HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
Update
December 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

MYLERAN (busulfan), antineoplastic agent

Insufficient clinical benefit in chronic myelogenous leukaemia and in conditioning regimens for stem cell transplantation

Main points

- MYLERAN (orally administered busulfan) has marketing authorisation in the treatment of chronic myelogenous leukaemia that is refractory to other therapies, or where other therapies are contraindicated, and for conditioning prior to haematopoietic stem cell transplantation**.**
- In conditioning regimens for stem cell transplantation, MYLERAN no longer has a role in the therapeutic strategy because the oral form of busulfan has greater toxicity than the intravenous form.
- In chronic myelogenous leukaemia, from the 2nd-line setting onwards, MYLERAN no longer has a role in the therapeutic strategy because more effective and better tolerated alternatives are available.

Therapeutic use

- **Chronic myelogenous leukaemia (CML)**

Second-line treatment of CML in the chronic, accelerated or blast phase involves tyrosine kinase inhibitors: imatinib (GLIVEC), dasatinib (SPRYCEL) or nilotinib (TASIGNA). In the third-line setting onwards, when these treatments have failed or are not tolerated, bosutinib (BOSULIF), cytarabine (ARACYTINE), hydroxycarbamide (HYDREA) and autologous haematopoietic stem cell transplantation (in eligible patients) may be considered.

- **Conditioning prior to haematopoietic stem cell transplantation**

The purpose of conditioning is to ensure sufficient immunosuppression of a recipient to allow the transplant and prevent rejection of the transplant. It must also, to a varying degree, destroy the tumour cells. Conditioning is therefore both immunosuppressant and myelotoxic.
Myeloablative conditioning involves various chemotherapy regimens that may include alkylating agents or antimetabolites (cyclophosphamide, busulfan IV, melphalan, thiotepa, cytarabine) and may be combined with total body irradiation (in malignant haematological diseases in particular).
Reduced intensity conditioning is based on the use of powerful immunosuppressants and in particular fludarabine in varying combinations with other immunosuppressants (anti-lymphocyte serum, mycophenolate mofetil), and low doses of chemotherapy (cyclophosphamide, busulfan IV, ARACYTINE) or low doses of total body irradiation.
The oral form of busulfan (MYLERAN), which is associated with significant individual variability in plasma concentrations, is no longer used in myeloablative conditioning regimens or reduced-intensity regimens. In fact, the development and administration of intravenous (IV) busulfan has reduced the variability of plasma concentrations in comparison with a fixed dose given orally, allowing toxicity (particularly hepatic veno-occlusive disease) and 100-day mortality to reduce.

- **Role of the medicinal product in the therapeutic strategy**

MYLERAN no longer has a role in the therapeutic strategy for managing CML, in accordance with current guidelines, or in conditioning prior to haematopoietic stem cell transplantation.

Clinical data

- No new data have been supplied by the company.

Special prescribing conditions

- For hospital prescription. Prescription restricted to oncology, haematology and medical oncology specialists and departments.

Benefit of the medicinal product

- The actual clinical benefit* of the proprietary medicinal product MYLERAN is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend continued inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 14 December 2016 (CT-10209) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.