



# Summary of Investigation Results

## Preparations containing amoxicillin hydrate

November 16, 2022

### Non-proprietary name

- a. Amoxicillin hydrate
- b. Potassium clavulanate/amoxicillin hydrate
- c. Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
- d. Vonoprazan fumarate/amoxicillin hydrate/metronidazole
- e. Rabeprazole sodium/amoxicillin hydrate/clarithromycin
- f. Rabeprazole sodium/amoxicillin hydrate/metronidazole

### Brand name (marketing authorization holder)

- a. Sawacillin Capsules 125, 250, Sawacillin Fine Granules 10%, Sawacillin Tablets 250 (LTL Pharma Co., Ltd), Pasetocin Capsules 125, Pasetocin Fine Granules 10% (Sandoz Pharma K.K.), and the others
- b. Augmentin Combination Tablets 125SS, 250RS, Clavamox Combination Dry Syrup for Pediatric (GlaxoSmithKline K.K.)
- c. Vonosap Pack 400, 800 (Takeda Pharmaceutical Company Limited)
- d. Vonopion Pack (Takeda Pharmaceutical Company Limited)
- e. Rabecure Pack 400, 800 (Eisai Co., Ltd.)
- f. Rabefine Pack (Eisai Co., Ltd.)

### Indications

See Attachment.

### Summary of revisions

a., b.

1. Anaphylaxis and acute coronary syndrome accompanying allergic reaction should be added to the precautions concerning a medical interview with regard to shock in the

IMPORTANT PRECAUTIONS section, and the precautions concerning the content of the medical interview should be added.

2. "Acute coronary syndrome accompanying allergic reaction" should be added to the Clinically Significant Adverse Reactions section.

c., d., e., f.

1. Anaphylaxis and acute coronary syndrome accompanying allergic reaction should be added to the precautions concerning a medical interview with regard to shock in <Amoxicillin hydrate> in the IMPORTANT PRECAUTIONS section, and the precautions concerning the content of the medical interview should be added.
2. "Acute coronary syndrome accompanying allergic reaction" should be added to <Amoxicillin hydrate> in the Clinically Significant Adverse Reactions section.

#### **Investigation results and background of the revision**

Cases involving acute coronary syndrome accompanying allergic reaction reported in Japan and overseas were evaluated. Cases for which a causal relationship between preparations containing amoxicillin hydrate and acute coronary syndrome accompanying allergic reaction was reasonably possible have been reported overseas. As a result of consultation with expert advisors, MHLW/PMDA concluded that revision of Precautions was necessary. Of note, the precautions regarding the content of the medical interview in the IMPORTANT PRECAUTIONS section also apply to anaphylaxis, which are already listed in the Clinically Significant Adverse Reactions section. Therefore, MHLW/PMDA concluded that it was appropriate to include anaphylaxis in the precautions concerning the medical interview as well.

#### **Number of cases and patient mortalities involving acute coronary syndrome accompanying allergic reaction reported in Japan and overseas during the previous 3 fiscal years**

No cases have been reported in Japan to date.

No cases have been reported overseas to date\*.

\*Cases which were presented as the basis for a revision of Company Core Data Sheet by



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the marketing authorization holders

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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Attachment

	Non-proprietary name	Indications
a.	Amoxicillin hydrate	<p>&lt;Applicable microorganisms&gt;            amoxicillin-susceptible strains of genus <i>Staphylococcus</i>, genus <i>Streptococcus</i>, <i>Streptococcus pneumoniae</i>, genus <i>Enterococcus</i>, <i>Neisseria gonorrhoeae</i>, <i>Escherichia coli</i>, <i>Proteus mirabilis</i>, <i>Haemophilus influenzae</i>, <i>Helicobacter pylori</i>, <i>Treponema pallidum</i></p> <p>&lt;Applicable conditions&gt;            Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, secondary infections following trauma, thermal burn, and surgical wound, secondary infections of erosions/ulcers, mastitis, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, prostatitis (acute/chronic), epididymitis, <i>Neisseria gonorrhoeae</i> infection, syphilis, intrauterine infection, uterine adnexitis, parametritis, dacryocystitis, hordeolum, otitis media, periodontal inflammation, pericoronitis, jaw inflammation, scarlet fever, <i>Helicobacter pylori</i> infection of the stomach after endoscopic treatment for gastric/duodenal ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach, idiopathic thrombocytopenic purpura, and early stage of gastric cancer, and <i>Helicobacter pylori</i> gastritis</p>

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	Non-proprietary name	Indications
		<p>&lt;Applicable microorganisms&gt;  Amoxicillin-susceptible strains of genus <i>Staphylococcus</i>, genus <i>Streptococcus</i>, <i>Streptococcus pneumoniae</i>, genus <i>Enterococcus</i>, <i>Neisseria gonorrhoeae</i>, <i>Escherichia coli</i>, <i>Proteus mirabilis</i>, <i>Haemophilus influenzae</i>, <i>Helicobacter pylori</i>, <i>Treponema pallidum</i></p> <p>&lt;Applicable conditions&gt;  Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, secondary infections following trauma, thermal burn, and surgical wound, secondary infections of erosions/ulcers, mastitis, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, prostatitis (acute/chronic), epididymitis, <i>Neisseria gonorrhoeae</i> infection, syphilis, intrauterine infection, uterine adnexitis, parametritis, dacryocystitis, hordeolum, otitis media, periodontal inflammation, pericoronitis, jaw inflammation, scarlet fever, and <i>Helicobacter pylori</i> infection of the stomach/duodenal ulcer</p>

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	Non-proprietary name	Indications
b.	Potassium clavulanate/amoxicillin hydrate	<p>&lt;Applicable microorganisms&gt;            Clavulanic acid/amoxicillin-susceptible strains of genus <i>Staphylococcus</i>, <i>Neisseria gonorrhoeae</i>, <i>Escherichia coli</i>, genus <i>Klebsiella</i>, genus <i>Proteus</i>, <i>Haemophilus influenzae</i>, genus <i>Bacteroides</i>, genus <i>Prevotella</i> (except <i>Prevotella bivia</i>)</p> <p>&lt;Applicable conditions&gt;            Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis, acute bronchitis, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, <i>Neisseria gonorrhoeae</i> infection, intrauterine infection, uterine adnexitis, and otitis media</p> <hr/> <p>&lt;Applicable microorganisms&gt;            Clavulanic acid/amoxicillin-susceptible strains of <i>Streptococcus pneumoniae</i> (minimum inhibitory concentration of penicillin G. 2 µg/mL and below), <i>Moraxella (Branhamella) catarrhalis</i>, <i>Haemophilus influenzae</i>, genus <i>Staphylococcus</i>, <i>Escherichia coli</i>, genus <i>Klebsiella</i>, genus <i>Proteus</i>, genus <i>Bacteroides</i>, genus <i>Prevotella</i> (except <i>Prevotella bivia</i>)</p> <p>&lt;Applicable conditions&gt;            Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis, acute bronchitis, cystitis, pyelonephritis, otitis media and sinusitis</p>

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	Non-proprietary name	Indications
c.	Vonoprazan fumarate/amoxicillin hydrate/clarithromycin	<p>&lt;Applicable microorganisms&gt; Amoxicillin/clarithromycin-susceptible strains of <i>Helicobacter pylori</i></p> <p>&lt;Applicable conditions&gt; <i>Helicobacter pylori</i> infection of the stomach after endoscopic treatment for gastric/duodenal ulcer, MALT lymphoma of the stomach, idiopathic thrombocytopenic purpura and early stage of gastric cancer, and <i>Helicobacter pylori</i> gastritis</p>
d.	Vonoprazan fumarate/amoxicillin hydrate/metronidazole	<p>&lt;Applicable microorganisms&gt; Amoxicillin/metronidazole-susceptible strains of <i>Helicobacter pylori</i></p> <p>&lt;Applicable conditions&gt; <i>Helicobacter pylori</i> infection of the stomach after endoscopic treatment for gastric/duodenal ulcer, MALT lymphoma of the stomach, idiopathic thrombocytopenic purpura and early stage of gastric cancer, and <i>Helicobacter pylori</i> gastritis</p>

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	Non-proprietary name	Indications
e.	Rabeprazole sodium/amoxicillin hydrate/clarithromycin	<Applicable microorganisms> Amoxicillin/clarithromycin-susceptible strains of <i>Helicobacter pylori</i> <Applicable conditions> <i>Helicobacter pylori</i> infection of the stomach after endoscopic treatment for gastric/duodenal ulcer, MALT lymphoma of the stomach, idiopathic thrombocytopenic purpura and early stage of gastric cancer, and <i>Helicobacter pylori</i> gastritis
f.	Rabeprazole sodium/amoxicillin hydrate/metronidazole	<Applicable microorganisms> Amoxicillin/metronidazole-susceptible strains of <i>Helicobacter pylori</i> <Applicable conditions> <i>Helicobacter pylori</i> infection of the stomach after endoscopic treatment for gastric/duodenal ulcer, MALT lymphoma of the stomach, idiopathic thrombocytopenic purpura and early stage of gastric cancer, and <i>Helicobacter pylori</i> gastritis