BIOTECH PRODUCT: GAMMAREC, RECOMBINANT HUMAN INF-GAMMA

Interferon gamma-1b

Summary

Interferon gamma-1b is a form of recombinant human interferon used to treat infections associated with chronic granulomatous disease and to slow the progression of severe malignant osteopetrosis.

Description

Brand Name	Gammarec
Generic Name	Interferon gamma-1b
N-terminal Sequence Analysis	Met-Gln-Asp-Pro-Tyr-Val-Lys-Glu-Ala-Glu-Asn-Leu-Lys-Lys-Tyr

Background

Human Interferon gamma-1b (140 residues), produced from *E. coli*. Production of Gammarec is achieved by fermentation of a genetically engineered *Escherichia coli* bacterium containing the DNA which encodes for the human protein. Purification of the product is achieved by conventional column chromatography. Gammarec is a high purified sterile solution consisting of non-covalent dimmers of two identical 16465 daltonsmonomers.

Specifications

Covalent Dimers & Oligomers	>2%, determined by size-exclusion chromatography (2.2.30)
Monomer and Aggregates	>2%, determined by size-exclusion chromatography (2.2.30)
Deamidated & Oxidised Forms & heterodimers	>3% for heterodimers and >10% for deamidated and oxidised forms , Examine by liquid chromatography (2.2.29)
SDS-PAGE	17 kDa
Potency	Estimated by evaluating the increase of the expression of human-leukocyte-antigen-DR (HLA-DR) due to the interferon gamma-1b present in test solutions during cultivation of the cells, and comparing this increase with the same effect of the appropriate International Standard of human recombinant interferon gamma. The estimated specific activity is 16-25 x10^6 IU/mg.
Endotoxin Level	<0.01 EU per 1 µg of the protein by the LAL method.
Purity	>97%, by SDS-PAGE with silver staining,
Host Cell Protein	<0.5 ng per µg of protein when tested by ELISA.

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Host Cell DNA	<0.0015 ng per µg of protein when tested by PCR.
Formulation	liquid from contains: 100 mcg of interferon gamma-1b formulated in 20 mg mannitol, 0.36 succinic acid, 0.05 mg Tween 20. See Certificate of Analysis for details.
Preparation and Storage	
Reconstitution	The product is ready to use and it doesn't need any reconstitution
Shipping	The product is shipped with polar packs. Upon receipt, store it immediately at 2-8° C. Do not freeze.
Stability & Storage	Shelf life: 24 month at 2-8° C. Left over time: 24 hours. Avoid excessive or vigorous agitation. Do not shake.

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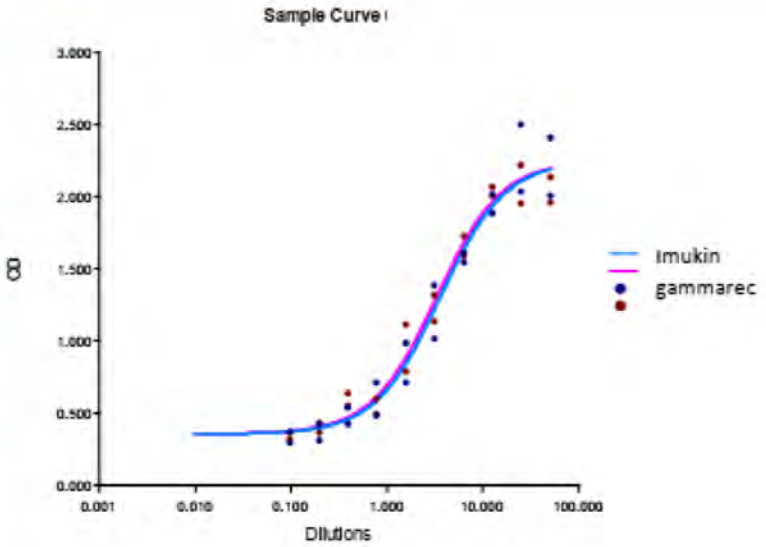
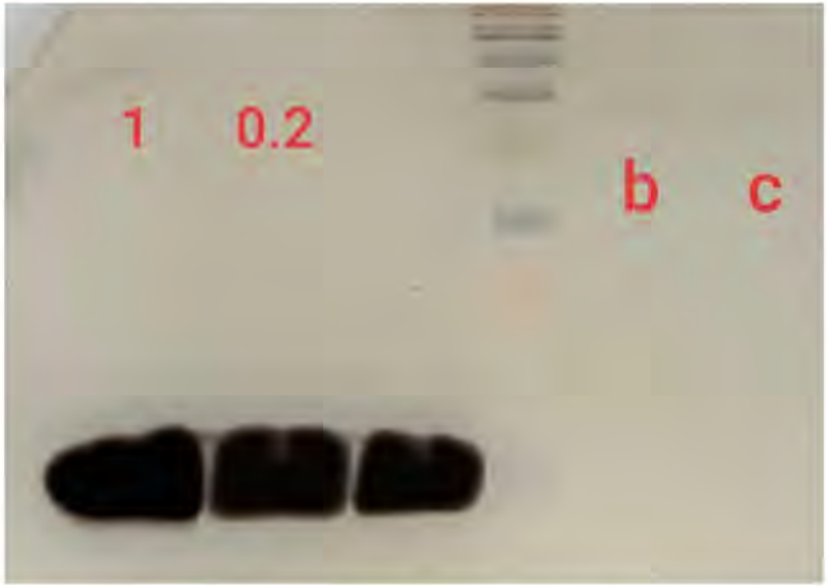
DATA



The expression of HLA-DR was increased by Gammarec. Calculations was done by Gen5 software and Imukin was used as the standard sample.



A 15% SDS-PAGE of protein expression levels of human Interferon gamma-1b and visualized by silver staining. It showed the single band at 17 kDa. Lane 1: sample contain 1 mg/ml interferon gamma-1b. Lane 2: sample contains 0.2 mg/ml interferon gamma-1b. Lane 3: CRS, Lane 4: Protein Ladder, Lane 4&5: reference solutions.

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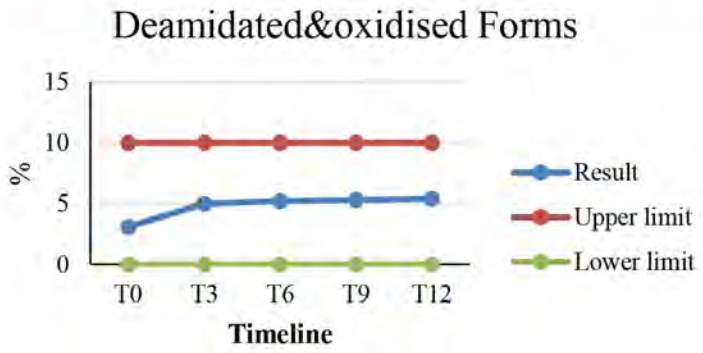
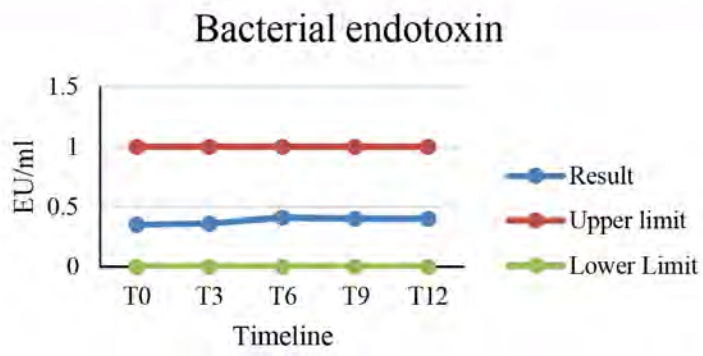
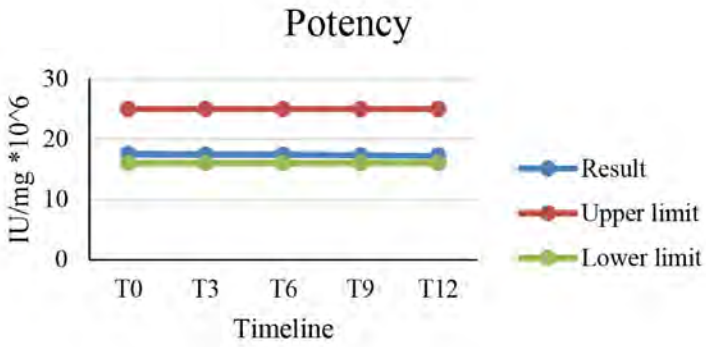
Stability Data







Stability data shows Gammarec maintain its original form without any visible changes under the long term storage condition.

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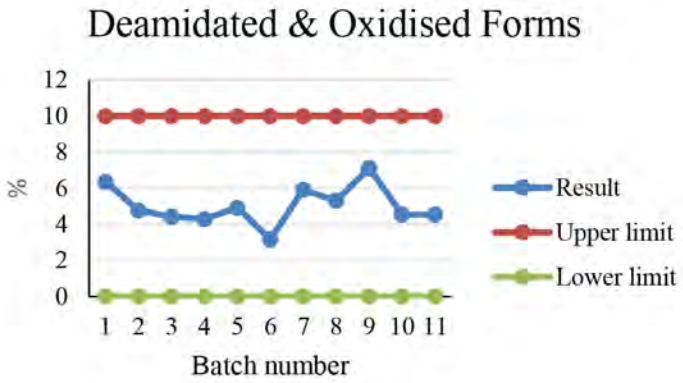
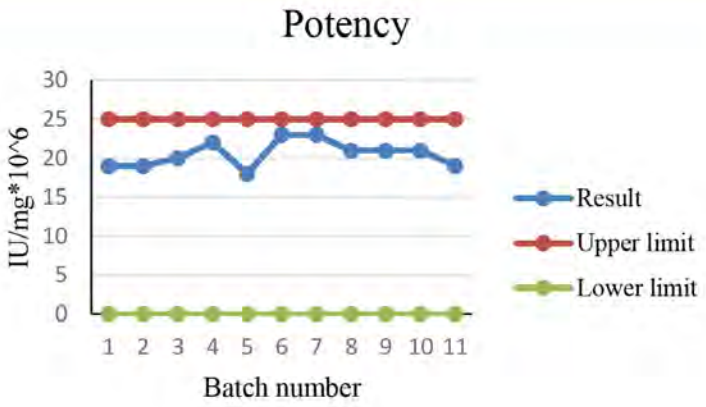
Assess Quality Consistency





Cp: 1.5, Cpk: 1.5

The quality control result indicated the maintenance of Gammarec consistency

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Manufacturing Specifications

Gammarec are produced according to relevant sections of the following documents: Good Manufacturing Practices for Biological Products; USP 42, and BP2019.
Quality system's focus includes:

- Documented processes and QA control of documentation and process changes
- Personnel training programs
- Raw material testing and vendor qualification/monitoring
- validated equipment, processes and test methods
- Equipment calibration schedules
- Facility maintenance, safety programs and pest control
- Material review process for variances
- Monitoring of stability over product shelf-life

Gammarec Pharmacokinetics

Interferon are not absorbed from the gastrointestinal tract. Peak plasma concentrations of interferon gamma-1b occur about 4 hours after intramuscular injection and about 7 hour after subcutaneous injection. Half-lives of 38 minutes (intravenous administration), 2.9 hours (intramuscular administration) and 5.9 hours (subcutaneous administration) have been reported.

Indication and Uses

Gammarec is indicated for reducing the frequency and severity of serious infections associated with Chronic Granulomatous Disease (CGD). Also, Gammarec plays important roles in the development and subsequent control of Leishmania infections. Nowadays Gammarec used for treatment CGD patients in Iran and for treatment leishmaniasis patients in turkey.

PSUR Report

The flu-like symptoms associated with this drug were seen in Gammarec injection and the dominant complaint was fever, which is also common with the brand product PSUR studies as reported internationally in documents and journals. The dominant side-effects as reported for one in ten of patients who they have administrated interferon gamma worldwide were also in line with Gammarec administration side effects and showed similar pattern and no un-common or serious side effects were seen or reported for the Gammarec injection during the study period.