

Regimen Monograph

[Regimen Name](#) | [Drug Regimen](#) | [Cycle Frequency](#) | [Premedication and Supportive Measures](#) | [Dose Modifications](#) | [Adverse Effects](#) | [Interactions](#) | [Drug Administration and Special Precautions](#) | [Recommended Clinical Monitoring](#) | [Administrative Information](#) | [References](#) | [Other Notes](#) | [Disclaimer](#)

A - Regimen Name

SILT Regimen

SILT

Disease Site	Hematologic - Rare Diseases Multicentric Castleman's Disease (MCD)
Intent	Palliative
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.
Rationale and Uses	For the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV)-negative and human herpes virus-8 (HHV-8)-negative and who have an ECOG performance status of ≤ 2 . Approval was based on a phase II study that showed an improvement in durable tumour and symptomatic response rate; a survival benefit has not been demonstrated.
Supplementary Public Funding	siltuximab New Drug Funding Program (Siltuximab - Multicentric Castleman's Disease (MCD)) (NDFP Website)

[back to top](#)

B - Drug Regimen

[siltuximab](#)

11 mg /kg

IV

Day 1

[back to top](#)

C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity.

[back to top](#)

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

For mild to moderate infusion-related reactions, consider pre-medication with antihistamine, acetaminophen and corticosteroid prior to the next infusion.

[back to top](#)

E - Dose Modifications

Refer to protocol by which patient is being treated.

Patients should be tested to confirm they are not HIV or HHV-8 positive before starting treatment. Infections, including localized ones should be treated prior to starting siltuximab.

Do not initiate treatment until ANC $\geq 1.0 \times 10^9/L$, platelets $\geq 75 \times 10^9/L$ and hemoglobin is < 170 g/L.

Dosage with toxicity

Dose reduction is not recommended. Doses may be delayed for toxicity for up to 3 weeks (van Rhee 2014).

Toxicity	Action
ANC < 1 x 10 ⁹ /L or platelets < 50 x 10 ⁹ /L	Hold* until recovery
Severe infection or non-hematologic toxicity	Hold* until recovery
Mild to moderate infusion-related reaction	Slow or hold infusion until recovery and treat. Consider pre-medication** prior to the next infusion.
Severe infusion-related reaction, anaphylaxis or cytokine-release syndrome	Discontinue and manage appropriately

*Do not retreat until ANC $\geq 1 \times 10^9/L$, platelets $\geq 50 \times 10^9/L$, non-hematologic toxicity \leq grade 2 or baseline

**Antihistamine, acetaminophen and corticosteroids

Hepatic Impairment

No formal studies have been conducted. Mild to moderate hepatic impairment had no significant effect on siltuximab pharmacokinetics.

Renal Impairment

No formal studies have been conducted. Mild to moderate renal impairment had no significant effect on siltuximab pharmacokinetics.

Dosage in the elderly

No major age-related changes in pharmacokinetics or safety were observed in clinical studies, but these did not include sufficient numbers of patients aged 65 and older to determine the effect of age on efficacy.

[back to top](#)

F - Adverse Effects

Refer to [siltuximab](#) drug monograph(s) for additional details of adverse effects

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> • Infection (including atypical and Hbv re-activation) • Diarrhea • Peripheral edema 	<ul style="list-style-type: none"> • Rash • Peripheral neuropathy • Nausea, vomiting • Night sweats • Abdominal pain • Hyperuricemia • Hyperlipidemia • Abnormal electrolytes • Headache • Hypertension • Myelosuppression +/- bleeding (may be severe) • Constipation • Increased creatinine (may be severe) • Increased LFTs • Musculoskeletal pain • Fever • Dizziness 	<ul style="list-style-type: none"> • Hypersensitivity, infusion-related reaction • GI perforation • Polycythemia

[back to top](#)

G - Interactions

Refer to [siltuximab](#) drug monograph(s) for additional details

- Binding of siltuximab to IL-6 may increase the metabolism of CYP450 substrates and reduce their efficacy.

-
- Use with caution and monitor closely with CYP3A4 and CYP2C9 substrates (e.g. cyclosporine, warfarin) that have a narrow therapeutic index
 - Siltuximab may reduce the efficacy of oral contraceptives. Consider alternative methods of contraception.

[back to top](#)

H - Drug Administration and Special Precautions

Refer to [siltuximab](#) drug monograph(s) for additional details

Administration

- Reconstitute with sterile water for injection as directed in the product monograph
- Gently swirl to mix; DO NOT shake or stir vigorously
- Do not use if visibly opaque particles are present and/or solution is discoloured
- Dilute reconstituted solution with D5W to the desired concentration
- Administer diluted solution over 1 hour using administration sets lined with PVC, PU or PE containing a 0.2-micron inline PES filter
- Diluted solution should be administered within 6 hours of preparation
- Siltuximab should be refrigerated between 2 to 8°C
- DO NOT freeze and protect from light

Contraindications

Patients who have a hypersensitivity to this drug or any of its components.

Other warnings/precautions

- Live, attenuated vaccines should not be given concurrently or within 4 weeks of starting treatment.
- Clinical studies excluded patients with significant infections, including patients positive for hepatitis B surface antigen. Cases of reactivated hepatitis B have been reported when siltuximab was given with chemotherapy in multiple myeloma patients.
- Use with caution in patients who may be at risk of GI perforation.
- Siltuximab is not recommended for use in pregnancy unless the benefit clearly outweighs the risk. Adequate contraception should be used by both sexes during treatment, and for at least 3 months after the last dose.
- As siltuximab can cross the placenta, exposed infants may be at increased risk of infection; caution is advised in the administration of live vaccines.
- Breastfeeding is not recommended.

[back to top](#)

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Blood pressure; Baseline and as clinically indicated
- CBC; Baseline and before each dose for the first 12 months and every 3 cycles thereafter
- Cholesterol and triglycerides; Baseline and periodic
- Liver and renal function tests; Baseline and as clinically indicated
- Clinical toxicity assessment for infection, bleeding, infusion-related reactions, GI effects; At each visit

- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

Hepatitis B serology; Especially in patients at risk of reactivation

[back to top](#)

J - Administrative Information

Pharmacy Workload (average time per visit) 35.850 minutes

Nursing Workload (average time per visit) 40.750 minutes

[back to top](#)

K - References

Siltuximab drug monograph, Cancer Care Ontario.

van Rhee F, Wong RS, Munshi N, et al. Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. *Lancet Oncol.* 2014 Aug;15(9):966-74.

November 2017 aligned disease site to QBP

[back to top](#)

M - Disclaimer

Regimen Abstracts

A 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). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

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.

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.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

[back to top](#)