Hodgkin Lymphoma is an uncommon neoplasm with estimated number of cases of 65,950 cases globally and 25,469 deaths worldwide. The incidence varies significantly by age, sex, ethnicity, geographic location and socioeconomic status. HL is more frequently a disease of young people between the ages of 20-35 with other cases diagnosed after the age of 55 years. HL accounts for 15% of all cancers in young adults globally with a high impact on quality of life. The current 5-year overall survival rate is up to 80% for patients with advanced and more than 90% for those with limited stage disease.

Two regimens are used to treat HL and all the drugs are already on the essential list except the G-CSF filgrastim.

1) The standard therapy is “ABVD”, including doxorubicin (Adriamycin®), bleomycin, vinblastine, and Dacarbazine., and
2) For high-risk patients we use “BEACOPP”, including bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine (Oncovin®), procarbazine, prednisone and G-CSF. [Eichenauer, D. A. et al. Hodgkin’s lymphoma: ESMO Clinical Practice
Many antineoplastic agents are cytotoxic to the bone marrow and prevent the development of granulocytes necessary to fight infection. Febrile neutropenia is a medical emergency and carries a substantial increase in morbidity, mortality, hospitalizations, and cost of care.

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

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
   Yes  
   G-CSF (Granulocyte-Colony Stimulating Factor) is a glycoprotein that stimulates the bone marrow to produce granulocytes, and promotes their survival, proliferation, and differentiation. When initiated early in the first cycle of chemotherapy and continued through all cycles of a chemotherapy regimen, CSFs substantially reduce the risk of febrile neutropenia. Recombinant G-CSF (filgrastim) has also been shown to reduce the risk of infection-related mortality in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever, while at the same time reducing the need for delays or dose reduction in chemotherapy treatment.

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

"Use of empiric G-CSF during ABVD has never been shown to be necessary or associated with less toxicity" (Evens AM, Cilley J, Ortiz T, et al)

(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  
   Rare cases of potentially fatal splenic rupture; evaluate if patient experiences left upper abdominal pain, left shoulder tip pain or both.
Rare cases of acute respiratory distress syndrome have been reported. Monitor for thrombocytopenia. Severe and sometimes fatal sickle cell crisis can occur.

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?
   Yes  

Filgrastim therapy should only be given in collaboration with an oncology center which has experience in hematology and has the necessary diagnostic facilities.

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

The reference drug is Neupogen® (filgrastim) from US Amgen. The 2 first biosimilar G-CSF were licensed by EMA in 2008, and there are currently eight biosimilar G-CSF products licensed for use in the EU. This has led to cost savings to European healthcare systems of approximately 25-30%. In 2014, Sandoz application was accepted by US FDA, the first time the FDA has accepted a filing for an approval of a biosimilar drug.

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

(9) Please comment briefly on issues regarding cost and affordability of this medicine.

Very few patients with Hodgkin Lymphoma will need the G-CSF. There are several biosimilars and they offer cheaper treatment option. Pegfilgrastim is much more expensive. However, guidelines generally remain accepting of both options, depending on patient circumstances and cost considerations within the health system concerned in the analysis.

(10) Any additional comments?
G-CSF should be used based on a physician-patient discussion of the risk-benefit ratio of the likelihood of developing FN, the potential consequences of a neutropenic event and the implications of reduced chemotherapy dose delivery.

(11) Please summarise the action you propose the Expert Committee takes.

I will recommend the addition of G-CSF filgrastim to the Essential Medicines List (inj vials 30MUI/0.5ml). The target population should be well identified for the prescription conditions (i.e.) patients receiving myelosuppressive chemotherapy treatment.
