Unit: Technical Assessment Unit

Public assessment report for biological products

Humaxin Tard

Administrative information:

Trade name of the medicinal product:	Humaxin Tard
INN (or common name) of the active substance(s):	Human Insulin Isophane 100 I.U./ml
Manufacturer of the finished product	Evapharma for Pharmaceutical Industries (2), Polaris Industrial District, Plot No. 27, North extensions area, 6th of October City, Giza - EGYPT
Marketing Authorization holder	Evapharma for Pharmaceutical Industries (2), Polaris Industrial District, Plot No. 27, North extensions area, 6th of October City, Giza - EGYPT
Applied Indication(s):	Anti-diabetic
Pharmaceutical form(s) and strength(s):	Suspension for S.C injection 100 I.U./ml
Route of administration	S.C injection
Type of registration (EMA/FDA – Local)	Local

List of abbreviations

S.C.	Subcutaneous
MA	Marketing Authorization
IPC	In process control
GMP	Good manufacturing practice
USP	United states pharmacopeia
BP	British pharmacopeia
CPP	Critical process parameter
SOPs	Standard operating procedures
EDQM	European Directorate for the Quality of Medicines & HealthCare
PVC/Alu	Aluminium Polyvinyl chloride

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1. **General introduction about the product including brief description of the AI, its mode of action and indications**

Humaxin Tard suspension for injection is a second brand product for the reference product Humulin N 100 IU/ml 3 ml for injection, Eli Lilly.
The active ingredient of the product is Human Insulin. The primary activity is the regulation of glucose metabolism. Insulin lowers blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. They are used in one fill volume 3 ml Cartridges. The pharmaceutical development of this product was straight forward depending on the data provided by Eli Lilly. Excipients were selected based on the same used in reference product (Humulin N 100 IU/ml 3 ml for injection, Eli Lilly).

2. **Quality aspects:**

2.2.1 Introduction

as mentioned above in the general introduction.

2.2.2 Drug Substance (Active ingredient)

Drug substance part is not assessed as it was previously approved in MA file of Humulin N 100 IU/ml 3 ml for injection, Eli Lilly.

2.2.3 Drug product:

- **Description and Composition of the Drug Product**

- Humaxin Tard suspension for injection is a white suspension which on standing deposits a white sediment and leaves a colorless to almost colorless supernatant liquid.
- The drug product composition has been fully detailed, including the active substance and accompanying excipients along with their respective functions.
- The container closure system consists of a Type I transparent glass cartridge, with chlorobutyl plunger on one side and Combiseal (Aluminum cap + Chlorobutyl) on the other side, with glass beads contained in the cartridge to facilitate resuspension.

- **Pharmaceutical Development including brief description on components of drug product**

- Human Insulin is used as active ingredient in Humaxin Tard Suspension for Injection. Human Insulin is procured from Eli Lilly which is White or almost white powder.
- The excipients used in the development of formulation are present in the reference product Humulin N 100IU/ml 3 ml for injection, Eli Lilly. No new excipients were tried in this second brand product.

All inactive ingredients used in the formulation are standard pharmaceutical substances complying with pharmacopeial monographs.

- **Formulation Development**

- The aim of the formulation development was to develop a formulation of Humaxin Tard Suspension for Injection that is equivalent to the reference product Humulin N 100IU/ml 3 ml for injection, Eli Lilly. Both reference and test products showed similar behavior in physical and chemical characteristics.
- A comparative study has been performed. This comparative study involves the comparison of the results obtained by the analytical testing of sample of the production of Humaxin Tard Suspension for Injection against a sample of a commercial batch of Humulin N 100IU/ml 3 ml for injection, Eli Lilly. The results are match closely and the deviation is negligible. Therefore, it can be concluded that Humaxin Tard Suspension for Injection is essentially similar to the reference product Humulin N 100IU/ml 3 ml for injection.
- The impurities in the finished product had their origin from the active pharmaceutical ingredient, Human Insulin.

- **Overages**

- The quantity of Human Insulin includes an overage to guarantee a final concentration of 100 IU/ml.

- **Physicochemical and Biological Properties**

- Human Insulin is White or almost white powder.
- The chemical formula and the molecular weight are mentioned.
- The physicochemical and biological properties include solubility, loss on drying, particle size, pH, particulate matter, aggregation, and biological activity & potency.

- **Manufacturing Process Development**

- All manufacturing steps and procedures have been performed following the latest GMP regulations.
- Detailed description of the development is well mentioned in the MA file.

- **Container closure system and their compatibility**

- Primary container: Transparent glass cartridges (Type I), with chlorobutyl plunger on one side and Combiseal (Aluminum cap + Chlorobutyl) on the other side with glass beads contained in the cartridge to facilitate resuspension.
- The stability study carried out for 6 months showed that the product is stable and compatible with this packaging where no change in physical appearance was observed and insignificant change in chemical properties.

- **Microbiological Attributes**

- Humaxin Tard Suspension for Injection is a sterile product. The finished product is supplied in multiple-dose Cartridges, and it is only opened prior to administration. Thus, the sterility of the product can be assured.

- **Manufacture of the drug product**

- **Description of manufacturing process and process controls along with manufacturers and responsibilities.**

The product is manufactured, packaged & released at Eva pharma for pharmaceutical industries (2), Polaris Industrial District, Plot No. 27, North extensions area, 6th of October City, Giza – EGYPT.

- **Manufacturing process:**

- Narrative description & flow diagram of the process is well illustrated in the MA file showing the preparation of the solution (insulin section & buffer section) followed by filtration, mixing & circulation procedures followed by filling.
- CPPs are shown on the flow diagram.
- The steps are controlled through various IPCs.

- **Control of critical steps and intermediates**

The CPPs are mentioned in the MA file with their limits.

- **Process validation and / or evaluation**

- Process validation has been performed for three consecutive production batches of Humaxin Tard Suspension for Injection. All equipment and procedures involved in the manufacturing of validation batches are the same as those used for normal production batches.

- **Product specification**

- Some specifications proposed for release and stability testing of the finished product comply with European Pharmacopoeia, BP, USP and In House based on Eli Lilly.
- Detailed SOPs, validation protocols & reports are provided.
- The specifications include physical & chemical characters and microbiological examination of the drug product.
- All the mentioned in-house tests were validated and met the criteria & the pharmacopoeial methods were verified.
- Justification of the drug product specifications at the release and during stability studies are provided.
- The used excipients are pharmacopeial.
- No excipient is found to be of human or animal origin or novel excipient.

- **Reference Standards or Materials**

- List of references were provided in the MA file with their corresponding potency and use.
  - The reference standard for Human Insulin was procured from EDQM.
  - The reference standards for Insulin Porcine for system suitability was procured from EDQM.

- **Container closure system**

- Primary container: Transparent glass cartridge made of glass type I, with chlorobutyl plunger on one side and Combiseal (Aluminum cap + Chlorobutyl) on the other side with glass beads contained in the cartridge to facilitate resuspension.
- Secondary container: Transparent PVC/Alu blister inside carton box.
- The specification for each component is provided in the MA file.

- **Stability of the drug product**

- Based on available stability data

- **Approved Shelf Life:**
  - 24 months

- **Approved Storage Conditions:**
  - Store in a refrigerator at temperature (2-8°C)
  - Do not freeze
  - Do not expose to excessive heat or direct sunlight.
- In-use storage conditions (after cartridge insertion):
  - Store in room temperature with shelf life 28 days (below 30 °C)

Adventitious agents:
NA

3. & 4. Non –clinical aspect & Clinical aspect:

The development, characterization and manufacture of Humaxin Tard Suspension for Injection have been adequately described. The manufacturing process is described in sufficient details and has been satisfactorily validated. The IPC tests are described and deemed suitable for controlling and monitoring the manufacturing process. The results indicate that the finished product can be reproducibly manufactured.
As a second brand for Humulin N, the comparability study was reviewed according to ICH Q5E & successfully demonstrated that there is no statistically significant difference between Humulin N and Humaxin Tard Suspension for Injection.
No major quality aspects impacting Humaxin Tard Suspension for Injection.
Thus, No need for preclinical and clinical evaluation.

5. General Conclusion and Recommendations if any:

Based on the review of CTD modules and other supplementary documents, the product is approved.