Medicine) – is ‘adequate’ good enough?
- The new ARK MTXII Assay re-sets the bar as best in class in terms of overall technical performance and clinical utility (accuracy, specificity and precision at clinical decision-making levels), helping laboratories streamline their workflow and support clinicians in making faster and safer decisions during HD-MTX therapy.



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