BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ERWINASE (Erwinia L-asparaginase), antineoplastic agent

Minor improvement in the treatment of acute lymphoblastic leukaemia in, mainly paediatric, patients who have developed hypersensitivity to native or pegylated E. coli asparaginase

Main points

For more than a decade, ERWINASE has been used in the setting of temporary usage authorisations (TUA). This proprietary medicinal product now has Marketing Authorisation in patients who have developed hypersensitivity (clinical allergy or silent inactivation) to:

- native E. coli asparaginase (KIDROLASE), which is recommended as first-line treatment in France or
- pegylated E. coli asparaginase: no proprietary medicinal product of this type currently has Marketing authorisation in France. Only ONCASPAR is available in the setting of temporary authorisations for use by named patients.

It is an alternative treatment for acute lymphoblastic leukaemia, mainly in paediatric care, in the event of the development of hypersensitivity (clinical allergy or silent inactivation) to native or pegylated L-asparaginase.

Therapeutic use

L-Asparagine is an amino acid that is essential for protein synthesis in the majority of leukaemia cells. Various chemotherapy protocols for the treatment of acute lymphoblastic leukaemia (ALL) include L-asparaginase, particularly in the induction and consolidation phases and mainly in children. In practice, the use of asparaginase in adults is more limited than in children (in particular because of the safety profile). At present, two proprietary medicinal products have Marketing Authorisation in France: KIDROLASE and ERWINASE. Another proprietary medicinal product based on asparaginase (ONCASPAR) is available for use in second-line treatment in the setting of a temporary usage authorisation. Because, in particular, of their pharmacokinetic and pharmacodynamic characteristics, their immunogenicity profiles and the differing dose regimens, these L-asparaginase-based proprietary medicinal products are not interchangeable.

Role of the medicinal product in the therapeutic strategy

ERWINASE, in combination with anticancer drugs, in the setting of therapeutic protocols for ALL, is an alternative treatment, mainly in paediatric care, in the event of the development of hypersensitivity (clinical allergy or silent inactivation) to native or pegylated L-asparaginase.

Clinical data

The available data come from three non-comparative studies in children with ALL that evaluated ERWINASE administered after hypersensitivity to:

- pegylated E. coli asparaginase, in two pharmacokinetics studies that evaluated the enzymatic activity in relation to the depletion of asparagine and in which no data on the clinical efficacy were collected;
- native E. coli asparaginase, in a study carried out in children with newly diagnosed ALL. Pharmacokinetic data were only available for 38 of the 42 children, with a median age of 5.5 years, who were treated with ERWINASE (administered by the IM route) following the development of hypersensitivity to E. coli L-asparaginase. After a median follow-up of 5.4 years, the median event-free survival was 86 months in 42 patients who received treatment with Erwinia L-asparaginase and 81 months in 170 patients without allergic reactions to E. coli L-asparaginase.

The safety profile is dominated by local or systemic hypersensitivity reactions, coagulation abnormalities that can lead to thromboembolic and haemorrhagic complications and pancreatic disorders (pancreatitis, hyperglycaemia).
In relation to the therapeutic use protocol put in place at the request of the FDA, the available data from 893 of the 1368 patients treated with ERWINASE revealed that at least one adverse event in the course of treatment was observed in 340 patients (36%). The adverse effects reported most frequently were allergic reactions (hypersensitivity: 14%, local hypersensitivity: 3%, anaphylaxis: 1%), infection/septicaemia (4%), pancreatitis (4%), fever (4%), hyperglycaemia (4%) and elevated transaminases (3%). Grade 3 or 4 adverse events were reported in 15% of patients.

No data have been provided for adults.

Special 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 ERWINASE is substantial.
- ERWINASE, in combination with anticancer drugs, provides minor clinical added value** (CAV IV) in the therapeutic strategy for acute lymphoblastic leukaemia in patients who present hypersensitivity (clinical allergy or silent inactivation) to native or pegylated E. coli asparaginase.
- Recommends inclusion on the list of reimbursable products for hospital use.

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* 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”.

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