STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Nexium capsules
ACTIVE INGREDIENT: Esomeprazole Magnesium Hydrate

Study No: D961HL00020
NCT02477475

Developmental Phase: post-marketing
Study Completion Date: February 2017
Date of Report: June 2017

OBJECTIVES:

The primary objective of the S-CEI was to confirm the treatment response to Nexium Capsule in patients with reflux oesophagitis when actually used in post-marketing clinical practice. The secondary objectives were to evaluate patient satisfaction, health-related quality of life (HRQOL), physician-reported severity and frequency of subjective symptoms, endoscopic healing rate, and nature and frequency of adverse drug reactions (ADRs).

METHODS:

Observational Study

RESULTS:

1 Efficacy

Treatment Response to Nexium Capsule

Treatment response to Nexium Capsule was evaluated using the GerdQ questionnaire, a patient-administered questionnaire specific for gastroesophageal reflux disease (GERD). The proportion of patients whose response to Questions 1, 2, 5 and 6 of the GerdQ were 0 or 1 day (i.e., treatment responders) at the final assessment, the primary endpoint of the S-CEI, was 81.4% (1034/1271 patients, exact 95% confidence interval [CI]: 79.1%, 83.5%). The proportion of treatment responders was 72.2% (771/1068 patients, exact 95% CI: 69.4%, 74.9%) at Week 4 and 83.3% (669/803 patients, exact 95% CI: 80.6%, 85.8%) at Week 8. Previous studies evaluating treatment response to Nexium

Capsule in patients with reflux oesophagitis using the GerdQ reported that approximately 70% to 85% of the patients responded to Nexium Capsule, which was similar to the result of the S-CEI.

In addition, multivariate logistic regression was used to investigate factors that may affect treatment response to Nexium Capsule. The following were identified as factors potentially affecting treatment response to Nexium Capsule: gender (higher treatment response in male patients than in female patients), BMI (higher treatment response in patients with BMI <18.5 or ≥30 than in those with BMI ≥18.5 to <25), and endoscopic finding at the start of treatment (higher treatment response in patients with Grade A/B or Grade C/D than in those with Grade N/M at the start of treatment).

Patient Satisfaction with Medication

A patient-administered questionnaire on patient satisfaction was used to determine use of medications at the start of Nexium Capsule treatment (prior medications) and patient satisfaction with prior treatment. In the subset of patients from the efficacy analysis set who had at least one prior medication for reflux oesophagitis, the proportion of patients with satisfaction or better response (i.e., "extremely satisfied", "very satisfied", or "satisfied") was 23.6% (48/203 patients, excluding non-responders), indicating that majority of the patients did not satisfy with their prior medications.

Then, the patient satisfaction questionnaire was used to assess patient satisfaction with Nexium Capsule.

The proportion of patients with satisfaction or better response (i.e., "extremely satisfied", "very satisfied", or "satisfied") was 84.2% (893/1061 patients), 88.8% (710/800 patients), and 87.7% (1100/1266 patients) at Week 4, Week 8, and at the final assessment, respectively. In summary, treatment with Nexium Capsule provided satisfaction for more than 80% of the patients as early as Week 4 and nearly 90% of the patients at Week 8.

Heatlh-Related Quality of Life

The acute form of the SF-8 (for one-week recall), a patient-administered questionnaire measuring overall health status, was used to assess HRQOL of the patients.

Mean (± SD) physical component summary (PCS) score was 49.198±6.128, 50.403±5.768, and 50.191±5.930 at Week 4, Week 8, and the final assessment, respectively; and mean (± SD) change from baseline in PCS score was 4.414±8.199, 5.612±8.753, and 5.326±8.634, respectively, which showed a large increase in the score at Week 4 and a further increase at Week 8.

A similar pattern was noted for mental component summary (MCS) score. Mean (± SD) MCS summary score was 50.192±6.097, 51.244±5.849, and 50.994±5.887 at Week 4, Week 8, and the final assessment, respectively; and mean (± SD) change from baseline in MCS score was 3.837±7.633, 4.931±7.817, and 4.470±7.712, respectively, which showed a large increase in the score at Week 4 and a further increase at Week 8.

These results indicate that continuous treatment with Nexium Capsule improved and/or resolved symptoms and thereby improved both physical and mental health of patients.

Efficacy Based on Subjective Symptoms

The proportion of patients experiencing improvement in a particular symptom was at least 85% for all of the subjective symptoms investigated and was more than 90% for the following subjective symptoms: vomiting (95.2%, 139/146 patients), inappetence (92.8%, 428/461 patients), heartburn

(91.6%, 1080/1179 patients), difficulty in swallowing (91.1%, 175/192 patients), and stomach discomfort (stomach feeling heavy) (91.0%, 765/841 patients).

The proportion of patients experiencing resolution of a particular symptom was at least 70% for all of the subjective symptoms investigated except for heartburn (69.6%, 820/1179 patients). The proportion of patients experiencing resolution was more than 80.0% for the following subjective symptoms: difficulty in swallowing (87.5%, 168/192 patients), vomiting (86.3%, 126/146 patients), and inappetence (85.9%, 396/461 patients).

Changes over time in severity of individual subjective symptoms were analysed using the set of patients for whom data at both baseline and final assessment were available as well as the set of patients for whom data at baseline, Week 4, and Week 8 were available. The analysis results indicated improvement in subjective symptoms at Weeks 4 and 8 compared with baseline.

Improvement in heartburn was assessed in terms of the heartburn reduction rate (i.e., proportion of patients with decreased frequency of heartburn compared with baseline among those with the number of days with heartburn ≥1 day/week at baseline). The heartburn increase rate was also determined as the proportion of patients with increased frequency of heartburn compared with baseline. The heartburn reduction rate was 92.0% (1015/1103 patients), while the heartburn increase rate was 1.1% (12/1103 patients) among patients with the number of days with heartburn ≥1 day/week at baseline and 12.5% (14/112 patients) among those without heartburn at baseline.

Among patients with the number of days with heartburn ≥1 day/week at baseline, 70.7% (780/1103 patients) had no heartburn at the final assessment.

Mean (±SD) number of days with heartburn was 4.0±2.2 days/week at baseline and decreased to 0.6±1.3 days/week at the final assessment.

Although direct comparison with the results from the CEI is difficult because of different patient background and treatment factors, the results of the S-CEI were similar to those from the CEI and again demonstrated improvement of subjective symptoms by treatment with Nexium Capsule.

Endoscopic Healing Rate

Of 1307 patients included in the efficacy analysis set of the S-CEI, 603 patients (46.1%) underwent endoscopy at baseline and only 54 patients had endoscopic data at both baseline and final assessment.

Among patients with baseline endoscopic data (n=603), endoscopic grade was N/M in 173 patients (28.7%), A/B in 360 patients (59.7%), and C/D in 70 patients (11.6%). Some patients had symptoms of GERD even without endoscopic GERD finding.

Of 54 patients for whom endoscopic data at both baseline and final assessment were available, 6 patients were graded as M at baseline. Among the remaining 42 patients, endoscopic grade changed to N or M in 42 patients (Grade N for 23 patients and Grade M for 19 patients), resulting in endoscopic healing rate of 87.5% (42/48 patients).

The endoscopic healing rate was 87.3% (165/189 patients) at Week 8 of treatment with Nexium Capsule 20 mg in a phase III study in Japan conducted before approval of Nexium Capsule and 78.9% (120/152 patients) at the final assessment in the CEI of Nexium Capsule. Although direct comparison of results is difficult because of different patient background and treatment factors as well as different timing of endoscopy, the rate reported in the S-CEI was similar to previously reported rates.

2 Safety

Adverse Drug Reactions and Infections

A total of 34 cases of adverse drug reactions (ADRs) were reported in 29 of 1367 patients (2.1%) included in the safety analysis set. Reported ADRs were chronic gastritis in 4 patients (0.3%), diarrhoea in 3 patients (0.2%), faeces soft and eczema in 2 patients (0.1%) each, and others in 1 patient (0.1%) each.

No serious ADR was reported. Reported unanticipated ADRs were chronic gastritis in 4 patients (0.3%), and nasopharyngitis, Parkinson's disease, eczema eyelids, asthma, rhinitis allergic, upper respiratory tract inflammation, enterocolitis, gastritis, oral discomfort, osteoporosis, muscle tightness, musculoskeletal stiffness, and feeling abnormal in 1 patient (0.1%) each.

Serious Adverse Events

A total of 3 cases of serious adverse events were reported in 2 of 1367 patients (0.1%) included in the safety analysis set. Reported events were 1 case each of pneumonia, pleura effusion and colon cancer. All of these serious adverse events were unanticipated events and were not considered to be related to Nexium Capsule.