Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

SMILE(PEG) Regimen

Steroid (dexamethasone)-Methotrexate (with leucovorin)-Ifosfamide (with mesna)-Pegaspargase-Etoposide

Disease Site
Hematologic
Lymphoma - T-cell

Intent
Curative

Regimen Category
Evidence-informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

This **Regimen Abstract** is an **abbreviated** version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Rationale and Uses
Treatment of extranodal natural killer/T-cell lymphoma (ENKTL)

Supplementary Public Funding
pegaspargase
New Drug Funding Program (Pegaspargase - Extranodal Natural Killer/T-cell Lymphoma)

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B - Drug Regimen

To be given as **inpatient**:

methotrexate	2000 mg /m²	IV	Day 1
leucovorin*	15 mg	IV / PO	q6h Days 2 to 4 (start 24h after start of methotrexate)
ifosfamide	1500 mg /m²	IV	Days 2 to 4
mesna	300 mg /m²	IV	Days 2 to 4, immediately before ifosfamide, and at 4 and 8 hrs post-ifosfamide
dexamethasone	40 mg	IV / PO	Days 2 to 4
etoposide	100 mg /m²	IV	Days 2 to 4

To be given as **outpatient**:†

pegaspargase	2500 units /m²	IV / IM	Day 8

*Also refer to local guidelines on urine alkalinization, methotrexate levels and alternative leucovorin dosing.

†ST-QBP funding applies to the outpatient portion of the regimen only.

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a usual total of 2 cycles (up to a maximum of 6 cycles), unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (Days 1 to 4)
Minimal (Day 8)

Febrile Neutropenia Risk: High

Primary prophylaxis with G-CSF is indicated. Refer to the Febrile Neutropenia Guideline.

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

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J - Administrative Information

Pharmacy Workload (average time per visit)	15.150 minutes
Nursing Workload (average time per visit)	37.50 minutes

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K - References

Caddell RJ, Saeed H, Nelson R, et al. Toxicity of a modified peg-asparaginase-based SMILE regimen is comparable to l-asparaginase-based SMILE in a non-Asian population. Blood (2019) 134 (Supplement 1): 5292. https://doi.org/10.1182/blood-2019-128435.

Kwong YL, Kim WS, Lim ST, et al. SMILE for natural killer/T-cell lymphoma: analysis of safety and efficacy from the Asia Lymphoma Study Group. Blood 2012 Oct 11;120(15):2973-80. doi: 10.1182/blood-2012-05-431460.

Li X, Cui Y, Sun Z, et al. DDGP versus SMILE in newly diagnosed advanced natural kliller/T-cell lymphoma: a randomized controlled, multicenter, open-label study in China. Clin Cancer Res. 2016 Nov 1;22(21):5223-5228. doi: 10.1158/1078-0432.

Wang X, Hu J, Dong M, et al. DDGP vs. SMILE in relapsed/refractory extranodal natural killer/T-cell lymphoma, nasal type: a retrospective study of 54 patients. Clin Transl Sci 2021;14(1):405-411. doi:

10.1111/cts.12893.

Wang X, Zhang L, Liu X, et al. Efficacy and survival in newly diagnosed advanced extranodal natural killer/T-cell lymphoma: A randomized, controlled, multicenter and open-labeled study with DDGP regimen versus SMILE regimen. Blood 2019; 134(Supp 1):463.

Yamaguchi M, Kwong YL, Kim WS, et al. Phase II study of SMILE chemotherapy for newly diagnosed stage IV, relapsed, or refractory extranodal natural killer (NK)/T-cell lymphoma, nasal type: the NK-Cell Tumor Study Group study. J Clin Oncol. 2011 Nov 20;29(33):4410-6.

September 2023 Updated the "Additional Information" section with pharmacy and nursing workload.

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M - Disclaimer

Regimen Abstracts

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Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended

that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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