



Summary of Investigation Results

Preparations containing vonoprazan fumarate

March 19, 2019

Non-proprietary name

- a. Vonoprazan fumarate
- b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
- c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole

Branded name (Marketing authorization holder)

- a. Takecab Tablets 10 mg., 20 mg. (Takeda Pharmaceutical Company Limited.)
- b. Vonosap Pack 400, 800 (Takeda Pharmaceutical Company Limited.)
- c. Vonopion Pack (Takeda Pharmaceutical Company Limited.)

Indications

- a. Treatment of gastric ulcer, duodenal ulcer, reflux esophagitis; prevention of recurrent gastric or duodenal ulcer associated with low-dose aspirin administration; and prevention of recurrent gastric or duodenal ulcer associated with non-steroidal anti-inflammatory drug administration

Adjunct therapy to *Helicobacter pylori* eradication in the following: Gastric or duodenal ulcer, gastric mucosa-associated lymphatic tissue (MALT) lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early-stage gastric cancer, or *Helicobacter pylori* gastritis

- b. <Applicable microorganisms>

Strains of *Helicobacter pylori* susceptible to amoxicillin and clarithromycin

<Applicable conditions>

Helicobacter pylori infection in the stomach and *Helicobacter pylori* gastritis after endoscopic treatment of gastric ulcer, duodenal ulcer, gastric mucosa-associated



lymphatic tissue (MALT) lymphoma, idiopathic thrombocytopenic purpura, or early-stage gastric cancer

c. <Applicable microorganisms>

Strains of *Helicobacter pylori* susceptible to amoxicillin and metronidazole

<Applicable conditions>

Helicobacter pylori infection in the stomach and *Helicobacter pylori* gastritis after endoscopic treatment of gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphatic tissue (MALT) lymphoma, idiopathic thrombocytopenic purpura, or early-stage gastric cancer

Summary of revisions

- a. “Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), erythema multiforme” should be added to the Clinically Significant Adverse Reactions section.
- b. A Clinically Significant Adverse Reactions section should be newly added for vonoprazan fumarate and “Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), erythema multiforme” should be listed.
- c. Same as b.

Investigation results and background of the revision

Cases of toxic epidermal necrolysis, oculomucocutaneous syndrome, and erythema multiforme have been reported in patients treated with vonoprazan fumarate in Japan. MHLW/PMDA concluded that revision of the package insert was necessary based on the results of their investigation of the currently available evidence and in consultation with expert advisors.

Number of adverse reactions and patient mortalities reported in Japan during the previous 3 fiscal years

1. Toxic epidermal necrolysis

a. Vonoprazan fumarate

A total of 6 cases involving toxic epidermal necrolysis have been reported to date

(including 1 case for which a causal relationship with the product could not be ruled out.)

1 instance of patient mortality has been reported to date (a causal relationship with the product could not be established in this case.)

b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin

1 case involving toxic epidermal necrolysis have been reported to date.* No patient mortalities have been reported to date.

c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole

No cases involving toxic epidermal necrolysis have been reported to date.

2. Oculomucocutaneous syndrome

a. Vonoprazan fumarate

A total of 8 cases involving oculomucocutaneous syndrome have been reported to date (including 2 case for which a causal relationship with the product could not be ruled out.) No patient mortalities have been reported to date.

b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin

14 cases involving oculomucocutaneous syndrome have been reported to date.* No patient mortalities have been reported to date.

c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole

No cases involving oculomucocutaneous syndrome have been reported to date.

3. Erythema multiforme

a. Vonoprazan fumarate

A total of 22 cases involving erythema multiforme have been reported to date (including 1 case for which a causal relationship with the product could not be ruled out.) No patient mortalities have been reported to date.

b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin

50 cases involving erythema multiforme have been reported to date.* No patient mortalities have been reported to date.

c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole

3 cases involving erythema multiforme have been reported to date.* No patient mortalities have been reported to date.



Pharmaceuticals and Medical Devices Agency

This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

* Causalities not assessed.

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