



Summary of investigation results

Products containing amoxicillin hydrate

October 17, 2017

Non-proprietary name

- a. amoxicillin hydrate
- b. potassium clavulanate/amoxicillin hydrate
- c. lansoprazole/amoxicillin hydrate/clarithromycin
- d. lansoprazole/amoxicillin hydrate/metronidazole
- e. rabeprazole sodium/amoxicillin hydrate/clarithromycin
- f. rabeprazole sodium/amoxicillin hydrate/metronidazole
- g. vonoprazan fumarate/amoxicillin hydrate/clarithromycin
- h. vonoprazan fumarate/amoxicillin hydrate/metronidazole

Brand name (marketing authorization holder)

- a. Sawacillin Capsules 125 and 250, Sawacillin Fine Granules 10%, Sawacillin Tablets 250 (Astellas Pharma Inc.), Pasetocin Capsules 125 and 250, Pasetocin Fine Granules 10%, Pasetocin Tablets 250 (Aspen Japan K.K.), and others
- b. Augmentin Combination Tablets 125 SS and 250 RS, Clavamox Combination Dry Syrup for pediatric (GlaxoSmithKline K.K.)
- c. Lansap 400, 800 (Takeda Pharmaceutical Company Limited)
- d. Lampion Pack (Takeda Pharmaceutical Company Limited)
- e. Rabecure Pack 400, 800 (Eisai Co., Ltd.)
- f. Rabefine Pack (Eisai Co., Ltd.)
- g. Vonosap Pack 400, 800 (Takeda Pharmaceutical Company Limited)
- h. Vonopion Pack (Takeda Pharmaceutical Company Limited)

Indications

Refer to the attachment below.

Summary of revision

- a. amoxicillin hydrate:
'Thrombocytopenia' should be added with regard to the precaution against 'granulocytopenia' in the Clinically Significant Adverse Reactions section.

Pharmaceuticals and Medical Devices Agency

Office of Safety I

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan

E-mail: safety.info@pmda.go.jp



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.

b. potassium clavulanate/amoxicillin hydrate:

'Thrombocytopenia' should be added with regard to "agranulocytosis and granulocytopenia" in the Clinically Significant Adverse Reactions section.

c, d, e, f, g, h. lansoprazole/amoxicillin hydrate/clarithromycin, lansoprazole/amoxicillin hydrate/metronidazole, rabeprazole sodium/amoxicillin hydrate/clarithromycin, rabeprazole sodium/amoxicillin hydrate/metronidazole, vonoprazan fumarate/amoxicillin hydrate/clarithromycin, vonoprazan fumarate/amoxicillin hydrate/metronidazole:

'Thrombocytopenia' should be added with regard to the precaution against 'granulocytopenia' (amoxicillin hydrate) in the Clinically Significant Adverse Reactions section.

Background of the revision and investigation results

Cases of thrombocytopenia have been reported in patients treated with amoxicillin hydrate and potassium clavulanate/amoxicillin hydrate in Japan. Following investigation results based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan (in and after FY 2014)

a. amoxicillin hydrate

A total of 3 cases associated with thrombocytopenia have been reported (the causal relationship to the product could not be ruled out in those patients). No fatality has been reported.

b. potassium clavulanate/amoxicillin hydrate

A total of 3 cases associated with thrombocytopenia have been reported (including 2 cases for which a causal relationship to the product could not be ruled out). No fatality has been reported.

c. lansoprazole/amoxicillin hydrate/clarithromycin

A total of 2 cases associated with thrombocytopenia have been reported*. No fatality has been reported.

d. lansoprazole/amoxicillin hydrate/metronidazole

No case associated with thrombocytopenia has been reported.

e. rabeprazole sodium/amoxicillin hydrate/clarithromycin

A case associated with thrombocytopenia has been reported*. No fatality has been reported.

f. rabeprazole sodium/amoxicillin hydrate/metronidazole

No case associated with thrombocytopenia has been reported.

g. vonoprazan fumarate/amoxicillin hydrate/clarithromycin

No case associated with thrombocytopenia has been reported.

h. vonoprazan fumarate/amoxicillin hydrate/metronidazole

No case associated with thrombocytopenia has been reported.

NOTE:

*Causal relationship has not been evaluated.



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.

Attachment

Non-proprietary name	Brand Name (Marketing Authorization Holder)	Indications
a. amoxicillin hydrate	Sawacillin Capsules 125, 250, Sawacillin Tablets 250 (Astellas Pharma Inc.), Pasetocin Capsules 125, 250, and Pasetocin Tablets 250 (Aspen Japan K.K.) and others	Applicable microorganisms: amoxicillin-susceptible strains of genus Staphylococcus, genus Streptococcus, Streptococcus pneumoniae, genus Enterococcus, Neisseria gonorrhoeae, Escherichia coli, Proteus mirabilis, Haemophilus influenza, Helicobacter pylori, Treponema pallidum Applicable conditions: 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, Neisseria gonorrhoeae infection, syphilis, intrauterine infection, uterine adnexitis, parametritis, dacryocystitis, hordeolum, otitis media, periodontal inflammation, pericoronitis, jaw inflammation, scarlet fever, Helicobacter pylori 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 Helicobacter gastritis
	Sawacillin Fine Granules 10% (Astellas Pharma	Applicable microorganisms: amoxicillin-susceptible strains of genus Staphylococcus, genus



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.

	Inc.) and Pasetocin Fine Granules 10% and (Aspen Japan K.K.) and others	<p>Streptococcus, Streptococcus pneumoniae, genus Enterococcus, Neisseria gonorrhoeae, Escherichia coli, Proteus mirabilis, Haemophilus influenza, Helicobacter pylori, and Treponema pallidum</p> <p>Applicable conditions: 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, Neisseria gonorrhoeae infection, syphilis, intrauterine infection, uterine adnexitis, parametritis, dacryocystitis, hordeolum, otitis media, periodontal inflammation, pericoronitis, jaw inflammation, scarlet fever, and Helicobacter pylori infection of the stomach/duodenal ulcer</p>
b. potassium clavulanate/ amoxicillin hydrate	Augmentin Combination Tablets 125SS, 250RS (GlaxoSmithKline K.K.)	<p>Applicable microorganisms: amoxicillin-susceptible strains of genus Staphylococcus, Neisseria gonorrhoeae, Escherichia coli, genus Klebsiella, genus Proteus, Haemophilus influenza, genus Bacteroides, genus Prevotella (except Prevotella bivia)</p> <p>Applicable conditions: Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis, acute bronchitis, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, Neisseria gonorrhoeae infection,</p>



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.

		intrauterine infection, uterine adnexitis, and otitis media
	Clavamox Combination Dry Syrup for pediatric (GlaxoSmithKline K.K.)	Applicable microorganisms: amoxicillin-susceptible strains of Streptococcus pneumoniae, (minimum inhibitory concentration of penicillin G. 2 µg/mL), Moraxella (Branhamella) catarrhalis, Haemophilus influenza, genus Staphylococcus, Escherichia coli, genus Klebsiella, genus Proteus, genus Bacteroides, genus Prevotella (except Prevotella bivia) Applicable conditions: Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis, acute bronchitis, cystitis, pyelonephritis, otitis media and sinusitis
c. lansoprazole/ amoxicillin hydrate/ clarithromycin	Lansap 400, 800 (Takeda Pharmaceutical Company Limited)	Applicable microorganisms: amoxicillin/clarithromycin-susceptible strains of Helicobacter pylori Applicable conditions: Helicobacter pylori 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 Helicobacter gastritis
d. lansoprazole/ amoxicillin hydrate/ metronidazole	Lampion Pack (Takeda Pharmaceutical Company Limited)	Applicable microorganisms: amoxicillin/metronidazole-susceptible strains of Helicobacter pylori Applicable conditions: Helicobacter pylori 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 Helicobacter gastritis



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.

e. rabeprazole sodium/ amoxicillin hydrate/ clarithromycin	Rabecure Pack 400, 800 mg (Eisai Co., Ltd.)	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 gastritis</i>
f. rabeprazole sodium/ amoxicillin hydrate/ metronidazole	Rabefine Pack (Eisai Co., Ltd.)	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 gastritis</i>
g. vonoprazan fumarate/ amoxicillin hydrate/ clarithromycin	Vonosap Pack 400, 800 (Takeda Pharmaceutical Company Limited)	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 gastritis</i>



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.

h. vonoprazan fumarate/ amoxicillin hydrate/ metronidazole	Vonopion Pack (Takeda Pharmaceutical Company Limited)	Applicable microorganisms: amoxicillin/metronidazole -susceptible strains of Helicobacter pylori Applicable conditions: Helicobacter pylori 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 Helicobacter gastritis
------------------------------------------------------------------	----------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------