Expert peer review on application for Imatinib

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes ✓ No (if no, please provide reference and information)

   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      With this medicine, 5-year survival rates have increased by over 35%. Complete cytogenetic response is seen in 75 - 80% of patients, with a Number Needed to Treat (NNT) of 1.6 patients to achieve a complete cytogenetic response at 18 months. Evidence from low- and middle-income countries, including South Africa, Mexico, China, and India, demonstrates the utility of this therapy in a variety of clinical and geographic contexts.

   c. Please provide any additional relevant information with reference

      The 6 years follow up of IRIS study shows continued clinical benefit, no cases of progression to AP or BC between the 5 and 6 year updates, OS was 88%, and EFS was 83%.

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes ✓ No (if no, please provide reference and information)

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      The comparison with other therapies (interferon-α (IFN) plus cytarabine) is clearly favourable to imatinib.

   c. Please provide any additional relevant information with reference

      In the IRIS study 6-year analysis, imatinib showed no new safety issues.

3. Assessment of cost and availability
   a. Have all relevant data on safety provided
      Yes ✓ No (if no, please provide reference and information)
b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

In India, where no product patent has been granted for imatinib, stiff generic competition has resulted in private sector prices as low as $3.5-$18 per gram (including the branded product). Using a survey of Indian retail prices, costs per year of treatment range from $454 to $2,623 (6-year costs of $2726 - $15,738)

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?

Generic manufacturers are now available in various countries.

4. Assessment of public health need
a. Please provide the public health need for this product (1-2 sentences)

The Glivec International Patient Assistance Program, GIPAP, has provided imatinib free of charge to nearly 18,000 patients in over 15 countries including Kenya, Nigeria, South Africa, Sudan, Argentina, Chile, El Salvador, Mexico, Russia, Georgia, China, India, Malaysia, Pakistan and Thailand. Here, the average age of diagnosis has been 38.7 years, significantly lower than in developed country settings, and the dominant age cohort is 31-40 years.

At diagnosis, over 11,000 of the 18,000 patients were in the chronic phase, just over 1,200 were in the accelerated phase and just under 1,000 were in blast crisis. Among these patients, imatinib has produced an 8-year event free survival of 81%.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international

NCCN Canada, ASH US (American Society of Haematology)

All international guidelines strongly recommend imatinib as the drug of choice for CML

5. Are there special requirements for use or training needed for safe/effective use?
If yes, please provide details in 1-2 sentences

Service delivery capacity to:

- diagnose Philadelphia chromosome positive

- define Cytogenetic Response (bone marrow aspirate and cytogenetic response)

6. Is the proposed product registered by a stringent regulatory authority?

Yes ☑ No

7. Any other comments
8. What is your recommendation to the committee (please provide the rationale)

The overall risk benefit profile of imatinib is clearly positive in the treatment of CML and data from trials and clinical practice show very high effectiveness of the drug. Data show a very high capacity of the drug to maintain over time its capacity to control the disease (estimated rate of being free of progression to AP and BC at 6 years was 93% (95% confidence interval (CI) 91–95). Annual rates of progression to AP/BC were 1.5, 2.8, 1.6, 0.9, 0.5 and 0%, in years 1–6, respectively. Data for estimated OS rate of patients randomized to imatinib was 88% at 6 years).
Given the magnitude of the expected benefit it is recommended that imatinib be included in EML.