

Medicine Shortage Communication

<Date>

<Holoxan/ Tronoxal / Mitoxana> (ifosfamide, <500 mg, 1 g and 2 g> powder for solution for injection): supply shortage

Dear Healthcare Professional,

Baxter is notifying healthcare professionals about a shortage of ifosfamide-containing medicinal products (Holoxan/Tronoxal/Mitoxana)

Overview of situation

- **A technical disruption at Baxter's contract manufacturing site has led to an interruption in the manufacturing and product release of <Holoxan/ Tronoxal / Mitoxana> (ifosfamide, <500 mg, 1 g and 2 g> , powder for solution for injection).**
 - **Baxter is the primary supplier of ifosfamide across the EU.**
 - **This has led, or is expected to lead, to a shortage of the medicine across all EU countries. While the timing of supply interruptions will differ between countries, the supply shortage is expected continue until Q1 2027.**
 - **Baxter is working with the manufacturing partner to restore supply as quickly as possible.**
 - **Available supplies will be allocated through a quota system until the shortage is fully resolved.**
 - **The shortage is not due to any safety, efficacy or quality concern with currently available supplies of ifosfamide.**
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Mitigation measures

To manage the shortage, Baxter is engaging with the European Medicines Agency and the National Competent Authority on mitigation measures.

During the shortage, healthcare professionals should:

- **ensure that sufficient supplies of ifosfamide are available to complete a treatment course, before starting any new patients on treatment.**
- **where necessary, ensure that patients who are already taking this medicine or for whom there are no suitable alternatives are prioritised for use of the limited supply.**
- **if necessary, consider prescribing an appropriate alternative treatment regime according to European treatment guidelines or local treatment protocols.**
- **consult EMA's shortage catalogue, your country's shortage register (where available) or your [national competent authority](#) for additional information on the shortage.**
- **advise concerned patients and caregivers to seek medical advice from their healthcare provider.**

Background on the shortage

Ifosfamide is a cytotoxic drug for the treatment of malignant disease. It is used in adults and children as a single agent and in combination with other drugs and radiotherapy for a wide range of malignant conditions,.

Baxter's contract manufacturing organisation recently experienced a technical disruption that affected site operations, including production planning and inventory systems. At the same time, the site has been implementing corrective actions following a regulatory inspection. Together, these factors have led to a short-term interruption in manufacturing and product release for <Holoxan/ Tronoxal / Mitoxana> (ifosfamide, <500 mg, 1 g and 2 g> powder for solution for injection).

Baxter, as the marketing authorisation holder, is working closely with the manufacturing partner to resolve the situation as quickly as possible. Manufacturing has now resumed at the facility; however capacity remains constrained.

Before initiating ifosfamide treatment for any new patients, healthcare professionals should ensure that sufficient supplies are available to complete a treatment course. It may be necessary to reserve supplies for patients already receiving ifosfamide treatment and for conditions where alternative treatment approaches are less optimal or have limited supporting evidence.

Treatment options for malignant conditions can be complex, nuanced and highly individualised to the patient. Baxter is not able to make individual clinical recommendations for alternative agents. As each clinical scenario is unique to the individual patient, relevant treatment guidelines, local treatment protocols and clinical opinion should inform alternative treatment options. Clinicians should be guided by clinical expertise and accepted alternative treatment regimens contained within local or regional or international treatment guidelines such as the European Society for Medical Oncology (ESMO), European Association of Neuro-Oncology (EANO) or the European Society for Paediatric Oncology (SIOPE) etc. See annex.

Company contact point

Please contact Baxter's Medical Information service, details of which can be found on Baxter's country-specific websites

Annex (EU): Independent Clinical Resources During the Ifosfamide Shortage

Scope

EU-focused signposting to independent guidance and protocol frameworks across tumour types in which ifosfamide is used in routine European practice (e.g., adult soft-tissue/uterine sarcoma, testicular germ-cell tumours, lymphomas, paediatric soft-tissue sarcomas).

ESMO–EURACAN–GENTURIS Soft Tissue & Visceral Sarcomas – Clinical Practice Guideline

Access: <https://www.esmo.org/guidelines/guidelines-by-topic/sarcoma-and-gist/soft-tissue-and-visceral-sarcomas>

EORTC Soft Tissue & Bone Sarcoma Group (STBSG) – Academic cooperative group information

Overview: https://www.eortc.org/research_field/sarcoma/

ESGO/EURACAN/GCIG – Uterine Sarcomas guideline (systemic therapy recommendations)

Access: <https://www.international-journal-of-gynecological-cancer.com/article/S1048-891X%2825%2900159-8/fulltext>

EAU Testicular Cancer Guidelines – full guideline hub + chemotherapy protocols appendix (BEP/EP/VIP)

Guideline hub: <https://uroweb.org/guidelines/testicular-cancer>

Chemotherapy appendix (VIP, etc.): <https://d56bochluxqnz.cloudfront.net/documents/guideline-appendices/testicular-cancer/Appendix-4.-Chemotherapy-Protocols.pdf>

ESMO–EURACAN – Testicular seminoma & non-seminoma guideline (Annals of Oncology)

Access: <https://www.annalsofoncology.org/article/S0923-7534%2822%2900007-2/fulltext>

EHA / ESMO Lymphoma Guidance – hubs/overviews for common lymphoma entities and salvage strategies

ESMO overview article link: <https://www.annalsofoncology.org/article/S0923-7534%2825%2900911-1/fulltext>

EHA guideline hub: <https://ehaweb.org/clinical-practice/guidelines-by-areas-of-disease/guidelines-on-lymphomas>

SIOP Europe (SIOPE) – European Standards of Care & disease-group resources (public)

Portal: <https://siope.eu>

European Standards of Care (PDF): <https://ccieurope.eu/wp-content/uploads/2025/09/European-Standards-of-Care-for-Children-and-Adolescents-with-Cancer-2025.pdf>

EpSSG – European paediatric Soft Tissue Sarcoma Study Group (peer-reviewed recommendations)

Example resource: <https://www.dovepress.com/pediatric-non-rhabdomyosarcoma-soft-tissue-sarcomas-standard-of-care-a-peer-reviewed-fulltext-article-CMAR>

EANO – Guideline index (includes EANO/SNO/EURACAN consensus materials for intracranial GCT management)

Access: <https://www.eano.eu/publications/eano-guidelines/>

Disclaimer

Baxter provides these links solely for clinicians' convenience and makes no therapeutic recommendations. Treatment choices, including any consideration of alternatives during the ifosfamide shortage, remain at the discretion of the responsible healthcare professionals according to applicable guidelines, clinical trial protocols, and local multidisciplinary team governance.

Communication Plan for Medicine Shortage Communication

| MSC COMMUNICATION PLAN | |
|---|--|
| Medicinal product(s)/active substance(s) | Holoxan / Tronoxal / Mitoxana (ifosfamide, 500 mg, 1 g and 2 g, powder for solution for injection) |
| Marketing authorisation holder(s) | Baxter |
| Purpose of the communication | To inform healthcare professionals about a shortage in supply affecting all Member States |
| MSC recipients | Oncologists, haematologists, hospital pharmacists |
| Member States where the MSC will be distributed | All EU/EEA Member States |
| Timetable <i>[Delete steps which are not applicable]</i> | |
| | Date |
| MSC and communication plan (in English) agreed by SPOC WP | 18 February 2026 |
| MSC and communication plan (in English) agreed by MSSG | 6 March 2026 |
| Submission of translated MSCs to the national competent authorities for review | 20 March 2026 |
| Agreement of translations by national competent authorities | 27 March 2026 |
| Dissemination of MSC | 3 April 2026 |