BC Cancer Protocol Summary for Treatment of Lymphoma using Intrathecal Methotrexate and Cytarabine

Protocol Code	*LYIT*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Laurie Sehn*

ELIGIBILITY:
- Large cell lymphoma or any other aggressive histology lymphoma (see Cancer Management Manual) with high risk of CNS involvement
- Primary or secondary CNS lymphoma with leptomeningeal involvement
- Prophylaxis for patients with high risk of CNS recurrence

TESTS:
- Baseline (required before treatment): CBC and differential, platelets, creatinine, bilirubin, ALT, CSF cytology, PTT, INR
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, HBcoreAb
- Weekly before treatment (twice weekly or weekly option) or once before treatment (single dose option): CBC and differential, platelets, PTT, INR
- Before each treatment: PTT, INR, Platelets
- With each treatment: CSF cytology

PREMEDICATIONS:
- not usually required

SUPPORTIVE MEDICATIONS:
If HBsAg or HBcoreAb positive, start lamiVUDine 100mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.

TREATMENT:

Twice weekly option is typically used, but weekly option can be considered based on physician discretion.

A. Twice Weekly Option

Drug	Dose	BC Cancer Administration Guideline • **by physician only** • **lumbar puncture tray required if no Ommaya reservoir**
methotrexate	12 mg on days 1, 8 and 15	Intrathecal (via lumbar puncture or Ommaya ventricular reservoir) qs to 6 mL with **preservative-free** NS
cytarabine	50 mg on days 4, 11 and 18	Intrathecal (via lumbar puncture or Ommaya ventricular reservoir) qs to 6 mL with **preservative-free** NS

B. Weekly Option

Drug	Dose	BC Cancer Administration Guideline • **by physician only** • **lumbar puncture tray required if no Ommaya reservoir**
methotrexate	12 mg on days 1, 15, and 29	Intrathecal (via lumbar puncture or Ommaya ventricular reservoir) qs to 6 mL with **preservative-free** NS
cytarabine	50 mg on days 8, 22 and 36	Intrathecal (via lumbar puncture or Ommaya ventricular reservoir) qs to 6 mL with **preservative-free** NS

C. Single Dose Option: Physicians may change the days of intrathecal chemotherapy. Ensure a minimum of 48 hours between doses.

Patients with established leptomeningeal disease should be continued on treatment for 6 doses after patient's CSF cytology reverted to negative for lymphoma.

For CNS prophylaxis: 6 doses total

Note: Anticoagulants should be held prior to IT treatment as per local guidelines for anticoagulation management.

Procedure for Injecting Chemotherapy into the Intraventricular Space Using an Ommaya Reservoir (By Physician Only)

1. Check that chemotherapy is mixed in **preservative free** normal saline.
2. Use sterile technique, gloves, mask, etc.
3. Have patient in the lying or sitting position.
4. Cleanse skin over the Ommaya reservoir and surrounding scalp with antiseptic after shaving away any recent hair growth.
5. Attach a 25 gauge butterfly needle to a 12 mL syringe.
6. Insert the 25 gauge needle perpendicular to the scalp until the back wall of the reservoir is contacted.
7. Slowly aspirate 6 mL of CSF. Send for cytology and/or culture if appropriate.
8. Attach chemotherapy syringe and inject slowly over about 5 minutes. A more rapid injection frequently causes acute or delayed headaches.
9. To facilitate the flow of the chemotherapy you may gently depress the Ommaya reservoir a few times. Another alternative to flush the system with 1-3 mL of preservative free saline after injecting the chemotherapy. This requires the removal of a similar volume of CSF with the initial CSF withdrawal.
10. Have patient remain at bedrest for 30 minutes after procedure in prone (abdomen down) position.

DOSE MODIFICATIONS:

1. **Hematological**:

ANC (x10^9/L)		Platelets (x10^9/L)	Dose (both drugs)
greater than or equal to 0.5	and	greater than or equal to 50	100%
less than 0.5	or	less than 50*	Delay

*For platelets less than 50x10^9/L, physicians may consider platelet transfusion prior to proceeding with treatment.

2. Coagulation tests:

INR		PTT	Dose (both drugs)
Less than 1.5	and	Less than or equal to the upper limit of normal	100%
Greater than or equal to 1.5	or	Greater than the upper limit of normal	Delay

3. **Symptomatic oral mucositis or arachnoiditis**: Delay until resolved.

PRECAUTIONS:

1. **Neutropenia**: There is some systemic absorption of intrathecal chemotherapy. This may be further complicated by systemic therapy if given concurrently or by poor marrow tolerance due to previous therapy. Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Dysfunction**: Methotrexate, given by any route, should be given with special caution if the creatinine clearance is less than 30 mL/minute with all subsequent doses determined based on hematologic and mucosal tolerance for the first dose given.
3. **Precautions for Intrathecal Administration**: refer to BC Cancer Intrathecal Policy.
4. **Hepatitis B Reactivation**: All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamiVUDine during chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

Call Dr. Laurie Sehn or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Dodd KC et al. Periprocedural antithrombotic management for lumbar puncture: Association of British Neurologists clinical guideline. Practical Neurology 2018:18 (6): 436-466