AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Nexium capsules
ACTIVE INGREDIENT: Esomeprazole Magnesium Hydrate

Study No: D961HC00010
NCT01434485

Developmental Phase: post-marketing
Study Completion Date: March/2014
Date of Report: July/2014

OBJECTIVES:

The objectives of the CEI were to investigate ADRs not expected from the Nexium JPI, and factors which may affect ADRs, safety and efficacy.

METHODS: Observational Study

RESULTS:

1. Safety
ADRs were observed in 45 patients in 3394 patients of the safety analysis set (1.3%). The ADRs developed in at least 3 patients were diarrhoea in 6 patients (0.2%), constipation in 4 patients (0.1%), and vomiting in 3 patients (0.1%). All events were non-serious ADRs. Serious ADRs observed in the CEI were cerebral infarction in 1 patient (outcome: recovered), and platelet count decreased in 1 patient (outcome: not yet recovered).
There was no ADR unexpected from the JPI and developed in more than 3 patients. All of the ADRs unexpected from JPI had involvement of concomitant disease or concomitant drugs. In addition, as the number of the ADRs was small, no new action is considered required.
ADR/infection development of each disease under investigation was reviewed, and there was no significant difference among them.
Fracture, community acquired pneumonia, and enterocolitis in association with *Clostridium difficile* infection were the events which had been considered possibly related

to PPIs, and for which safety information should be collected and after marketing. No patient experienced fracture or enterocolitis in association with *Clostridium difficile* infection in the CEI. The event of pneumonia was collected in two patients as community acquired pneumonia. However, causal relationship between the event and Nexium was ruled out in both of the events.
ADR development in patients with peptic ulcer (gastric ulcer and duodenal ulcer), and those with gastro-oesophageal reflux (reflux oesophagitis and non-erosive oesophagitis) was reviewed by each patient demography factor and treatment which may affect safety. Significant difference ($p < 0.05$) in ADR frequencies were observed in the following factors: inpatient vs. outpatient, past medical history Yes vs. No, previous treatment for the disease under investigation Yes vs. No, and discontinuation of Nexium during the investigation Yes vs. No in patients with peptic ulcer, and smoking habit Yes vs. No, allergy Yes vs. No, concomitant diseases Yes vs. No, concomitant therapies Yes vs. No, change of Nexium dose during the investigation Yes vs. No, and discontinuation of Nexium during the investigation Yes vs. No in those with gastro-oesophageal reflux. However, no new action is considered required.

2. Efficacy
Efficacy confirmed on endoscopy was as follows: endoscopic healing rates were: 82.2% (254/309) in patients with gastric ulcer, 91.6% (98/107) in those with duodenal ulcer, and 78.9% (120/152) in those with reflux oesophagitis. The ulcers also resolved in two patients with anastomotic ulcer and in one patient of Zollinger-Ellison syndrome.
Efficacy confirmed on subjective symptoms was as follows: improving rates of epigastric pain were: 98.3% (588/598) in patients with gastric ulcer, 97.3% (285/293) in those with duodenal ulcer, and 87.5% (7/8) in those with anastomotic ulcer. The improvement rates of heartburn were 93.2% (1285/1379) in patients with reflux oesophagitis, and 89.9% (213/237) in those with non-erosive gastro-oesophagus reflux disease.
The factors which may affect efficacy in demography and treatment factors were reviewed. There was significant difference ($p< 0.05$) in endoscopic healing rates in following demographic factors: age, inpatient vs. outpatient, and concomitant drugs in gastric ulcer Yes vs. No. However, there was no issue which may require a new action. There was no factor which showed significant difference in the patients with duodenal ulcer or reflux oesophagitis.
Significant difference ($p < 0.05$) of the disappearance rate of heartburn was observed in following factors: BMI, disease duration after the initial onset, previous treatment for the disease under investigation Yes vs. No, unit dose of Nexium at the first prescription, and Nexium dose change during the investigation Yes vs. No in patients with reflux oesophagitis, BMI, disease duration after the initial onset, past medical history Yes vs. No, previous treatment for the disease under investigation Yes vs. No, concomitant drug Yes/No, and discontinuation of Nexium during the investigation Yes vs. No in those with non-erosive gastro-oesophagus reflux disease.
As above, new safety and efficacy concerns which may require new actions were not identified in the CEI. Updated information on the appropriate use concerning dosage and administration will be sought from spontaneous reports, and assessment/review will be conducted for updated ADR information.