Proposed medicines(s) for treatment of Testicular Germ Cell Tumors (refer to application for specific protocols):

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EML</th>
<th>Addition</th>
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<tbody>
<tr>
<td>bleomycin</td>
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<tr>
<td>etoposide</td>
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<tr>
<td>cisplatin</td>
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<tr>
<td>ifosfamide</td>
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<tr>
<td>mesna</td>
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<tr>
<td>G-CSF</td>
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(1) Does the application adequately address the issue of the public health need for the treatment of the disease?

√ Yes ☐ No ☐

Comments:

As testicular germ cell tumours occur in young men between 15 and 40 year old and are lethal if left untreated, there is a public health need for access to chemotherapy drugs which enable cure of disease.

(2) Have all important studies that you are aware of been included in the application?

√ Yes ☐ No ☐

Comments: It would be worthwhile adding the study of Aapro and colleagues (2006) in support for routine use of G-CSF with BEP.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the proposed treatment regimen(s)?

√ Yes □ No □

Comments:
The evidence provided supports the claim for efficacy of the proposed treatment regimen.

(4) Does the application provide adequate evidence of safety for the proposed treatment regimen(s)? Are there any adverse effects of concern, or that may require special monitoring?

√ Yes □ No □

Comments:
The application provides adequate evidence of safety of the proposed treatment regimen and a comprehensive review of side effects.

Other potential side effects which may need monitoring:
1. Ototoxicity
   Cisplatin induced ototoxicity may occur; patients should be monitored for signs and symptoms.

2. Peripheral neuropathy
   Assess prior to each cycle. If a patient experiences > grade 2 a dose reduction or delay of treatment may be required; review by medical officer before commencing treatment.

3. Pulmonary function
   Baseline clinical assessment and pulmonary function tests (including DLCO), repeat with each cycle.

4. Chest x-rays may be considered where clinically indicated.

5. Blood tests
   Blood tests: Baseline and repeat prior to each cycle FBC, EUC, LFTs, calcium and magnesium. For cycle 1, repeat EUC on day 8.

Note. In addition, cisplatin is a highly emetogenic agent. Correct anti-emetic regimen needs to be prescribed with the chemotherapy (Ondansetron, dexamethasone).

Additional monitoring for VIP chemotherapy
For ifosfamide, it is important to monitor for bladder toxicity and neurotoxicity.
Ifosfamide infusion
Prior to administration
- assess neurological function at baseline and prior to each ifosfamide dose
- Inpatients: 4 hourly assessments until 24 hours after ifosfamide infusion is completed
Outpatients: advise patient/carer of the potential for neurotoxicity
- perform baseline urinalysis and monitor for haematuria prior to each ifosfamide dose
(note the administration of mesna will cause a false positive for ketonuria)

ADDITIONAL CONSIDERATIONS:

(5) Are there special requirements or training needed for the safe, effective and/or appropriate use of the proposed treatment(s)?

Yes ☑ No ☐

Comments:

Patients should be preferably treated in centers that are experienced in the management of germ cell tumours.
Medical Oncologists only can prescribe and supervise chemotherapy for ovarian germ cell tumours. Chemotherapy –trained nurses only can administer the drugs.

(6) Are there any issues regarding the registration of the proposed medicines by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes ☐ ☑ No ☐

Comments:

Not that we are aware.

(7) Comment briefly on issues regarding cost and affordability of treatment.

As drugs used in BEP regimen are off patent use and widely used in treatment of testicular cancer, the cost and affordability of treatment should not pose any additional significant burden on the health systems of different countries, especially as its aim is to treat a rare and potentially curable disease of the young males.

(8) Any additional comments on the application?

These life-saving treatments for germ cell tumours should be made accessible to all young males who suffer from this disease.

(9) Please summarise the action(s) you propose the Expert Committee take.

Ensure that Cisplatin and G-CSF are added on the WHO of essential medicine for treatment of ovarian germ cell tumours in males.