



Medication Policy Manual

Policy No: dru269

Topic: Erwinaze™, asparaginase *Erwinia chrysanthemi*

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IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Asparaginase *Erwinia chrysanthemi* (Erwinaze) is an injectable medication for acute lymphoblastic leukemia (ALL). It is indicated as second-line therapy in patients who have developed hypersensitivity to *E. coli*-derived asparaginase.

Policy/Criteria

- I. Most contracts require prior authorization approval of asparaginase *Erwinia chrysanthemi* prior to coverage. Asparaginase *Erwinia chrysanthemi* may be considered medically necessary in patients with clinical documentation of hypersensitivity to *E. coli*-derived asparaginase preparations.

- II. Administration, Quantity Limitations, and Authorization Period
 - A. RegenceRx does not consider asparaginase *Erwinia chrysanthemi* to be a self-administered medication.
 - B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

- Acute lymphoblastic leukemia is the most common form of cancer in children. Asparaginase is a standard component of ALL therapy and it is used in remission induction and intensification treatment in every pediatric regimen for ALL.^[1]
- Asparaginase depletes circulating asparagine, which is necessary for leukemic cells.
- *Erwinia*-asparaginase (Erwinaze) is a standard therapy with years of clinical experience internationally. It has also been available in the U.S. through compassionate use protocols.^[2-4]
- Two *E.coli*-derived asparaginase products were available in the U.S. prior to Asparaginase *Erwinia chrysanthemi* (Erwinaze) approval: *E.coli*-asparaginase (Elspar) and *E.coli*-pegaspargase (Oncaspar). One of the main concerns with asparaginase products is the development of hypersensitivities and cross-sensitivities.
- Asparaginase *Erwinia chrysanthemi* (Erwinaze) is an immunologically distinct asparagine specific enzyme approved for treatment of patients with ALL who have developed a hypersensitivity to *E. coli*-derived asparaginase.
- Retrospective analyses have suggested improved efficacy (event-free survival [EFS]) in acute lymphoblastic leukemia (ALL) with completion of scheduled doses of asparaginase.^[5,6] *Erwinia*-asparaginase provides clinical value in patients who developed hypersensitive to *E. coli*-asparaginase to allow completion of scheduled therapies.

Clinical Efficacy

- Approval of *Erwinia*-asparaginase (Erwinaze) was based on a clinical pharmacology trial demonstrating an acceptable trough asparaginase activity level (N= 58). Serum trough asparaginase activity ≥ 0.1 International Units/ mL has been demonstrated to correlate with asparagine depletion (asparagine < 0.4 mcg/mL or 3 μ M) and to serum levels that predict clinical efficacy.^[7]

- While the contribution of *Erwinia*-asparaginase (Erwinaze) as part of ALL regimen has not been isolated through controlled clinical trials, indirect evidence of its benefit is so widely accepted by the community that the conduct of RCTs would not be feasible at this time.^[8] Therefore, the FDA accepts measurement of serum asparaginase activity as the surrogate endpoint for efficacy.
- There is low certainty in the body of evidence that at therapeutic dose, one asparaginase preparation is superior to another at therapeutic doses.^[9,10]

Safety

- *Erwinia*-asparaginase (Erwinaze) has been available overseas for over 20 years^[11] and it has a track record of safety in patients who are hypersensitive to *E. coli*-derived asparaginase (Elspar, Oncaspar).^[3,4,11]
- Other than different rates of hypersensitivity, there is no reliable evidence that differentiates relative safety between different asparaginase preparations (Elspar, Oncaspar).
- All asparaginase preparations share similar adverse events, including serious hypersensitivity reactions, pancreatitis, abnormal transaminases, and thrombosis and hemorrhage.^[7,12,13]
- Development of anti-asparaginase antibodies may lead to clinical hypersensitivity reactions and/or cause rapid inactivation of the asparaginase, resulting in suboptimal asparagine deletion and therapeutic failure.^[1]
- Clinical hypersensitivity reactions are most common in native *E. coli*-asparaginase (Elspar) ranging from 32.5% to 75%^[12] and less prevalent in *E. coli*-pegaspargase (Oncaspar) ranging from 3% to 10%^[13] and *Erwinia*-asparaginase (Erwinaze) which is 5%^[7]. Clinical hypersensitivity occurs almost exclusively in postinduction regimens (i.e. intensification, reinduction) when asparaginase has not been given for weeks or months.^[1]
- Switching between *E. coli*-asparaginase preparations in the setting of hypersensitivity reactions is not recommended, due to cross-sensitivity and potential for silent inactivation of anti-asparaginase antibodies.^[1]

Codes	Number	Description
HCPCS	J9020	Injection, asparaginase (Elspar), 10,000 units
HCPCS	J9266	Injection, pegaspargase (Oncaspar), per single dose vial

References

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