BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

GLIVEC (imatinib), tyrosine kinase inhibitor

Major improvement in the treatment of children with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL)

Main points

- GLIVEC now has Marketing Authorisation in the treatment of children with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), integrated with chemotherapy.
- Integrated with chemotherapy, it represents a major therapeutic advance in terms of event-free survival and overall survival at 4 years in this indication.

Pre-existing indications

- GLIVEC has Marketing Authorisation in numerous other indications:
  - treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment.
  - treatment of adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis.
  - treatment of adults with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy.
  - treatment of adult patients with relapsed or refractory Ph+ ALL as monotherapy.
  - treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements.
  - treatment of adult patients with advanced hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL) associated with FIP1L1-PDGFRα rearrangement.
  - treatment of adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST).
  - adjuvant treatment of adult patients who are at significant risk of relapse following resection of Kit (CD117)-positive GIST
  - treatment of adult patients with unresectable dermatofibrosarcoma protuberans (DFSP) and adult patients with recurrent and/or metastatic DFSP who are not eligible for surgery.

- This summary does not cover these indications.

Therapeutic use

- The treatment of ALL, tailored to the risk factors of the individual patient and possibly combined with supportive care, includes:
  - Induction treatment aimed at achieving full cytological remission with low residual disease. This chemotherapy generally comprises vincristine, L-asparaginase and possibly an anthracycline such as daunorubicin) in combination with a corticosteroid.
  - Post-induction treatment (also termed consolidation/intensification) comprising, depending on the protocol, 6-mercaptopurine, cyclophosphamide, cytarabine, etoposide, an anthracycline.
  - Maintenance therapy comprising 6-mercaptopurine and methotrexate.
  - Neuro-meningeal prophylaxis and/or an allogeneic haematopoietic stem cell transplant may be considered where appropriate.

The inclusion of a tyrosine kinase inhibitor is recommended in the different treatment phases in young patients (aged 15-39 years).

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Role of the medicinal product in the therapeutic strategy

GLIVEC in combination with chemotherapy (induction, consolidation and maintenance) is the treatment of choice in children with newly diagnosed Ph+ ALL.

Clinical data

The efficacy of GLIVEC in the treatment of newly-diagnosed Ph+ ALL in children was evaluated on the basis of a historical cohort controlled study that included 93 Ph+ ALL patients. In the group of 50 Ph+ ALL patients treated with GLIVEC in combination with chemotherapy (reinduction, intensification, and maintenance), event-free survival at 4 years was 69.6% versus 31.6% in the historical control group treated with chemotherapy alone (HR = 0.28, 95% CI [0.16; 0.49], p <0.0001) and overall survival 4 years after inclusion was 83.6% versus 44.8% in the historical control group (HR = 0.23, 95% CI [0.11; 0.49], p <0.0001).

Safety data in children with Ph+ ALL are limited; the adverse effects reported in this population were similar to those observed in adults with Ph+ ALL. Questions do, however, remain about the risk of delayed weight gain and growth in children.

Benefit of the medicinal product

The actual benefit* of GLIVEC is substantial.
GLIVEC integrated with chemotherapy provides major clinical added value** (CAV I) in the therapeutic strategy for children with newly diagnosed Ph+ ALL.

** The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

This document was created on the basis of the Transparency Committee Opinion of 28 May 2014 (CT-13248) and is available at www.has-sante.fr

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