# BC Cancer Protocol Summary for Treatment of Lymphoma using Glofitamab

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| ***Protocol Code*** | *ULYOGLOFIT* |
| ***Tumour Group*** | *Lymphoma* |
| ***Contact Physicians*** | *Dr. Laurie Sehn* |

**ELIGIBILITY:**

Patients must have:

- One of the following indications for use for relapsed or refractory disease:
  - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified,
  - DLBCL transformed from indolent lymphoma,
  - High grade B-cell lymphoma,
  - Primary mediastinal B-cell lymphoma, or
  - Follicular lymphoma Grade 3b,

and

- Previously received:
  - Two or more lines of systemic therapy, and
  - CAR T-cell therapy unless unable to receive,

and

- Access to a treatment center with expertise to manage cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), and
- BC Cancer “Compassionate Access Program” request approval prior to treatment

Patients should have:

- No signs or symptoms of active infection

Notes:

- At time of subsequent disease progression, glofitamab retreatment (with one dose of oBINutuzumab administered 7 days prior to first glofitamab dose) is allowed for an additional 12 cycles if:
  - Complete response, partial response, or stable disease on previous glofitamab treatment,
  - Progression-free interval of 6 months or greater from previous glofitamab, or
  - Patients have stopped glofitamab for reasons other than progression (e.g., toxicity or complete response)
  - CAP approval not required for retreatment

Treatment Planning:

| Treatment Day | Drug | Treatment Setting | Post-Infusion Requirement |
|---|---|---|---|
| Cycle 1 Day 1 | oBINutuzumab | Ambulatory care | Observation in treatment facility for 30 minutes after infusion completed |
| Cycle 1 Day 8 | glofitamab Step-up dose 1 | Inpatient | Inpatient observation during infusion and for at least 24 hours after infusion completed |
| Cycle 1 Day 15 | glofitamab Step-up dose 2 | Inpatient if ***any grade*** CRS with Step-up dose 1 | Inpatient observation during infusion and for at least 24 hours after infusion completed |
| | | or | or |
| | | Ambulatory care, if no CRS of ***any grade*** with Step-up dose 1, and if no treatment interruption* | Patient to remain in proximity of treating facility for at least 24 hours after infusion completed** |
| Cycle 2 | glofitamab First full dose | Inpatient if Grade 2 or higher CRS with Cycle 1 Day 15 | Inpatient observation during infusion and for at least 24 hours after infusion completed |
| | | or | or |
| | | Ambulatory care if no CRS of Grade 2 or higher with Cycle 1 Day 15, and if no treatment interruption* | Patient to remain in proximity of treating facility for at least 24 hours after infusion completed** |
| Cycle 3 onward | glofitamab | Inpatient if Grade 2 or higher CRS with previous dose | Inpatient observation during infusion and for at least 24 hours after infusion completed |
| | | or | or |
| | | Ambulatory care if no CRS of Grade 2 or higher with previous dose, and if no treatment interruption* | No post-glofitamab requirements, unless clinically indicated |

* See Dose Modifications and Treatment Interruptions sections, below

** Cycle 1 Day 15 and Cycle 2:
Treatment in the ambulatory care setting for Cycle 1 Day 15 and Cycle 2 requires a local plan in place for rapid assessment and intervention of suspected CRS and ICANS following ambulatory care administration. An adequate local plan must ensure the patient:

- Remains within the proximity of the treating facility for at least 24 hours following completion of glofitamab infusion,

- Is monitored for signs and symptoms of CRS and ICANS,
- Is counselled on the signs and symptoms associated with CRS and ICANS and on seeking immediate medical attention should they occur at any time

**TESTS:**

- Baseline: CBC & Diff
- Baseline, if clinically indicated: creatinine, sodium, potassium, urea, uric acid, total bilirubin, ALT, alkaline phosphatase, phosphate, calcium, albumin, LDH, random glucose, immunoglobulin panel (IgA, IgG, IgM)
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with Cycle 2): HCAb, HBsAg, HbsAb, HbcoreAb
- Prior to each dose of glofitamab: CBC & Diff, vital signs
- If clinically indicated: creatinine, sodium, potassium, phosphate, calcium, magnesium, uric acid, albumin, total bilirubin, ALT, alkaline phosphatase, LDH, random glucose, GGT, immunoglobulin panel (IgA, IgG, IgM), HBV viral load (see protocol SCHBV)

**SUPPORTIVE CARE MEDICATIONS:**

- Very high risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV
- Antiemetics not usually required
- Antiviral prophylaxis against herpes virus infections is recommended prior to initiation of treatment. Patients should take valACYclovir 500 mg PO daily while on treatment and for 3 months following completion of glofitamab treatment
- Pneumocystis jirovecii (PJP) prophylaxis: cotrimoxazole 1 DS tablet PO 3 times each week (Monday, Wednesday and Friday) and for 3 months following completion of glofitamab treatment

**PREHYDRATION:**

- Optional prehydration with 500 mL NS IV over 30 minutes prior to glofitamab can be considered, to minimize risk of hypotension related to CRS

**PREMEDICATIONS:**

**Premedication for oBINutuzumab to prevent infusion-related reactions (IRRs):**

Cycle 1 Day 1:

- 60 minutes prior to oBINutuzumab infusion:
  - dexamethasone 20 mg IV
- 30 minutes prior to oBINutuzumab infusion:
  - acetaminophen 650 to 975 mg PO
  - diphenhydrAMINE 50 mg PO/IV

**Note:** Alternative glucocorticoids include methylPREDNISolone 80 mg IV. *Hydrocortisone is ineffective and not recommended as a premedication for oBINutuzumab but may still be used for an infusion-related reaction.*

**Premedication for glofitamab to prevent CRS and IRRs:**

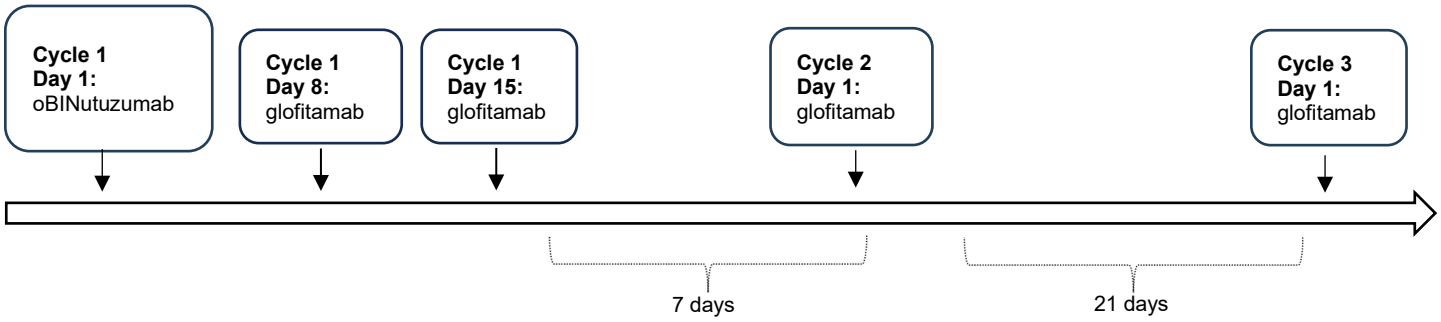
Cycle 1 Days 8 and 15, Cycle 2, and Cycle 3:

- 60 minutes prior to glofitamab:
  - dexamethasone 20 mg IV
- 30 minutes prior to glofitamab:
  - diphenhydrAMINE 50 mg PO/IV, and
  - acetaminophen 650 to 975 mg PO

Cycle 4 to 12:

- If patient experienced *any grade* CRS with previous dose, 60 minutes prior to glofitamab: dexamethasone 20 mg IV
- All patients, regardless if prior CRS, 30 minutes prior to glofitamab:
  - acetaminophen 650 to 975 mg PO, and
  - diphenhydrAMINE 50 mg PO/IV

**Treatment schema:**




- First dose oBINutuzumab followed by glofitamab dose escalation with Step-up dosing schedule mandatory at initiation of treatment and after treatment interruptions if indicated (see Treatment interruptions, below). Do not skip or modify doses. Follow schedule outlined below
- Do not initiate next glofitamab infusion until all CRS symptoms have been resolved for at least 72 hours

**TREATMENT:**

**Cycle 1 Day 1:**

| Drug | Treatment Day | Dose | BC Cancer Administration Guideline |
|---|---|---|---|
| oBINutuzumab | 1 | 1000 mg | IV in 250 mL NS* |
| glofitamab | 8 | Step-up dose 1 2.5 mg | IV in 25 mL NS over 4 hours** |
| | 15 | Step-up dose 2 10 mg | IV in 50 mL NS over 4 hours**† |

* Initiate oBINutuzumab infusion at **50 mg/hour**; after 30 minutes, increase by 50 mg/hour every 30 minutes until rate = 400 mg/hour unless toxicity occurs. Refer to protocol appendix for oBINutuzumab infusion rate titration table.

** Additional line required to ensure minimum rate required to keep vein open (TKVO). Infuse NS IV at 20 mL/h continuous infusion during glofitamab administration via Y-site connector placed immediately before the injection site.

† if CRS of any grade with previous dose of glofitamab, duration of infusion extended to 8 hours

**Day 1 (oBINutuzumab):**

- Vital signs not required, unless symptomatic
- Due to the risk of infusion-related reactions, patients are to be under constant visual observation during all dose increases and for 30 minutes after infusion completed

**Day 8 (glofitamab):**

- In addition to IV for treatment, insert saline lock for emergency management
- Observation: All patients must be hospitalized for monitoring for treatment-related adverse events, in particular CRS and ICANS, during infusion and for at least 24 hours following completion of Cycle 1 Day 8 (Step-up dose 1)
- Vital signs: (including blood pressure, heart rate, temperature and pulse oximetry) to be done prior to Cycle 1 Day 8, every hour during infusion, at the end of the infusion, and as clinically indicated
- If clinical evidence of CRS or ICANS, notify provider immediately. See Dose Modifications, below

**Cycle 1 Day 15 (glofitamab):**

- Ambulatory care treatment:
  - If no CRS and no treatment interruption with Cycle 1 Day 8, patient to be treated in ambulatory care setting for Cycle 1 Day 15
  - Vital signs prior to treatment, at the end of the infusion, and as clinically indicated
  - Patient to remain in proximity of treating facility for at least 24 hours after infusion completed. Patients must be counselled on the signs and symptoms of CRS and ICANS and to seek immediate medical attention should they occur. See treatment planning, above

- Inpatient treatment:
  - If *any grade* CRS or treatment interruption with Cycle 1 Day 8, patient to be admitted during Cycle 1 Day 15 infusion and for at least 24 hours following completion
  - In addition to IV for treatment, insert saline lock for emergency management
  - Observation and vital signs per Cycle 1 Day 8

**Cycle 2** (to be given 7 days after Cycle 1 Day 15)**:**

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| glofitamab | 30 mg on Day 1 | IV in 100 mL NS over 4 hours*† |

* If rate of glofitamab is below 20 mL/hr, infuse NS IV at 20 mL/h continuous infusion during glofitamab administration via Y-site connector placed immediately before the injection site

† if CRS of *any grade* with previous dose of glofitamab, duration of infusion extended to 8 hours

- Ambulatory care treatment:
  - If no Grade 2 or higher CRS and no treatment interruption with previous dose
  - Vital signs prior to treatment, at the end of the infusion, and as clinically indicated
  - Patient to remain in proximity of treating facility for at least 24 hours after infusion completed. Patients must be counselled on the signs and symptoms of CRS and ICANS and to seek immediate medical attention should they occur. See treatment planning, above
- Inpatient treatment:
  - If Grade 2 or higher CRS with previous dose, patient to be admitted to hospital during infusion and for at least 24 hours following completion
  - In addition to IV for treatment, insert saline lock for emergency management
  - Observation and vital signs per Cycle 1 Day 8

**Cycles 3 to 12**:

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| glofitamab | 30 mg on Day 1 | IV in 100 mL NS over 2 hours† |

† if CRS of *any grade* with previous dose of glofitamab, duration of infusion should be maintained at 4 hours

- Ambulatory care treatment:
  - If no Grade 2 or higher CRS and no treatment interruption with previous dose
  - Vital signs prior to treatment, at the end of the infusion, and as clinically indicated
  - Post-treatment monitoring only if clinically indicated
- Inpatient treatment:
  - If Grade 2 or higher CRS with previous dose, patient to be admitted to hospital during infusion and for at least 24 hours following completion
  - In addition to IV for treatment, insert saline lock for emergency management

- Observation and vital signs per Cycle 1 Day 8

**Repeat every 21 days to a maximum of 12 cycles, or until disease progression or unacceptable toxicity.** Retreatment may be allowed (see Eligibility)

**DOSE MODIFICATIONS:**

- No dose reductions are recommended for oBINutuzumab or glofitamab. The infusion may be discontinued, held or its rate reduced as appropriate.

**1. Infusion- Related Reactions to oBINutuzumab:**

- Refer to SCDRUGRX protocol for management guidelines

| Infusion reactions | Management (oBINutuzumab) |
|---|---|
| Grades 1 or 2 (mild or moderate) | • Reduce infusion rate and treat symptoms<br>• Once symptoms resolved, may resume infusion<br>• Titrate infusion rate at appropriate increments– see Administration Guideline for oBINutuzumab, above |
| Grade 3 (severe) | • Hold infusion and treat symptoms<br>• Once symptoms resolved, may resume infusion at no more than half of the rate when reactions occurred (see table below)<br>• Titrate infusion rate at appropriate increments– see Administration Guideline for oBINutuzumab, above |
| Grade 4 (life-threatening) | Stop infusion and discontinue oBINutuzumab therapy |

- hydrocortisone may be used but more potent corticosteroids such as methylPREDNISolone may be required for oBINutuzumab-related infusion reactions

**Infusion rate when resuming oBINutuzumab infusion after Grade 3 symptoms are resolved:**

| oBINutuzumab Infusion Rate When Reactions Occur (mg/h) | Maximum oBINutuzumab Infusion Rate When Resuming Infusion (mg/h) |
|---|---|
| 25 | 10 |
| 50 | 25 |
| 100 | 50 |
| 150 | 50 |
| 200 | 100 |
| 250 | 100 |
| 300 | 150 |
| 350 | 150 |
| 400 | 200 |

## 2. Cytokine Release Syndrome (CRS):

- See management of cytokine release syndrome protocol (SCCRS)
- Cycle 1 Day 15 (glofitamab Step-up dose 2) to be given as inpatient if *any grade* CRS with Step-up dose 1
- Cycle 2 onward: If patient experiences Grade 2 or greater CRS, subsequent dose to be given in inpatient setting

| Grade | Management (glofitamab) |
|---|---|
| 1 | **If CRS symptoms during infusion:**<br>• Hold until resolution<br>• Manage per SCCRS (infusion should be interrupted)<br>• Once symptoms resolve, restart infusion at 50% of rate at which symptoms occurred<br>• If recurrent symptoms after restarting infusion, discontinue current infusion<br>**Subsequent dose:**<br>• Should not be given until CRS symptoms resolved for at least 72 hours<br>• Given per treatment interruption section, below<br>• Administer at 50% rate of previous dose |
| 2 | **CRS symptoms during infusion:**<br>• Discontinue current infusion and do not restart<br>• Manage per SCCRS (infusion should not be restarted)<br>**Subsequent dose:**<br>• Should not be given until CRS symptoms resolved for at least 72 hours<br>• Given per Treatment Interruptions, below<br>• Administer at 50% rate of previous dose |
| 3 | **If CRS symptoms during infusion:**<br>• Manage per SCCRS<br>**Subsequent dose:**<br>• Should not be given until CRS symptoms resolved for at least 72 hours<br>• Given per Treatment Interruptions, below<br>• Administer at 50% rate of previous dose<br>• If recurrent Grade 3 or higher CRS with subsequent infusion, discontinue glofitamab treatment |
| 4 | **If CRS symptoms during infusion:**<br>• Discontinue glofitamab treatment<br>• Manage per SCCRS |

**3. Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS):** see management of ICANS protocol (SCICANS)

| Grade | Management (glofitamab) |
|---|---|
| 1 or 2 | • Manage per SCICANS |
| 3 | • Manage per SCICANS<br>• If resolution takes longer than 7 days, consider discontinuing glofitamab<br>Subsequent dose:<br>• Should not be given until symptoms resolved for at least 7 days<br>• Given per Treatment Interruptions, below |
| 4 | • Discontinue glofitamab treatment<br>• Manage per SCICANS |

**4. Hematological:**

- Proceed with Cycle 1 Day 1 oBINutuzumab regardless of blood counts

| ANC ($x10^9$/L) | | Platelets ($x10^9$/L) | Management (glofitamab) |
|---|---|---|---|
| Greater than or equal to 0.5 | and | Greater than or equal to 50 | 100% |
| Less than 0.5 | and/or | Less than 50 | • Delay* until ANC 0.5 and platelets 50, then<br>• Restart per Treatment Interruptions, below |

* No delay required if decreased counts are due to disease

## 5. Treatment Interruptions:

- Treatment schedule and dose may be affected
- Give oBINutuzumab premedications per Cycle 1 Day 1 if repeating oBINutuzumab after treatment interruption
- Give glofitamab premedication per Cycles 1 to 3 if restarting glofitamab after treatment interruption
- Follow Administration Guideline for applicable dose, above, for appropriate rate of administration

| Last Treatment Administered | Time from last dose administered | Action for Next Dose |
|---|---|---|
| oBINutuzumab | More than 1 week (First dose glofitamab is delayed) | Restart treatment; repeat oBINutuzumab per Cycle 1, Day 1, followed by glofitamab Step-up dosing schedule |
| glofitamab 2.5 mg (Step-up dose 1) | Less than 2 weeks | • Administer 10 mg,<br>• Then resume the recommended dosage schedule |
| | 2 to 6 weeks | • Repeat 2.5 mg, then 10 mg the following week, followed by 30 mg one week later,<br>• Then resume the recommended dosing schedule |
| | More than 6 weeks | • Restart treatment as per Cycle 1, beginning with oBINutuzumab on Day 1 |
| glofitamab 10 mg (Step-up dose 2) | Less than 2 weeks | • Administer 30 mg,<br>• Then resume the recommended dosing schedule |
| | 2 to 6 weeks | • Repeat 10 mg, then 30 mg the following week,<br>• Then resume the recommended dosing schedule |
| | More than 6 weeks | • Restart treatment as per Cycle 1, beginning with oBINutuzumab on Day 1 |
| glofitamab 30 mg | 6 weeks or less | • Administer 30 mg,<br>• Then resume the recommended dosing schedule |
| | More than 6 weeks | • Restart treatment as per Cycle 1, beginning with oBINutuzumab on Day 1 |

**PRECAUTIONS**:

1. **oBINutuzumab Infusion Reactions,** including anaphylaxis, may occur within 24 hours of infusion, usually with the first infusion and decreasing with subsequent infusions. Cycle 1 Day 1 infusion reactions have been most frequently reported at 1 to 2 hours from the start of infusion. Risk factors include a high tumour burden. Infusion reactions may require rate reduction, interruption of therapy, or treatment discontinuation. Patients are to be under constant visual observation during all dose increases and for 30 minutes after infusion is completed. Vital signs are not required unless symptomatic. Monitor patients with pre-existing cardiac or pulmonary conditions closely. Consider temporarily withholding antihypertensive therapies for 12 hours prior to, during, and for 1 hour after infusion.

2. **Infusion-Related Reactions to glofitamab** can occur and may be clinically indistinguishable from CRS. **Treat as signs or symptoms of CRS** (See SCCRS).

3. **Cytokine release syndrome (CRS)** is reported in patients receiving glofitamab and can recur. Most patients experience Grade 1 or 2 reactions, but serious or life-threatening events can occur. Signs and symptoms of CRS may include fever, chills, hypoxia, hypotension, dyspnea, tachycardia, and elevated liver enzymes. Most events occur during Cycles 1 and 2. The incidence of CRS is highest after Step-up dose 1 (glofitamab 2.5 mg) and decreases with each subsequent dose. Median time to onset after Step-up dose 1 is 13 hours. See BC Cancer Drug Manual for details.

   To reduce the risk of CRS, pretreatment with oBINutuzumab is administered 7 days prior to the first dose of glofitamab to deplete the circulating and lymphoid B cells, and glofitamab is initiated with a Step-up dosing regimen. Premedication with antihistamine, antipyretic, and corticosteroid prior to glofitamab is recommended.

   Closely monitor patients for signs and symptoms of CRS. At first sign of CRS, admit patient to hospital for further monitoring if not already admitted. CRS may be managed with acetaminophen, intravenous fluids, tocilizumab, corticosteroids, and other symptomatic measures – see management of cytokine release syndrome protocol SCCRS. Permanently discontinue glofitamab for recurrent Grade 3 and Grade 4 CRS.

   Do not initiate the next glofitamab infusion until all CRS symptoms have been resolved for at least 72 hours. If patients present with symptoms suggestive of CRS after Cycle 3, especially after successful full dose free of CRS, other causes such as infection should be thoroughly investigated and ruled out prior to concluding CRS is the cause.

4. **Neurologic toxicity**, including **immune effector cell-associated neurotoxicity syndrome (ICANS)** can occur during treatment with glofitamab. The majority of neurological adverse events occur during Cycle 1 and 2. The onset varies depending on the dose. See BC Cancer Drug Manual for details. Most events are mild to moderate in severity, but serious or fatal neurologic toxicity such as **immune effector cell-associated neurotoxicity syndrome (ICANS)** can occur. Clinical

manifestations of ICANS may include headache, confusion, disorientation, speech disturbances, altered levels of consciousness, seizures, muscle weakness, agitation, and tremor. Management of ICANS may include temporary dose interruption, corticosteroids, anti-seizure medications, and supportive care.

If ICANS occurs, admit patient to hospital for further monitoring if not already admitted. Neurology consult may be required. Hold glofitamab until neurologic toxicity has resolved for at least 7 days. Symptoms are managed depending on their severity and whether they occur concurrently with CRS. Permanently discontinue glofitamab for Grade 4 ICANS. Consider discontinuation for Grade 3 ICANS that takes more than 7 days to resolve. Patients experiencing reduced consciousness or any symptoms that might affect their ability to drive or use machines, should refrain from driving or operating heavy machinery until symptoms resolve. See management of immune effector cell-associated neurotoxicity protocol, SCICANS.

5. **Infections,** including bacterial, fungal, and new or reactivated viral infections have been reported in patients treated with oBINutuzumab and glofitamab. These may be severe or life-threatening. Fatalities have been reported. oBINutuzumab and glofitamab should not be given to patients with an active infection; use cautiously in patients with recurring or chronic infections. Fever or other evidence of infection must be assessed promptly and treated aggressively. Prophylaxis against viral infections and PJP should be administered as per above. Consider IVIG prophylaxis in patients with recurrent infections and low immunoglobulin levels.

6. **Tumour Lysis Syndrome (TLS)** including acute renal failure can occur within 12 to 24 hours after the first infusion of oBINutuzumab. TLS has also been reported in patients treated with glofitamab. Patients considered to be at increased risk for TLS should receive hydration and prophylactic treatment with uric acid lowering agents. Patients should be monitored closely for signs and symptoms of TLS, especially patients with high tumour burden, rapidly proliferative tumours or reduced renal function. Monitor blood chemistries regularly and manage abnormalities promptly.

7. **Hepatitis B Reactivation:** See SCHBV protocol for more details.

8. **Vaccination:** Patients should not receive live or live attenuated vaccines within 4 weeks of starting treatment and at any point during treatment.

9. **Progressive Multifocal Leukoencephalopathy (PML)** may occur caused by reactivation of the JC virus during treatment with oBINutuzumab. Patients should be evaluated for PML if presenting with new neurologic symptoms such as confusion, vision changes, changes in speech or walking, dizziness or vertigo.

10. **Cardiovascular events**, such as myocardial infarction and dysrhythmias have been reported with oBINutuzumab and are sometimes fatal; patients with pre-existing cardiac disease may experience worsening of their cardiovascular disease.

11. **Tumour flare** has been reported with glofitamab, likely due to the activated immune response and T-cell influx towards tumour sites. Symptoms may include pain and swelling at lymphoma sites with tumour inflammation. Manage as indicated, using analgesics, corticosteroids, antihistamines and supportive care.

12. **Drug Interactions:** The initial release of cytokines associated with the start of glofitamab treatment could suppress CYP450 enzymes, resulting in increased exposure of CYP substrates. See BC Cancer Drug Manual.

**REFERENCES:**


1. Hutchings M, Morschhauser F, Iacoboni G, et al. Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell-Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial. J Clin Oncol. 2021 Jun 20;39(18):1959-1970.
2. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2022 Dec 15;387(24):2220-2231.
3. Glofitamab (Columvi) CADTH [Canada's Drug Agency (CDA-AMC)] Reimbursement Recommendation. Canadian Journal of Health Technologies Feb 2024; 4(2): 1-27.
4. CADTH [Canada's Drug Agency (CDA-AMC)] Reimbursement Review. Provisional Funding Algorithm. Large B cell lymphoma. Aug 2024.

## Appendix. oBINutuzumab infusion rate titration table

### Cycle 1: Day 1

| **oBINutuzumab 1000 mg IV in 250 mL NS<br>Total volume = 315 mL** | | |
|---|---|---|
| **TITRATION** | **INFUSION RATE** | **VOLUME TO BE INFUSED (VTBI)** |
| 50 mg/h x 30 min | 16 mL/h | 8 mL |
| 100 mg/h x 30 min | 32 mL/h | 16 mL |
| 150 mg/h x 30 min | 47 mL/h | 24 mL |
| 200 mg/h x 30 min | 63 mL/h | 32 mL |
| 250 mg/h x 30 min | 79 mL/h | 39 mL |
| 300 mg/h x 30 min | 95 mL/h | 47 mL |
| 350 mg/h x 30 min | 110 mL/h | 55 mL |
| 400 mg/h x 45 min | 126 mL/h | 95 mL |