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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</tbody>
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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:
The application stated that TGCT account for 1% of all newly diagnosed male cancers worldwide and were the most commonly found cancer in young males ages 20 to 40. The backbone of standard therapy included cisplatin-based combination chemotherapy. The studies we added also agree with that.

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

Yes ☐ No ☒

Comments:
The application included some RCTs and reviews. We added seven guidelines and four systematic reviews (N=24, n=10131) through systematic searching.

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

Yes ☒ No ☑

Comments:
The application stated that cisplatin-based combination chemotherapy had significant improvements in response rates and overall survival rates, were extremely important for more advanced TGCT (Stage II disease had a cure rate of >95%, stage III disease with good, intermediate, and poor prognosis had cure rate of >95%, 75% and 50% respectively). The studies we added also agree with that.

(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 safety and adverse effects of the proposed treatment regimen were concerned adequately in the application:
1. Men treated with cisplatin commonly suffered peripheral neuropathy, nephrotoxicity, and ototoxicity.
2. With cisplatin, close monitoring of routine labs and aggressive intravenous hydration pre and post-chemotherapy were necessary to avoid significant declines in renal function, and prophylactic intravenous anti-emetics due to cisplatin with highly emetogenic.
3. During chemotherapy, serum markers should be monitored to prevent risk of recurrence and adverse prognosis.
4. To address potential adverse events caused by the treatment itself, including marrow suppression, neutropenic fever, bleomycin-induced pulmonary toxicity, and gastrointestinal toxicity.
The studies we included also agree with that.

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:
The safe, effective, and appropriate use of cisplatin had been stated in the application (see question 4)
The studies we included also agree with that.

(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:
The application stated that cisplatin had been registered by EMA (European Medicines Agency) and FDA (US Food and Drug Administration) for testicular tumors. We found cisplatin had also been registered in CFDA (China Food and Drug Administration) for testicular tumors.
(7) Comment briefly on issues regarding cost and affordability of treatment. Neither the application nor our added studies provide any evidence about cost evaluation. We calculated the cost of cisplatin with the price of the tertiary hospital which we worked in, and we found that the cost using cisplatin for a course of treatment was ¥723.6~964.8 ($115.7~154.3). Since it was in health insurance directory of China and the government will pay the fees, the affordability of cisplatin was good for patients in China.

(8) Any additional comments on the application? None.

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

We recommend cisplatin be listed in WHO EML for TGCT, due to:
Adequate evidence of effectiveness and good affordability.