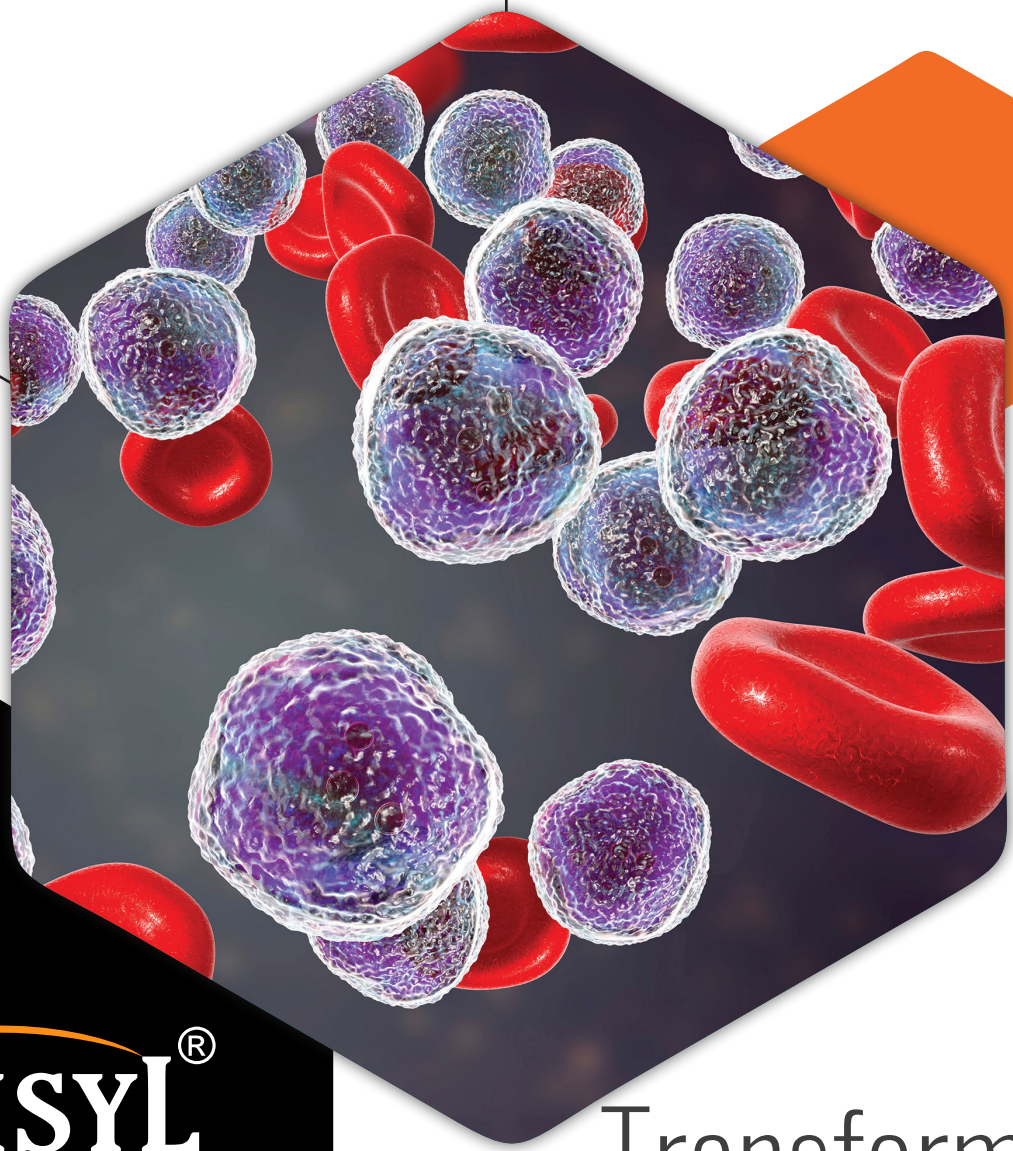
GENNOVA

Acute Lymphoblastic Leukemia

Pegaspargase



HAMSYL®

Indicated as a component of multi agent chemotherapeutic regimen for the treatment of patients with Acute Lymphoblastic Leukemia (ALL) which is an orphan disease.

Transforming Healthcare

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ALL
A RARE CHILDHOOD CANCER

GLOBALLY
2 IN 100,000
ANNUAL INCIDENCE[1]

USA
~3,000
ANNUAL INCIDENCE

INDIA
~6,000
ANNUAL INCIDENCE[2]

Acute Lymphoblastic Leukemia (ALL) is a cancer of the blood and bone marrow. ALL is the most common type of childhood cancer yet it is considered a rare disease. ALL is curable with survival rates up to 90% in developed economies under a standardized chemotherapy regimen but fatal if untreated.

ALL is a **rare disease** and occurs **2 in 100,000** people annually[1]. The risk of developing ALL is highest in children below 5 years of age and in adults above the age of 50.

Globally, there are more than **0.8 million** prevalent cases of ALL. There are about **15,600 prevalent cases in India** making ALL the commonest cancer in children[2].

CURRENT TREATMENT ISSUES

Asparaginase, an enzyme obtained from microbial source is a critical component of multidrug treatment of ALL. There are three kinds of asparaginase available in the market

- Native asparaginase from *E. coli* – native asparaginase
- PEGylated version of the native asparaginase from *E. coli* – Pegaspargase
- Native asparaginase from *Erwinia chrysanthemi* – Erwinase

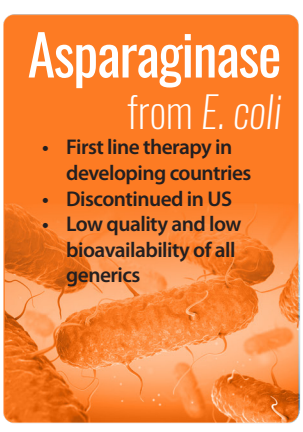
Patients develop hypersensitivity to 'native asparaginase', since it is obtained from a microbial source, and need to be switched to pegaspargase, the PEGylated form of 'native asparaginase'.

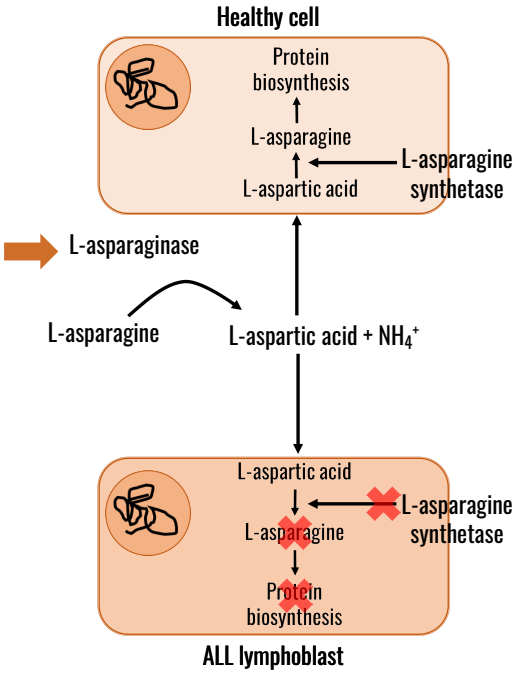
Since hypersensitivity is a known outcome, in developed nations pegaspargase is used as a first line treatment and Erwinase as second line treatment for ALL. **Pegaspargase** is very expensive and thus forces the developing countries to use the non-PEGylated version, 'native asparaginase', which invariably sensitizes the patients during a course of chemotherapy.

Pegaspargase is preferred over native asparaginase due to its longer half life, the requirement of fewer dose and sustained therapeutic activity through the course of treatment.

There are two major problems with pegaspargase - affordability and accessibility.

The current treatment is very expensive and the liquid preparation has inherent **challenges with cold-chain shipment, handling, and storage** of this drug in harsh environments prevalent in India and other tropical countries.





Pegaspargase is prepared by the pegylation of native *E. coli* asparaginase.

Pegaspargase is safe, effective, and economical for the treatment of ALL considering the half-life and hypersensitivity of the native L-Asparaginase. Considering these facts **pegaspargase has been included in the WHO essential list of medicine 2021**[3].

GENNOVA'S INNOVATION

Gennova is committed to this orphan disease and is walking the path to create solutions for various asparaginase formulations.

The development of recombinant asparaginase is a novel way of ensuring quality as it is governed by stringent regulatory rules which are globally harmonized.

Gennova was the first company in India to rise to the cause of the ALL, an orphan disease. In 2014, Gennova **launched an affordable quality-assured pegaspargase, Hamsyl®**, bringing the **drug cost down to one-third the price of the innovator product**. This launch ensured that patients of ALL in India have access to the best medications. The product quality was **independently attested by the paediatric and haematology clinical community** & this is the only generic to **establish its clinical bioequivalence with the innovator product**.

Gennova's **innovation around high cell density fermentation, genetic manipulations for its microbial products, and cost-effective PEGylation technology** puts itself in a unique position to address the availability of the asparaginase portfolio of products.

Gennova has developed a novel storage stable formulation of pegaspargase and **have filed Patent Corporation Treaty (PCT) to protect its IP.**

CLINICALLY PROVEN TO BE BIOEQUIVALENT TO INNOVATOR PRODUCT

Randomized, Parallel Group, Open-Label Bioequivalence Trial of Intramuscular Pegaspargase in Patients With Relapsed Acute Lymphoblastic Leukemia

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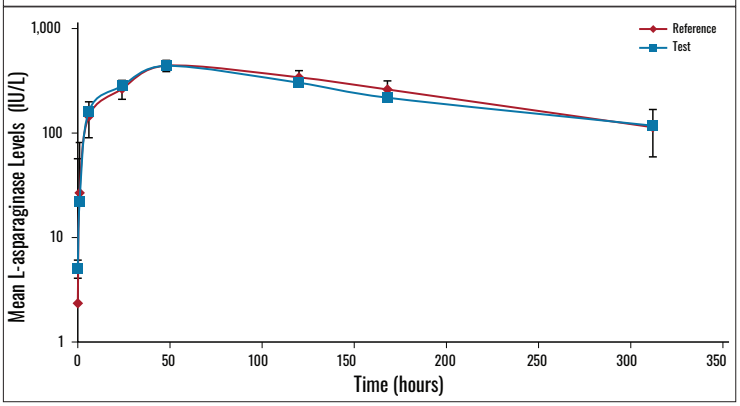
PURPOSE Pegylated asparaginase is comparatively safer than native asparaginase in the management of acute lymphoblastic leukemia (ALL). However, the high price and nonavailability in low- and middle-income countries limits its use. In 2014, the first generic of pegaspargase (Hamsyl) was approved in India for use as a second-line treatment option for ALL. The aim of this study was to assess whether the generic pegaspargase (the test product) was bioequivalent with the reference product (Oncaspar).



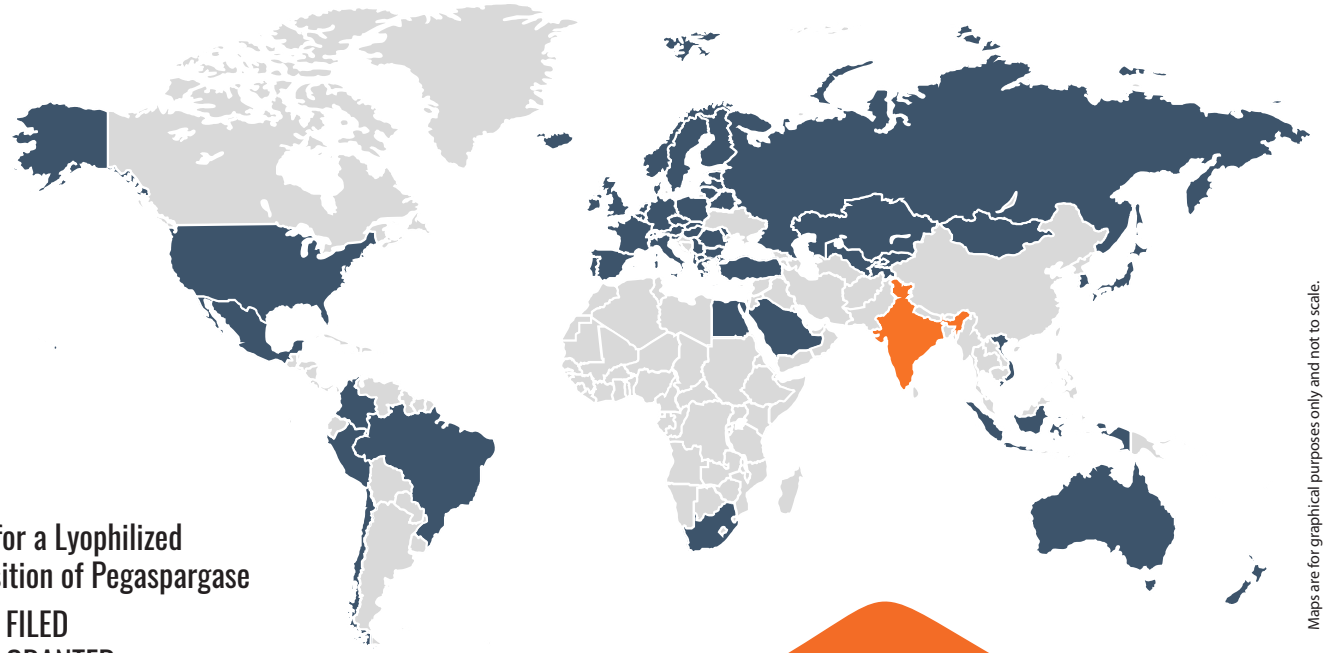
Mean ± standard deviation of L-asparaginase plasma activity–time profiles in the test and reference arms

Human Clinical Study[4]

A prospective, open label, randomized, active control, parallel design, comparative PK study of IM Hamsyl® versus Oncaspar® in pediatric patients with relapsed cases of ALL

- Hamsyl® is bioequivalent to innovator product in this study.
- Trough asparaginase level of >100 IU/L with Hamsyl® at 1000 IU/m2 observed to be comparable with innovator product.
- Overall survival rate of Pegaspargase treatment in relapsed cases of ALL >70% at 2 year.
- Hamsyl® was well tolerated and found to be safe and efficacious in the relapsed patients of ALL.

1. Acute lymphoid leukemia — Level 4 cause. Institute for Health Metrics and Evaluation https://www.healthdata.org/results/gbd_summaries/2019/acute-lymphoid-leukemia-level-4-cause (2020)
2. https://vizhub.healthdata.org/gbd-results/
3. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02
4. https://pubmed.ncbi.nlm.nih.gov/32628582/



Maps are for graphical purposes only and not to scale.

Patent for a Lyophilized Composition of Pegaspargase

- FILED
- GRANTED

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Gennova Biopharmaceuticals Limited, headquartered in Pune, India, is a biotechnology company dedicated to the development, production and commercialization of bio-therapeutics to address life-threatening diseases across various indications. Incorporating recombinant DNA technologies together with innovative bio-manufacturing practices, Gennova has created cost effective solutions for manufacturing and successfully commercializing bio-therapeutics across cardiovascular, neurology, nephrology and oncology markets. Gennova has developed an mRNA-based platform technology for a COVID-19 vaccine.

GENNOVA

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