BC Cancer Protocol Summary for the Treatment of Malignant Mesothelioma using Platinum, Pemetrexed and Pembrolizumab

Protocol Code	*LUMMPPPMB*
Tumour Group	*Lung*
Contact Physician	*LU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Histologically confirmed unresectable advanced or metastatic malignant pleural mesothelioma (MPM), and
- No prior systemic treatment

Patients should have:

- Good performance status,
- Adequate hepatic and renal function,
- Asymptomatic/stable brain metastases (if applicable), and
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab

Note:

- Patients who were started on first-line platinum doublet treatment prior to 1 Mar 2026 and received less than 4 cycles may switch to LUMMPPPMB provided they have not experienced progression and all eligibility criteria are met.
- Patients discontinuing first line treatment with LUMMIPNI or LUMMIPNI3 due to serious adverse effects or toxicity related to dual immunotherapy may switch to LUMMPPPMB provided they have not experienced progression and all eligibility criteria are met.
- At time of subsequent disease progression, pembrolizumab retreatment (with or without chemotherapy) is allowed for an additional 1 year of treatment:
  - Retreatment without CAP approval is allowed for an additional 18 cycles for 3-weekly dosing or 9 cycles for 6-weekly dosing (or a combination of both) if patient has completed the initial pembrolizumab treatment without disease progression.

CAUTIONS:

- Active, known or suspected autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)
- Evidence of interstitial lung disease
- Known history or any evidence of active noninfectious pneumonitis

TESTS:

- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol
- Baseline, if clinically indicated: BNP, troponin, creatine kinase, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), ECG, echocardiogram, chest x-ray
- Before each treatment: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, random glucose, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, ECG, troponin, creatine kinase
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional).

PREMEDICATIONS:

Cycles 1 to 6 only:

- **Vitamin supplementation mandatory** starting at least 7 days prior to the first cycle, and to continue while on treatment, until 21 days after last pemetrexed dose:
  - folic acid 0.4 to 1 mg PO daily
  - vitamin B12 1000 mcg IM every 9 weeks
- Prophylaxis for skin rash: dexamethasone 8 to 12 mg PO prior to treatment, then 4 mg PO every 12 hours for 4 doses.
- Antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA)
- **If prior infusion reactions to pembrolizumab**: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

Cycle 7 onwards (pembrolizumab maintenance):

- Antiemetics are not usually required.
- **If prior infusion reactions to pembrolizumab**: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT:

Cycles 1 to 6:

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter**
pemetrexed	500 mg/m^2	IV in 100 mL NS over 10 minutes**
CISplatin	75 mg/m^2	IV in 500 mL NS over 60 minutes†

* select dose per Dose Banding Table (appendix)
** pembrolizumab and pemetrexed may be given during the pre-hydration period
† pre- and post-hydration protocol for high-dose CISplatin required according to institutional guidelines (e.g., prehydration with 1 L NS over 60 minutes, CISplatin in 500 mL NS with potassium chloride 20 mmol, magnesium sulfate 1 g and mannitol 30 g)

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter
pemetrexed	500 mg/m^2	IV in 100 mL NS over 10 minutes
CARBOplatin	AUC 5 or 6 Dose = AUC x (GFR†† +25)	IV in 250 mL NS over 30 minutes

*select dose per Dose Banding Table (appendix)
†† GFR may be determined by nuclear renogram or estimated by the Cockcroft formula, at the discretion of the attending physician:

$$GFR = \frac{N \times (140\text{-age in years}) \times \text{wt (kg)}}{\text{Serum creatinine (micromol/L)}} \qquad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

The estimated GFR should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.

- Repeat every 3 weeks for up to 6 cycles unless unacceptable toxicity, then proceed to maintenance treatment (Cycle 7 onwards).
- Retreatment may be allowed (refer to Eligibility).

Cycle 7 onwards (maintenance):

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*select dose per Dose Banding Table (appendix)

- Repeat every **3 weeks**

OR

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	4 mg/kg* (maximum 400 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*select dose per Dose Banding Table (appendix)

- Repeat every **6 weeks**

- Duration of treatment:
  - Initial pembrolizumab treatment: until disease progression or unacceptable toxicity, up to a maximum of 35 cycles for 3-weekly dosing or 18 cycles for 6-weekly dosing (or a combination of both including doses given with chemotherapy) or 2 years of treatment.
- Patients may have treatment breaks for reasons other than progression (e.g., toxicities, treatment holiday, vacation).
- Retreatment may be allowed (refer to Eligibility).

DOSE MODIFICATIONS:

No specific dose modifications for pembrolizumab. Toxicity managed by treatment delay and other measures (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).

1. HEMATOLOGY

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
Greater than or equal to 1.5	and	Greater than or equal to 100	100%
Less than 1.5	or	Less than 100	**Delay**

2. RENAL DYSFUNCTION

Creatinine Clearance (mL/min)	CISplatin Dose	Pemetrexed Dose
Greater than or equal to 60	100%	100%
45 to less than 60	80% CISplatin or use CARBOplatin option	100%
Less than 45	Hold	Hold regardless of type of platinum

3. MUCOSITIS

For next cycle:

Mucositis Grade	CISplatin dose	Pemetrexed dose
0 to 2	100%	100%
3 to 4	100%	50% previous dose*
***Discontinue treatment after two dose reductions**		

4. OTHER TOXICITIES:

- For any other Grade 3 or higher toxicity, delay treatment until toxicity resolves, then resume with 25% dose decrease if considered appropriate to resume by attending oncologist.

PRECAUTIONS:

1. **Serious immune-mediated reactions** can be severe to fatal and usually occur during the treatment course with pembrolizumab, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).
2. **Infusion-related reactions:** Isolated cases of severe infusion reactions have been reported with pembrolizumab. Discontinue pembrolizumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive pembrolizumab with close monitoring, reduced rates of administration and use of premedication. Refer to BC Cancer SCDRUGRX protocol.

3. **Vitamin supplements**: Appropriate prescription of folic acid and vitamin B12 is essential. The incidence of adverse events such as febrile neutropenia related to pemetrexed is higher without vitamin supplementation.
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
5. **NSAIDs**: Concurrent nonsteroidal anti-inflammatory agents should be avoided as they may decrease the renal clearance of pemetrexed.
6. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Use caution with pre-existing renal dysfunction.
7. **Neurotoxicity**: CISplatin is neurotoxic and may have to be discontinued if functionally important neuropathy develops. Particular caution must be used in individuals with existing neuropathy.
8. **Ototoxicity**: CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.

Contact the LU Systemic Therapy physician at your regional cancer centre or the LU Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Chu Q, Perrone F, Greillier L, et al. Pembrolizumab plus chemotherapy versus chemotherapy in untreated advanced pleural mesothelioma in Canada, Italy, and France: a phase 3, open-label, randomised controlled trial. Lancet. 2023 Dec 16;402(10419):2295-2306.
2. Pembrolizumab (Keytruda) CDA-AMC Reimbursement Recommendation. Canadian Journal of Health Technologies 2025; 5(7): 1-25.

Appendix. Dose Bands

PEMBROLIZUMAB DOSE BANDING TABLE (2 mg/kg capped 200 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	**To:**	
Less than 70		**Pharmacy prepares specific dose**
70	80.49	**75**
80.5	92.49	**85**
92.5	110.49	**100**
110.5	137.49	**125**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	200	**200**

PEMBROLIZUMAB DOSE BANDING TABLE (4 mg/kg capped 400 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	**To:**	
Less than 137.5		**Pharmacy prepares specific dose**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	221.49	**200**
221.5	242.49	**225**
242.5	264.49	**250**
264.5	284.49	**275**
284.5	332.49	**300**
332.5	374.49	**350**
374.5	400	**400**