HAUTE AUTORITÉ DE SANTÉ

HAEMATOLOGY
New medicinal product
September 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

LONQUEX (lipegfilgrastim), granulocyte colony stimulating factor

Substantial clinical benefit in the reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients receiving cytotoxic chemotherapy, but no clinical benefit demonstrated compared to NEULASTA (pegfilgrastim).

Key points

- LONQUEX has MA in the reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients receiving cytotoxic chemotherapy for a malignant condition (except for chronic myeloid leukaemia and myelodysplastic syndromes).
- It is a long-acting granulocyte colony stimulating factor, the efficacy of which has been demonstrated in two non-inferiority studies versus NEULASTA on the duration of severe neutropenia (DSN) in the 1st chemotherapy cycle.
- The post-authorisation safety study descriptive data requested by the EMA do not suggest a short-term excess mortality risk in non-small cell lung cancer, unlike that which had been observed in another clinical study.

Care pathway

- The use of colony stimulating factors (G-CSF) in cancerology is recommended in patients following a protocol carrying a risk of febrile neutropenia higher than 20%, even 10% in some patients for whom the individual risk factors justify it.
- The curative use of colony stimulating factors must be limited only to those patients presenting with chemotherapy-induced neutropenia, who are not likely to respond to the appropriate antibiotic treatment and who are likely to develop life-threatening infectious complications.
- Several G-CSF are already available:
  - filgrastim (NEUPOGEN) and its biosimilars,
  - lenograstim (GRANOCYTE),
  - the pegylated filgrastim formulation, pegfilgrastim (NEULASTA), and its biosimilars, improving the convenience of use of filgrastim and the quality-of-life of patients by extending the half-life: one single injection per chemotherapy cycle instead of a daily injection.

Role of the medicinal product in the care pathway

LONQUEX (lipegfilgrastim) is a therapeutic option in the same way as NEULASTA (pegfilgrastim) in the reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients receiving cytotoxic chemotherapy for a malignant condition (except for chronic myeloid leukaemia and myelodysplastic syndromes) with a risk of febrile neutropenia higher than 20%, or even 10% according to the individual risk factors.

Clinical data

- Two randomised studies on efficacy demonstrated the non-inferiority of lipegfilgrastim versus pegfilgrastim on the duration of severe neutropenia (DSN) during the 1st chemotherapy cycle:
  - Study XM22-03, in 202 female patients with high risk stage II, stage III or IV breast cancer, and treated with cytotoxic chemotherapy with a difference between the treatments of -0.218 days, 95%CI = [-0.498; 0.062]) therefore an upper limit of the confidence interval lower than 1 day, non-inferiority threshold predefined.

- Study XM22-ONC-305, in elderly patients with aggressive B-cell non-Hodgkin's lymphoma (NHL) treated with an R-CHOP-21 protocol, with a difference in DSN between the treatments of -0.3 days, 95%CI = [-0.70; 0.19]) therefore an upper limit of the confidence interval lower than 1 day, non-inferiority threshold predefined.

- A phase III, comparative, randomised, placebo-controlled, double-blind study XM22-04, having included patients with non-small cell lung cancer, suggested higher short-term mortality (D85) with lipegfilgrastim (12.5%, 31/248 patients) than with the placebo (7.2%, 9/125 patients). The patients included in this study had a lower risk of febrile neutropenia than the MA population. This study was not selected therefore to demonstrate the efficacy of lipegfilgrastim. Further to this excess mortality signal, a post-authorisation clinical safety study (PASS, XM22-ONC-40041), requested by the EMA when granting MA, was conducted in order to collect data on the use of lipegfilgrastim or pegfilgrastim or a placebo, especially on disease progression and mortality in patients with stage IIIB/IV non-small cell lung cancer. In this study on 303 patients, analysis of the Kaplan-Meier curves demonstrated median progression-free survival by centralised analysis of 5.9 months (95%CI [5.20; 7,90]) in the lipegfilgrastim group, 4.6 months (95%CI [4.10; 5.80]) for the pegfilgrastim group and 5.8 months (95%CI [5.20; 7.10]) in the placebo group. Median overall survival was 11.7 months (95%CI [9.60; 14.50]) in the lipegfilgrastim group, 10.7 months (95%CI [9.10; 14.80]) in the pegfilgrastim group and 11.9 months (95%CI [10.00; 14.80]) in the placebo group. The descriptive data (absence of statistical assumption issued in the statistical analysis plan) for this new post-authorisation safety study requested by the EMA do not suggest a short-term excess mortality risk in non-small cell lung cancer, unlike that which was observed in the clinical study XM22-04.

Specific prescribing conditions

- Medicinal product subject to initial quarterly hospital prescription.

Benefit of the medicinal product

- The clinical benefit* of LONQUEX is substantial.
- LONQUEX does not provide any clinical added value** (CAV V) compared to NEULASTA (pegfilgastrim).
- Positive opinion issued for retail pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 18 September 2019 (CT-17679) available at **www.has-sante.fr**

* The clinical benefit of a 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 clinical benefit, which may be substantial, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) corresponds to the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV level from I, major, to IV, minor. A level V CAV (equivalent to "no clinical added value") denotes a "lack of clinical improvement"