



Submitted by:

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NCCN Guidelines Panel: Bone Cancer

On behalf of BTG, I respectfully request the NCCN Bone Cancer panel review the enclosed publications as support for inclusion of the use of glucarpidase as supportive care for patients being treated with high dose methotrexate, and experiencing delayed methotrexate elimination due to renal impairment.

We propose that the following recommendation be made as a footnote to mentions of high dose methotrexate for osteosarcoma in the systemic therapy agents section of the guideline (based on published consensus guidelines and recommendations, enclosed):

"In the event a patient receiving high dose methotrexate experiences delayed elimination due renal impairment, glucarpidase is strongly recommended in the context of a rising serum creatinine if the 36-hour plasma methotrexate level is above 30 µM, 42-hour level is above 10 µM, or 48-hour level is above 5 µM. Optimal administration of glucarpidase is within 48 to 60 hours from the start of methotrexate infusion."

Rationale: In support of the proposed change, an international panel of clinicians convened to provide expert consensus guidelines for the use of glucarpidase in patients who develop acute kidney injury and delayed methotrexate excretion during methotrexate therapy. The guideline provides specific methotrexate plasma concentrations and times that would indicate when glucarpidase should be given, and recommend administration optimally within 48 to 60 hours from start of methotrexate infusion. These guidelines have been adopted by the Children's Oncology Group, and are also referenced in UpToDate, and therefore should be reflected in the NCCN guidelines as well.

The following articles are submitted in support of this proposed change.

1. Ramsey LB, et al. Consensus Guideline for Use of Glucarpidase in Patients with High Dose Methotrexate Induced Acute Kidney Injury and Delayed Methotrexate Clearance. *The Oncologist* 2018 2018 Jan;23(1):52-61.
2. LaCasce AS. Therapeutic use and toxicity of high-dose methotrexate. In: UpToDate, Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>

Sincerely,

A handwritten signature in blue ink that reads "Suzanne Ward".

Suzanne Ward
Senior Director Medical Strategy
BTG International Inc.