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Summary of Investigation Results

Preparations containing vonoprazan fumarate (excluding aspirin/vonoprazan fumarate combination tablets)

October 6, 2020

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 lymphoid 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

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

Summary of revisions

a.

1. “Shock, anaphylaxis” should be added to the Clinically Significant Adverse Reactions section.
2. “Hepatic impairment” should be added to the Clinically Significant Adverse Reactions section.

b, c

1. “Shock, anaphylaxis” should be added to the Clinically Significant Adverse Reactions section (vonoprazan fumarate).
2. “Hepatic impairment” should be added to the Clinically Significant Adverse Reactions section (vonoprazan fumarate).

Investigation results and background of the revision

Cases of shock, anaphylaxis or hepatic impairment have been reported in patients treated with vonoprazan fumarate in Japan. MHLW/PMDA in consultation with expert advisors concluded that revision of the package insert was necessary.

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

Cases involving shock or anaphylaxis

a. A total of 8 cases have been reported to date (including 1 case for which a causal relationship between the drug and event was reasonably possible).
   No patient mortalities have been reported to date.
b. A total of 9 cases* have been reported to date.
   No patient mortalities have been reported to date.
c. 1 case* has been reported to date.
   No patient mortalities have been reported to date.

Cases involving hepatic impairment

a. A total of 39 cases have been reported to date (including 7 cases for which a causal relationship between the drug and event was reasonably possible).
   4 patient mortalities have been reported to date. (A causal relationship with the drug and event could not be established in any of these cases.)
b. 1 case* has been reported to date.
   No patient mortalities have been reported to date.
c. 1 case* has been reported to date.
   No patient mortalities have been reported to date.

*The possibility of a causal relationship between vonoprazan fumarate and events was not assessed in these cases because effects of the antimicrobials used in combination with vonoprazan fumarate could not be ruled out.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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