



Summary of Investigation Results

Preparations containing vonoprazan fumarate

October 29, 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

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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. “Thrombocytopenia, agranulocytosis, leukopenia, or pancytopenia” should be added to the Clinically Significant Adverse Reactions section.
- b. “Thrombocytopenia, agranulocytosis, leukopenia, or pancytopenia” should be added to the Clinically Significant Adverse Reactions section for vonoprazan fumarate.
- c. Same as b.

Investigation results and background of the revision

Cases of thrombocytopenia, agranulocytosis, leukopenia, and pancytopenia 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 cases and patient mortalities reported in Japan during the previous 3 fiscal years

1. Cases involving thrombocytopenia
 - a. Vonoprazan fumarate

A total of 19 cases involving thrombocytopenia have been reported to date (including 2 cases for which a causal relationship between the drug and event could not be ruled out). 2 patient mortalities have been reported to date (a causal relationship between the

- drug and event could not be established for either of these cases)
- b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
No cases involving thrombocytopenia have been reported to date.
 - c. Vonoprazan fumarate/amoxicillin hydrate/ metronidazole
No cases involving thrombocytopenia have been reported to date.
2. Cases involving agranulocytosis, leukopenia
- a. Vonoprazan fumarate
A total of 15 cases involving agranulocytosis, leukopenia have been reported to date (including 4 cases for which a causal relationship between the drug and event could not be ruled out). 2 patient mortalities have been reported to date (a causal relationship between the drug and event could not be established for either case.)
 - b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
No cases involving agranulocytosis, leukopenia have been reported to date.
 - c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole
No cases involving agranulocytosis, leukopenia have been reported to date.
3. Pancytopenia
- a. Vonoprazan fumarate
A total of 17 cases involving pancytopenia have been reported to date (including 2 cases for which a causal relationship between the drug and event could not be ruled out). No patient mortalities have been reported to date.
 - b. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
No cases involving pancytopenia have been reported to date.
 - c. Vonoprazan fumarate/amoxicillin hydrate/metronidazole
No cases involving pancytopenia have been reported to date.