Nexium: Summary of Specific Clinical Experience Investigation in Children

In May 2018, the investigation was started with the target number of registration as 200 patients. In Jan 2020, 240 patients were registered. In Nov 2020, CRFs were collected for 239 patients and the investigation was completed.

The target diseases (main lesion) in 212 patients for safety analysis included Gastric ulcer (35 patients, 16.5%), Duodenal ulcer (17 patients, 8.0%), Anastomotic ulcer (0 patient, 0%), Reflux oesophagitis (124 patients, 58.5%), Non-erosive reflux disease (36 patients, 17.0%), and Zollinger-Ellison syndrome (0 patient, 0%).

The observation period (day) in 212 patients for safety analysis was 40.4±22.7[1,129].

The Nexium administration period (day) in 212 patients for safety analysis was 40.4±22.7[1,129].

For 113 of 212 patients for safety analysis (53.3%), Nexium was stopped. The reasons for discontinuation were “improvement of the symptoms” for 93 patients, “lack of effect” for 7 patients, “no revisit (transferred to other hospital, change of address, etc.)” for 6 patients, “other reasons” for 4 patients, and “adverse event” for 3 patients.

ADRs, etc. developed in 3 of 212 patients for safety analysis (1.4%). The events of ADRs included “Iron deficiency anaemia”, “Abdominal pain”, “Diarrhoea”, “Alanine aminotransferase increased”, “Aspartate aminotransferase increased”, and “Gamma-glutamyltransferase increased” in one patient each (0.5%). There was no development of serious ADR.

Although it is difficult to directly compare the results due to the different background of the patients, the ADR incidence rate was lower than that in the domestic Phase I/III clinical studies in Japanese children (4.0%, 2/50 patients) which were conducted prior to the approval.

The target diseases (main lesion) in 184 patients for efficacy analysis included Gastric ulcer (29 patients, 15.8%), Duodenal ulcer (15 patients, 8.2%), Anastomotic ulcer (0 patient, 0%), Reflux oesophagitis (109 patients, 59.2%), Non-erosive reflux disease (31 patients, 16.8%), and Zollinger-Ellison syndrome (0 patient, 0%).

The improvement rate of subjective symptoms at the latest evaluation was 90.6% (48/53 patients) for heartburn, 95.9% (47/49 patients) for acid reflux, 95.3% (101/106 patients) for epigastric pain, and 93.0% (93/100 patients) for upper abdominal discomfort. The deterioration rate was 0.9% (1/116 patients) for heartburn, 2.5% (3/120 patients) for acid reflux, 0.9% (1/106 patients) for epigastric pain in the patients “with symptoms“ at the start of Nexium, 1.5% (1/65 patient) for epigastric pain

in the patients “without symptoms“ at the start of Nexium, and 4.3% (3/70 patients) for upper abdominal discomfort.

For all of the subjective symptoms, the improvement rate was 90% or more and the deterioration rate was 5% or less.

The disappearance rate of each subjective symptoms was 86.8% (46/53 patients) for heartburn, 83.7% (41/49 patients) for acid reflux, 90.6% (96/106 patients) for epigastric pain, and 84.0% (84/100 patients) for upper abdominal discomfort.

For all of the subjective symptoms, the disappearance rate was 83% or more.

In the transition of the severity of each subjective symptoms by time, improvement was observed for all subjective symptoms compared to those at the start of Nexium administration.

The rate of patients underwent endoscopy among 44 patients with peptic ulcer was 38.6% (17/44 patients) at the baseline and 6.8% (3/44 patients) at the latest evaluation. There were only 2 patients who had endoscopic findings both at the baseline and after Nexium administration. Both of the patients were cured (baseline: A2 → after Nexium administration: S1 or S2).

The rate of patients underwent endoscopy among 109 patients with reflux oesophagitis was 11.0% (12/109 patients) at the baseline and 0.9% (1/109 patients) at the latest evaluation. There was no patient who had endoscopic findings both at the baseline and after Nexium administration.

As stated above, the safety and efficacy of Nexium in children under actual use were reviewed, and the investigation result showed no specific safety concern and no efficacy issue.