A Report on Comparative Safety and Efficacy of Fexuprazan in the treatment of Acid Peptic Diseases

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Introduction

The parietal cell undergoes dramatic morphologic changes from the resting status to the stimulated state, when activated by stimuli such as histamine and acetylcholine, the gastric H^+-K^+ ATPase pumps the gastric acid[1, 2]. Proton pump inhibitors (PPIs) irreversibly block the gastric H^+-K^+ ATPase, inhibiting gastric acid secretion[3]. Proton pump inhibitors (PPIs) were clinically introduced more than 25 years ago and have since proven to be invaluable, safe, and effective agents for the management of a variety of acid-related disorders. Although all members in this class act in a similar fashion, inhibiting active parietal cell acid secretion, there are slight differences among PPIs relating to their pharmacokinetic properties, metabolism, and Food and Drug Administration (FDA)-approved clinical indications. Nevertheless, each is effective in managing gastroesophageal reflux disease and uncomplicated or complicated peptic ulcer disease[4-6]. Despite an excellent safety profile throughout their first two decades of use, the nearly universal popularity of PPIs has prompted several concerns about both their short- and long term effects[7,8]. Potassium-competitive acid blockers (P-CABs) were developed and have beneficial effects including rapid, long-lasting, and reversible inhibition of the gastric hydrogen potassium ATPase, the proton pump of the stomach. Vonoprazan was recently innovated as a novel, orally active, P-CAB. It is currently indicated for the treatment of gastric and duodenal ulcers, reflux esophagitis, and prevention of low-dose aspirin- or nonsteroidal anti-inflammatory drug-related gastric and duodenal ulcer recurrence in Japan[9]. Vonoprazan, a potassium-competitive acid blocker, inhibits acid secretion by competitively blocking availability of potassium to hydrogen-potassium ATPase in both active and resting proton pumps[10, 11].

Fexuprazan, a next-generation, novel potassium-competitive acid blocker (P-CAB) developed by Daewoong Pharmaceuticals, which reversibly blocks the proton pump that secretes gastric acids located in the cannalicular membrane. These agents are widely used for gastroesophageal reflux disease (GERD). A phase 3 clinical trial of

Fexuprazan was conducted in Korea in patients with erosive esophagitis, and additional clinical trials are ongoing for other acid-related diseases[12].

Mechanism of action

Conventional PPIs: Proton pump inhibitors (PPIs) irreversibly block the gastric H^+-K^+ ATPase, inhibiting gastric acid secretion. They block only active parietal cell acid secretion[3, 4].

Potassium Competitive Acid Blockers (P-CABs): Potassium-competitive acid blockers, inhibit acid secretion by competitively blocking availability of potassium to H^+-K^+ ATPase in both active and resting proton pumps[10, 11].

Patent Information (INH Patents sheet) – Product Patent Expiry – US: 8th Jul, 2036; IND/JP/CN: 27th Apr, 2036; KR: 3rd Feb, 2036.

Comparison of Efficacy[12-15]

Outcome	Fexuprazan	Esomeprazole	Vonoprazan
Mucosal Healing Rate – Erosive Esophagitis	4 weeks – 90.3%	4 weeks – 88.5%	88% - 96% (Severe Reflux Esophagitis)
	8 weeks – 99.1%	8 weeks – 99.1%	
Symptom Relief for Moderate-Severe Heartburn (Day 3)	22.4% (~ 3×Esomeprazole)	7.9%	-
24 hour pH	Day 1 – 5.8 ± 0.3	Day 1 - 4.0 ± 1.7	Day 1 – 5.7 ± 0.4
	Day 7 – 6.5 ± 0.3	Day 7 – 5.2 ± 0.9	Day 7 – 6.6 ± 0.1
24 hour pH >4 holding time (%)	Day 1 – 91.3 ± 4.1	Day 1 – 54.3 ± 15.9	Day 1 – 85.3 ± 8.3
	Day 7 – 99.2 ± 1.9	Day 7 – 68.0 ± 14.3	Day 7 – 100 ± 0.0

Fexuprazan HCl strength[16] – 40mg – OD

Indications (Adis Insight) - Phase III: Gastritis; Gastro-Oesophageal Reflux Disease; Peptic Ulcer[17].

As per a study, Fexuprazan (a P-CAB under active development) promise to emulate the superior efficacy and benefits seen with vonoprazan in the treatment of acid-related diseases[14].

Innovator Claims[12, 15]:

The phase 3 clinical trial in patients with erosive esophagitis was conducted in 25 hospitals in Korea. Fexuprazan showed 99% of mucosal healing rate at week 8 and was well tolerated in the patients and additional clinical trials are ongoing for other acid-related diseases.

Sengho Jeon, CEO of Daewoong, said, "We are committed to developing a novel and improved therapeutic options, and are very excited that Fexuprazan will be a valuable addition to the current treatment for acid-related diseases. We expect accelerated development of Fexuprazan through partnerships and will soon have a unique opportunity to commercialize Fexuprazan in the global markets such as US and China.

In January, Daewoong signed an agreement with Moksha8, a leading pharmaceutical company in Latin America. As Daewoong began the successful entry into the global market, Fexuprazan is expected to position as a next global blockbuster drug in the anti-acid secretion agent market valued $37 billion.

Conclusions

- Fexuprazan, a next-generation, novel potassium-competitive acid blocker (P-CAB) developed by Daewoong Pharmaceuticals, which reversibly blocks the proton pump that secretes gastric acids. The company has recently released clinical trials phase – III results for the drug.
- As per the reported results, Fexuprazan is more efficacious than Esomeprazole in all the parameters compared, the efficacy of Fexuprazan is similar to that of Vonoprazan. As reported by a study Fexuprazan may emulate the superior efficacy and benefits seen with Vonoprazan.
- As per the innovator, they signed an agreement with Moksha8 pharmaceutical company in Latin America and will soon have more

partnerships which will get them an opportunity to commercialize Fexuprazan in global markets such as the US and China.

- Therefore, looking at the trial results and considering the claims being made by the innovator, it is quite evident that the product seems to have good potential in the coming future.

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