HAUTE AUTORITÉ DE SANTÉ

HAEMATOLOGY
New medicinal product
November 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

OBIZUR (susoctogog alfa), porcine recombinant factor VIII

No clinical benefit demonstrated in current treatment of severe bleeding in patients with acquired haemophilia

Main points

- OBIZUR has Marketing Authorisation only in the treatment of bleeding episodes in patients with acquired haemophilia due to factor VIII antibodies.
- Laboratory monitoring of its efficacy is possible, based on the measurement of FVIII activity, in addition to clinical monitoring.
- Clinical efficacy data are limited and the safety profile is poorly documented. There is no clinical information on the development of anti-OBIZUR inhibitor antibodies after repeated administration, the main risk related to the treatment.

Therapeutic use

- The therapeutic management of bleeding in acquired haemophilia must be quick because it is life-threatening for the patient. In case of severe bleeding, two therapeutic options can be considered:
  - first-line use of an agent short-circuiting the inhibitor: factor VIIa (NOVOSEVEN) or prothrombin complex concentrates (FEIBA).
  - use of high doses of FVIII concentrates. This strategy, the efficacy of which is limited when the inhibitor titre is high and which is ineffective in many patients, is rarely used in practice.
- The choice of NOVOSEVEN or FEIBA depends on the clinical context, the availability of medicinal products and prescribing habits. No studies are available comparing FEIBA and NOVOSEVEN. Each of these medicinal products may prove ineffective in some patients and it is possible that patients who do not respond to one may respond to the other. These treatments expose patients to a thrombotic risk and there is no specific laboratory test to monitor their efficacy.
- **Role of the proprietary medicinal product in the therapeutic strategy**

  OBIZUR is a first-line treatment in severe bleeding in patients with acquired haemophilia.

  In the presence of an elevated titre of porcine anti-FVIII antibodies, the use of a bypass agent (FEIBA or NOVOSEVEN) rather than OBIZUR should be considered. There is no argument justifying a therapeutic attitude different from that usually applied in congenital haemophilia A in the presence of an elevated level of inhibitors.

  Compared to “bypassing” agents, whose efficacy monitoring is based solely on clinical response, OBIZUR has the advantage of also allowing laboratory monitoring by measurement of factor VIII activity.

  The main disadvantage of OBIZUR, already known for the previous plasma-derived porcine FVIII available, is the risk of resistance to treatment due to the presence of anti-porcine FVIII antibodies. As there is no clinical information on the development of anti-OBIZUR inhibitor antibodies after repeated administration, OBIZUR must be administered only when it is considered clinically necessary.

  Particular attention must be given to possible thrombotic events. This risk is increased in the case of elevated and constant levels of circulating factor VIII.

  Unlike FEIBA and NOVOSEVEN, OBIZUR does not have Marketing Authorisation in prevention of bleeding before a surgical procedure, or in case of congenital haemophilia A with inhibitors.

Clinical data

- The efficacy and safety of OBIZUR were evaluated in an uncontrolled study with a small number of subjects:
  - the bleeding managed was primarily muscular or articular, in patients with a mean age of 70 years;
  - 24 hours after the first administration of OBIZUR, a positive response to treatment was observed in all 28 patients included (treatment considered effective or partially effective on the basis of clinical elements and FVIII activity). For 86% of patients, the initial bleeding episode was controlled.
  - the doses of OBIZUR and the frequencies of administration were highly variable between patients. Almost one quarter of the patients included died during or shortly after the study, mainly due to bleeding or infection.
- Development of porcine anti-FVIII antibodies was observed in 25% of patients who did not have this at inclusion. Two catheter occlusions were reported in the same patient (not confirmed by imaging tests). Discussion points:
  - Nearly 30% of the patients had received FEIBA, NOVOSEVEN or tranexamic acid just before administration of OBIZUR. The bleeding control rate in these patients did not appear to be greater than that observed in patients who received OBIZUR as first-line.
  - The available data do not enable an assessment of the risk of resistance to a subsequent treatment due to the presence of porcine anti-FVIII antibodies.
  - The data do not support a conclusion on the efficacy of OBIZUR based on the location of the bleeding.

Special prescribing conditions

- Medicinal product for hospital prescription
- Medicinal product reserved for hospital use

Benefit of the medicinal product

- The actual benefit* of OBIZUR is substantial.
- OBIZUR does not provide clinical added value** (CAV V) in the current treatment strategy for severe bleeding in patients with acquired haemophilia.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 30 November 2016 (CT-15521) and is available at **www.has-sante.fr**

* The actual benefit (AB) 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 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”.