Public assessment summary report

Name of the Finished Pharmaceutical Product	Inigast 40 tablets
Manufacturer of the Finished Product	BDA HEALTHCARE PVT. LTD., Plot No.: B-1, 2, 3, Near Gov. ITI MIDC, Parseoni – 441105, Taluka: Parseoni, District: Nagpur, M.S., India
Active Pharmaceutical Ingredient(s) (API)	Esomeprazole magnesium trihydrate

1. Introduction

Based on in depth review of quality, safety and efficacy data, the authority granted a marketing authorization for Inigast 40 tablets, from BDA healthcare pvt Ltd. The active ingredient of Inigast is Esomeprazole magnesium trihydrate. Esomeprazole is in a class of medications called Proton Pump Inhibitors.

The product is indicated for Gastro-Oesophageal Reflux Disease (GORD). A compressive description of the indications and posology is given in the SmPC.

2. Assessment of quality

Active pharmaceutical Ingredient (API)

INN name: Esomeprazole Magnesium Trihydrate

Chemical name: 5-methoxy-2-[(R)-[(4-methoxy-3, 5-dimethylpyridin-2-yl) methane] sulfinyl]-1H-1, 3-benzodiazole

The active substance is a white to slightly colour crystalline powder, slightly hygroscopic. It's soluble in methanol, slightly soluble in water and practically insoluble in heptanes. Esomeprazole Magnesium is the magnesium salt of esomeprazole, the S-isomer of omeprazole, with gastric proton pump inhibitor activity. In the acidic compartment of parietal cells, esomeprazole is protonated and converted into the active achiral sulphenamide; the active sulphenamide forms one or more covalent disulfide bonds with the proton pump hydrogenpotassium adenosine triphosphatase (H+/K+ ATPase), thereby inhibiting its activity and the parietal cell secretion of H+ ions into the gastric lumen, the final step in gastric acid production. H+/K+ ATPase is an integral membrane protein of the gastric parietal cell. The enantiomeric purity of this active substance is controlled routinely by HPLC on a chiral AGP column.

The proposed manufacturing process has been adequately described; critical steps and accompanying in-process controls have been defined to ensure quality of the final compound.
In-process controls performed during the synthesis are suitable to control the reaction progress. Appropriate specifications for starting materials, solvents and reagents have been established.

Evidence of the structure has been confirmed by various methods. Potential impurities originating from starting materials, intermediates, by-products, and degradation products have been discussed in relation to their origin and potential carry-over into the final drug substance. Residual solvents and heavy metals are routinely controlled.

The substance complies with the requirements of the Ethiopian medicine registration guideline for potential impurities.
The specifications reflect all relevant quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. Testing methods are adequately drawn up and sufficiently validated. The reference materials used by the active substance manufacturer and the drug product manufacturer for the control of the substance are adequately characterised. Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch to batch consistency of the production.

Stability data have been obtained. The data show the substance to be stable. Based on the data submitted appropriate retest periods and storage conditions have been set.
GMP compliance of the API manufacture is demonstrated by document review.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture:

The aim of the pharmaceutical development was to esomeprazole 40mg tablets generic version to the reference innovator product.

A satisfactory package of data on development pharmaceutics has been presented. Brief Discussion on reasons for inclusion and quantity of excipients has been provided.
The compositions and the pharmaceutical tests evaluated during development of the final Formulation is included in the documentation.

As a result of development studies product with the following composition, appearance and Packaging was obtained. The used excipients were: Lactose Maize Starch, Ethylene Diamine Tetra acetic acid (EDTA), Polyvinyl Pyrrolidone, Methylene dichloride (MDC) or Dichloromethane, Croscarmellose Sodium, Aerosil, Talc purified, Sodium Starch Glycolate, HPMC 5cps, PEG 6000, Isopropyl Alcohol, Methylene Dichloride, Magnesium stearate, microcrystalline cellulose, dibutyl phthalate, Talcum, titanium dioxide. HPMC Phthalate was used as coating agent. All excipients used comply with their respective Ph. Eur. monographs, with the exception of film-coating, which complies with USP/BP monographs.

Inigast 40 mg tablets White, oval shaped, biconvex, plain on both side and enteric coated tablets.

The enteric-coated tablets are packaged in ALU-ALU Blister Pack with insert.

With regard to dissolution and impurity profile, the product is shown to be similar to the reference product. A description and flow chart of the manufacturing method has been provided. Appropriate in-

process controls are included in the manufacturing process. Satisfactory batch formulae were also presented. GMP compliance of the manufacturing site has been demonstrated.

Specifications:

The finished product specification is satisfactory. The acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form in house monograph. Appropriate control strategy was selected. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification. Certificates of analysis for three productions are presented. Certificates of analysis were also provided for the working standard used.

The container closure system

Inigast 40 mg blisters:

Alu-Alu blister pack of pack size 3X10 was the container closure system used for production batches.

Stability testing:

Same blisters as those proposed for routine storage were used for the stability studies.
Finished product stability studies have been conducted in accordance with the current medicine registration guideline of Ethiopia. Based on the results a shelf-life of 36 months with storage conditions: *"Store below 30°C and protect from light."* is considered acceptable for inigast 40 mg tablet.

3. Assessment of bioequivalence

Randomized, Open-Label, Two-Way Crossover Study to Compare The Bioequivalence of test product inigast 40 (Esomeprazole 40 mg) comparing with the reference product NEXIUM (Esomeprazole 40 mg) , Astra Zeneca AB, Sweden in healthy Male volunteers.

Based on the acceptance criteria (ln transformed value of Cmax and AUC0-t, 80-125) Inigast 40 (Esomeprazole 40 mg) manufactured by BDA healthcare pvt. ltd ,India is bioequivalent with Nexium (Esomeprazole 40mg) manufactured by AstraZeneca AB, Sweden.

Conclusion

Based on assessment of data on quality, bioequivalence, safety and efficacy the assessors considered that the benefit–risk profile of Inigast 40 mg enteric-coated tablets manufactured by BDA healthcare pvt. ltd ,India was acceptable for the following indication: Gastroesophageal Reflux Disease (GERD), In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori, Patients requiring continued NSAID therapy, Prolonged treatment after I.V. induced prevention of rebleeding of peptic ulcers and Treatment of Zollinger Ellison Syndrome