20th Expert Committee on Selection and Use of Essential Medicines

Peer Review Report #2a

[Granulocyte-Colony Stimulating Factor (G-CSF) for Testicular Germ Cell Tumor (TGCT)] (section 8.2)

(1) Does the application adequately address the issue of the public health need for the medicine?

Yes ☒ No ☐

Please provide brief details:
The application suggested that prophylactic use of G-CSF during chemotherapy to reduce the risk of Febrile neutropenia (FN) and infection-related mortality. The studies we included also agree with that.

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

Yes ☐ No ☒

Please provide brief comments on any relevant studies that have not been included: The application did not include any study about use of G-CSF for TGCT. One randomized, multicenter phase III trial (n=380) and four observational studies (n=22), we added, were related the use of G-CSF for TGCT.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?

Yes ☐ No ☒

Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine: The application did not provide any relevant evidence of the efficacy about G-CSF for TGCT, but only for FN. We added insufficient evidence of efficacy about G-CSF for TGCT, including one RCT and four low-quality observational studies. The RCT reported that the routine use of G-CSF significantly improved the delivery of the planned treatment schedule but no effect on overall survival. So the evidence did not support the routine use of G-CSF during standard chemotherapy with BEP.

(4) Is there evidence of efficacy in diverse settings and/or populations?

Yes ☐ No ☒

Please provide brief details:
Neither the application nor our added studies provided the evidence about efficacy of G-CSF in diverse settings or populations.

(5) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?
   Yes ☐ No ☒

Please provide brief details:
The application did not state the safety and adverse effects of GCSF.
We found that adverse effects of G-CSF for TGCT were generally well tolerated in one RCT. Two case reports showed that Sweet’s syndrome and the transient elevations of serum lactate dehydrogenase (LDH) level may be caused by the administration of G-CSF.

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?
   Yes ☒ No ☐

Please provide brief details:
Neither the application nor our added studies provide the special requirements or training needed for the use of the G-CSF.
G-CSF required to be subcutaneous or intravenous injection, so it should be used in medical institutions which can provide such conditions.

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)
   Yes ☒ No ☐

Please provide brief details:
The application stated that G-CSF had been granted regulatory approval in the USA by FDA (US Food and Drug Administration) and also approved in EMA (European Medicines Agency), which indicated to cancer patients receiving myelosuppressive chemotherapy, chemotherapy and patients with severe chronic neutropenia.
We found G-CSF had been registered in CFDA (China Food and Drug Administration) for cancer patients with neutropenia during chemotherapy.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?
   Yes ☐ No ☒

Please provide brief details:
There is no WHO GRC-approved Guideline for TGCT or G-CSF.

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
The application stated that for low-risk patients, those with a less than 20% risk of developing FN, routine use of GCSF was not considered cost-effective. The studies we included also suggested this conclusion.

(10) Any additional comments?
The evidence did not support the routine use of G-CSF for TGCT during standard chemotherapy with BEP. Only if the anticipated risk of FN and/or medical consequences from FN is high, prophylactic G-CSF might be considered.

(11) Please summarise the action you propose the Expert Committee takes.
We do not recommend G-CSF be listed in WHO EML for TGCT as routine use due to the current poor evidence.