BIOCON'S
INSULIN GLARGINE STORY

A Commitment to Effective Diabetes Management

Biocon embarked upon the Insulin Glargine development journey after successful launch of Insugen® (recombinant human Insulin) in India. We are driven by our passion to develop affordable biopharmaceuticals and are committed to make insulin-based therapy increasingly accessible for people with diabetes globally.

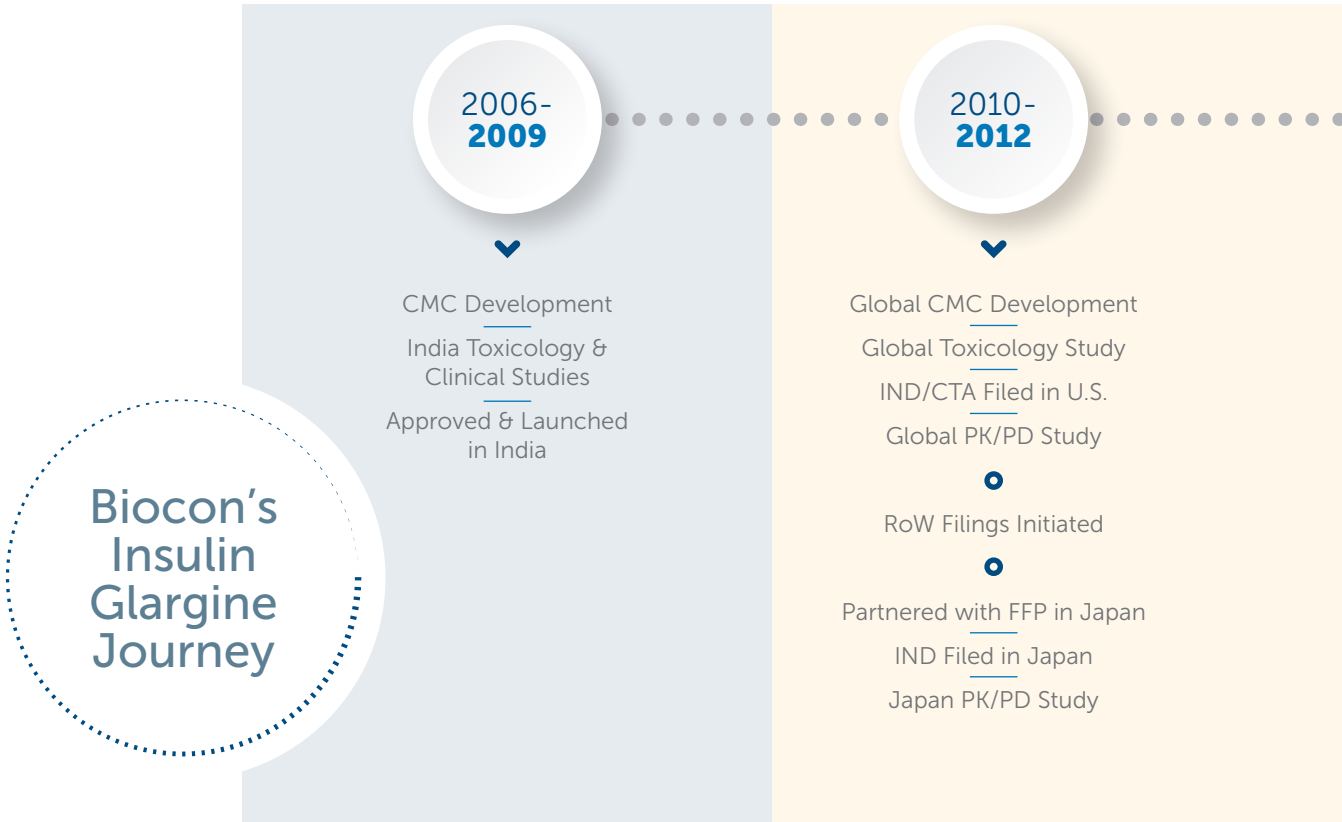
Insulin Glargine is a long-acting insulin analog that offers better glucose control with the convenience of once daily injection versus the discomfort of multiple daily injections and reduces the possibility of developing hypoglycemia (low blood sugar). It is prescribed for adults with Type 2 diabetes as well as adults and pediatric patients (children 2 years and older) with Type 1 diabetes.

Initial Development

The biological process of manufacturing Insulin Glargine starts with a yeast cell, *Pichia pastoris*, which is genetically engineered to express the human Insulin Glargine protein, when grown in culture, which is then purified and formulated. The quality of the Insulin Glargine is established and controlled using multiple orthogonal analytical techniques.

The CMC development, non-clinical and clinical studies for Insulin Glargine in India culminated in its approval and subsequent launch under the brand name BASALOG® in 2009.

To take Insulin Glargine to people with diabetes worldwide, Biocon initiated its global CMC development program in 2010. Our comparative pharmacokinetics / pharmacodynamics (PK/PD), Phase I trials demonstrated the bioequivalence



of biosimilar Insulin Glargine with the reference product in glucose clamp studies.

Global Trials

In 2013, we expanded an existing global partnership with U.S.-based Mylan to include insulin analogs, Glargine, Aspart and Lispro. Subsequently, we initiated the global INSTRIDE clinical program to establish the efficacy, safety and immunogenicity of biosimilar Insulin Glargine in comparison to the reference product in patients with Type 1 and Type 2 diabetes. INSTRIDE 1 was a 52-week study in 558 Type 1 diabetes patients, while INSTRIDE 2 was a 24-week study in 560 Type 2 diabetes patients. In both the studies, patients were randomized to receive either biosimilar Insulin Glargine or the reference product once daily and the primary endpoint was change from baseline in HbA1c after 24 weeks. Secondary endpoints included glycemic endpoints such as change from baseline in fasting plasma glucose and insulin dose, as well as, safety endpoints like systemic reactions, device-related safety issues and immunogenicity.

On conclusion of the trials, we made a regulatory submission with the European Medicines Agency (EMA) in 2016, which included analytical, functional and pre-clinical data, as well as results from the PK/PD and confirmatory efficacy/safety global clinical trials for biosimilar Insulin Glargine.

Approvals Across the Globe

In 2015, our product became the first Insulin Glargine to be approved in Mexico as per the country's biologics approval pathway.

Subsequently, we achieved a major regulatory milestone with approval of our Insulin Glargine in Japan. The approval followed the successful completion of initial development by Biocon and local comparative Phase I followed by Phase III clinical studies in over 250 Type 1 diabetes patients

2013-2015

Partnered with Mylan

Global INSTRIDE Clinical Studies

Tech Transfer To Malaysia & Scale-Up

Disposable Pen, Basalog One™, Launched in India

Approved in Mexico

Japan Phase III Clinical Study

NDA Filed in Japan

2016-2017

Final Similarity Package

MAA Filed in EU & Australia

NDS Filed in Canada

NDA Filed in U.S.

Approved in Japan, Malaysia, UAE, Algeria

Product Launched in Japan, Malaysia, UAE, Algeria

2018

Approved in EU, Australia, S. Korea, Russia

by our Japanese partner. This was Biocon's first biosimilar approval in a developed market and the first biosimilar from a company in India to be approved in Japan. The approval and launch of our Insulin Glargine disposable pen in Japan in 2016 was an important continuing endorsement of our product quality.

Till date, 1,700 patients and healthy volunteers have been evaluated in comparative clinical studies conducted across the U.S., EU, Japan, India, Canada and other countries for establishing the safety and efficacy of Biocon's Insulin Glargine.

In January 2018, the EMA's Committee for Medicinal Products for Human Use (CHMP) recommended Insulin Glargine co-developed by Biocon and Mylan for approval. After CHMP's positive opinion, the European Commission approved the sale of the biosimilar Insulin Glargine, Semglee™ 100 units/mL 3 mL prefilled disposable pen, in March 2018. It is the first biosimilar from Biocon and Mylan's joint portfolio to be approved in Europe.

Our biosimilar Insulin Glargine has also been approved in Australia, Russia, Mexico, South Korea, Malaysia and 28 other countries, enabling us to provide an affordable treatment option to millions of people with diabetes worldwide.

It is a proud achievement for Biocon that takes us closer to realizing our aspiration of reaching 'one in five' insulin dependent people with diabetes worldwide.