HAUTE AUTORITÉ DE SANTÉ

RARE DISEASE
New indication
November 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ILARIS (canakinumab), interleukin 1 inhibitor

Minor improvement in the treatment of 3 inflammatory syndromes

Main points

- ILARIS has Marketing Authorisation in the treatment of three forms of hereditary recurrent fevers in adults, adolescents and children aged 2 years and older:
  - TNF-associated periodic syndrome (TRAPS),
  - hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD), and
  - familial Mediterranean fever (FMF).
- Its superiority relative to placebo has been demonstrated in these 3 diseases in terms of resolution of the initial attack at 15 days and absence of new flare-up within 4 months after treatment.
- ILARIS has not shown to have a long-term effect in the prevention of secondary amyloidosis, a source of morbidity and mortality.

Pre-existing indications*

- ILARIS also has Marketing Authorisation in treatment of cryopyrin-associated periodic syndromes, frequent attacks of gout and systemic idiopathic juvenile arthritis

Therapeutic use

- Diagnosis and initial management of the 3 syndromes falls under reference or expert centres.
- As there is no curative treatment for these three forms of periodic recurrent fevers, management is based on symptomatic treatment of attacks and their prevention with the goal of avoiding complications, including those related to amyloidosis, and preserving the quality of life of patients.
- Treatment of inflammatory attacks involves the use of analgesics, antipyretics, nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroid therapy, which will be for the shortest possible duration. Adjuvant stress management and pain therapies may also be proposed.
- There is no basic treatment validated by a Marketing Authorisation in TRAPS or HIDS/MKD. The following products are used in paediatrics, off-label (without Marketing Authorisation):
  - etanercept (anti-TNF) and anakinra (another anti-IL 1) in TRAPS,
  - anti-TNF (etanercept, adalimumab) and anakinra in HIDS/MKD.
- Colchicine in the only specific basic treatment for FHF validated by a Marketing Authorisation. Anakinra (off label) is reserved for those rare patients who are resistant to colchicine despite proper adherence and dosage.
- **Role of the medicinal product in the therapeutic strategy**
  ILARIS must be reserved for severe patients, with frequent autoinflammatory febrile attacks or with persistent chronic biological inflammatory syndrome for TRAPS and HIDS/MKD.
  For FMF, ILARIS must be reserved for patients resistant or intolerant to properly conducted treatment with colchicine.

* This summary does not cover these indications.

Clinical data

- The efficacy and safety of canakinumab were assessed in the three periodic syndromes in a study conducted versus placebo in 4 phases and 3 cohorts (one per disease). A total of 280 patients were included. After 12 weeks of observation, 181/280 (64.6%) who had a flare-up were selected and randomised to be treated with either canakinumab 150 mg every 4 weeks (or 2 mg/kg in patients ≤ 40 kg) or placebo for 16 weeks. Then, the patients who responded to canakinumab from the 3 cohorts were randomised again, double-blinded, to receive either canakinumab 150 mg every 8 weeks or placebo for an additional 24 weeks. The primary endpoint was the proportion of patients who responded, i.e. who achieved a resolution of the initial flare-up on D15 after the start of treatment and no new flare-up of the disease during the first 16 weeks of treatment. The superiority of canakinumab compared with placebo on this criteria was demonstrated in each cohort:
  - 61.3% (19/31) in the canakinumab group versus 6.3% (2/32) in the placebo group in the FMF cohort;
  - 35.1% (13/37) in the canakinumab group versus 5.7% (2/35) in the placebo group in the HIDS/MKD cohort;
  - 45.5% (10/22) in the canakinumab group versus 8.3% (2/24) in the placebo group in the TRAPS cohort.
- To date, the ability of canakinumab to prevent secondary amyloidosis has not been demonstrated based on the available data.
- The safety profile of ILARIS seems comparable to that already known for CAPS. Long-term data in its indications are limited.

Special prescribing conditions

- Medicinal product for hospital prescription.
- Initial and repeat prescription reserved for specialists in rheumatology, internal medicine, dermatology or paediatrics.
- Medicinal product requiring special monitoring during treatment.
- Exception drug status.

Benefit of the medicinal product

- The actual benefit* of ILARIS is substantial.
- ILARIS provides minor clinical added value (CAV IV) in the treatment strategy for these three inflammatory syndromes (TRAPS, HIDS/MKD and FMF resistant to colchicine).
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 09 November 2017 (CT-16220) 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”.