HAUTE AUTORITÉ DE SANTÉ

**RARE DISEASE**
**New medicinal product**
**April 2015**

**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **SYLVANT** (siltuximab), monoclonal antibody

**Minor clinical benefit in the management of multicentric Castleman's disease in adults not infected with HIV and HHV-8**

## Main points

- SYLVANT is the first medicinal product with Marketing Authorisation in the treatment of adult patients with multicentric Castleman's disease (MCD) not infected with human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8)
- In these patients, it has shown its efficacy in terms of tumour response (partial and complete).
- Clinical efficacy data remain limited and have not shown any gain in overall survival.

## Therapeutic use

- The strategy for treating MCD has not been clearly established. In practice, several treatments can be combined, including in particular:
  - surgical excision of the affected lymph nodes,
  - multidrug cytotoxic chemotherapies such as CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine),
  - immunomodulators: interferon alfa, corticosteroids, thalidomide,
  - biotherapies: MABTHERA (rituximab), ROACTEMRA (tocilizumab), VELCADE (bortezomib).

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

At present, SYLVANT is the only biotherapy to have Marketing Authorisation for the treatment of adult patients with MCD who are not infected with HIV and HHV-8 and is the biotherapy of choice in this indication.

## Clinical data

- In a randomised double-blind study in 79 patients, the percentage partial and complete tumour response (primary endpoint) was 34% (32.1% partial response and 1.9% complete response) in the group treated with siltuximab in combination with optimal symptomatic treatment versus 0% in the placebo group in combination with optimal symptomatic treatment (95% CI [11.1; 54.8]; p = 0.0012). After median follow-up of 422 days, median overall survival was not achieved in either of the two treatment groups.
- Safety data in patients with MCD not infected with HIV and HHV-8 are very limited. The main adverse effects reported in these patients were upper airways infections, neutropenia, thrombocytopenia, rash, hypertriglyceridaemia, abdominal pain, localised oedema and weight gain.
- The main adverse effects requiring special attention are anaphylactic reactions, infections, cytopenia, skin reactions and secondary malignant tumours.

## Prescribing conditions

- Medicinal product reserved for hospital use
- Medicine restricted to haematologists or doctors trained in blood diseases.

# Benefit of the medicinal product

- The actual benefit* of SYLVANT is moderate.
- SYLVANT provides clinical added value** (CAV IV, minor) in the management of multicentric Castleman's disease in adult patients not infected with HIV and HHV-8
- 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 15 April 2015 (CT-13885) and is available at **www.has-sante.fr**

* 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".