



Conservation Strategies for Fludarabine in Oncology Care

The following considerations have been developed with the input of provincial cancer leads and other clinical experts with the objective of reducing overall intravenous (IV) fludarabine use in the cancer system, and conserving supplies for the highest priority circumstances. Regional programs and hospitals may want to consider local and regional strategies to ensure high priority needs are identified and closely monitored.

A. General Recommendations

For the duration of this supply interruption:

- Sites are encouraged to share locally with hospitals in their Local Health Integrated Network (LHIN) or a neighbouring LHIN to address any acute supply issues. Contact your LHIN drug lead who can facilitate this process.
- Strongly consider prioritizing your patients, conserving IV fludarabine for those who need it most (*e.g., indications with curative intent*).
- Consider not initiating therapy for indications with non-curative intent unless no other therapeutic options are available.
- Consider alternative fludarabine dosage forms (substituting IV for oral where public or private drug coverage allows) for patients currently stabilized on therapy or for those initiating therapy for non-curative indications.
- If modifications to the treatment plan are required:
 - Ensure that modifications are based on the best available evidence, and consider the risk of changing therapy.
 - Seek consultation with clinical experts as appropriate.
 - **Inform patients of any modifications to their treatment plan and the potential impact on overall outcomes.**

B. Clinical Recommendations

Hematologic Cancers

- **Allogeneic Stem Cell Transplantation:** Fludarabine IV is used as part of the conditioning regimen for patients undergoing reduced-intensity (non-myeloablative) or myeloablative allogeneic stem cell transplantation. **For these indications, fludarabine IV use should be given the highest priority for new and pre-booked patients.**

- **Acute Myeloid Leukemia (AML):** Fludarabine IV, as part of the FLAG-IDA regimen, is used with curative intent as front-line induction (followed by consolidation) or as salvage therapy in patients with high risk and/or relapsed or refractory AML. **Fludarabine IV should be prioritized for new and existing patients for this indication.** Alternative induction/re-induction/consolidative regimens could be considered on a case-by-case basis depending on local and regional supply issues.
 - In AML for which the treatment intent is no longer curative, the use of fludarabine-based regimens should be avoided during this shortage as alternative options are available.
- **Chronic Lymphocytic Leukemia (CLL):** A fludarabine-based regimen with rituximab (with or without cyclophosphamide) remains a standard front-line treatment for younger patients with good performance status. For these select patients in whom FC or FCR is the preferred treatment option, consideration should be given towards using oral fludarabine. Oral fludarabine is an eligible Limited Use (LU) benefit under the Ontario Drug Benefit (ODB) formulary for the first-line treatment of CLL in combination with rituximab (with or without cyclophosphamide) (LU code 424). Patients must be ODB eligible in order to qualify.
 - A fludarabine-based regimen may also be used in the second line setting for relapsed or refractory CLL and oral fludarabine is ODB eligible for patients who have failed or are intolerant to chlorambucil (LU code 379).
- **Follicular or other low grade lymphoma:** Fludarabine is used for the treatment of advanced stage follicular or other indolent B-cell histology lymphomas. While there is insufficient data to support the use of fludarabine as initial therapy in these groups of patients, fludarabine is an acceptable option for patients requiring treatment following disease progression after first-line therapy.
 - Given the natural history of this disease, multiple treatment approaches may be considered for recurrent/relapsing disease and no one recommendation is suitable for all patients. Unless no other therapeutic options are available, a non-fludarabine-based regimen should be strongly considered.
 - For select patients in whom fludarabine or a fludarabine-based regimen may be the preferred option, should no other treatment options be available, consideration should be given towards substituting IV with oral fludarabine. Please note that for this indication (low grade non-Hodgkin's lymphoma), oral fludarabine can be considered on a case-by-case basis through the Ministry of Health and Long-Term Care's Exceptional Access Program or for those with private insurance coverage.

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