



Summary of investigation results

**Amoxicillin hydrate, potassium clavulanate/amoxicillin hydrate,
lansoprazole/amoxicillin hydrate/clarithromycin,
lansoprazole/amoxicillin hydrate/metronidazole,
rabeprazole sodium/amoxicillin hydrate/clarithromycin,
rabeprazole sodium/amoxicillin hydrate/metronidazole**

January 9, 2015

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

Brand Name (Marketing Authorization Holder)

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



Indications

See annex

Summary of revision

- a. amoxicillin hydrate
 - ‘Erythroderma (dermatitis exfoliative)’ should be added in the toxic epidermal necrolysis, oculomucocutaneous syndrome, erythema multiforme, and acute generalised exanthematous pustulosis subsection in the Clinically significant adverse reactions section.
 - ‘Meningitis aseptic’ should be added in the Clinically significant adverse reactions section.
- b. potassium clavulanate/amoxicillin hydrate
 - ‘Erythroderma (dermatitis exfoliative)’ should be added in the toxic epidermal necrolysis, oculomucocutaneous syndrome, and erythema multiforme subsection in the Clinically significant adverse reactions section.
 - ‘Meningitis aseptic’ should be added in the Clinically significant adverse reactions section.
- c, d, e, f. lansoprazole/amoxicillin hydrate/clarithromycin, lansoprazole/amoxicillin hydrate/metronidazole, rabeprazole sodium/amoxicillin hydrate/clarithromycin, and rabeprazole sodium/amoxicillin hydrate/metronidazole
 - ‘Erythroderma (dermatitis exfoliative)’ should be added in the toxic epidermal necrolysis, oculomucocutaneous syndrome, erythema multiforme, and acute generalised exanthematous pustulosis subsection of amoxicillin hydrate in the Clinically significant adverse reactions section.
 - ‘Meningitis aseptic’ should be added in the Clinically significant adverse reactions section of amoxicillin hydrate.

Background of the revision and investigation results

Cases of erythroderma (dermatitis exfoliative) have been reported in patients treated with amoxicillin hydrate in Japan and in foreign countries, and the company core datasheet (CCDS)* has been revised to include information on erythroderma (dermatitis exfoliative). Following an investigation based on the opinions of expert advisors and available evidence, the MHLW/PMDA concluded that revision of the package inserts was necessary.

Cases of meningitis aseptic have been reported in patients treated with amoxicillin hydrate in foreign countries, and the CCDS* has been revised to include information on meningitis aseptic. Following an investigation based on the opinions of expert advisors and available evidence, the MHLW/PMDA concluded that revision of the package inserts was necessary.



The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan

- Erythroderma (dermatitis exfoliative)
 - a. amoxicillin hydrate
No case of erythroderma (dermatitis exfoliative) has been reported.
 - b. potassium clavulanate/amoxicillin hydrate
A case of erythroderma (dermatitis exfoliative) has been reported. Causality could not be ruled out in this case. No fatality has been reported.
 - c. lansoprazole/amoxicillin hydrate/clarithromycin
A case of erythroderma (dermatitis exfoliative) has been reported. Causality has not been assessed in this case. No fatality has been reported.
 - d. lansoprazole/amoxicillin hydrate/metronidazole
No case of erythroderma (dermatitis exfoliative) has been reported.
 - e. rabeprazole sodium/amoxicillin hydrate/clarithromycin
No case of erythroderma (dermatitis exfoliative) has been reported.
 - f. rabeprazole sodium/amoxicillin hydrate/metronidazole
No case of erythroderma (dermatitis exfoliative) has been reported.

- Meningitis aseptic
 - a. amoxicillin hydrate
No case of meningitis aseptic has been reported.
 - b. potassium clavulanate/amoxicillin hydrate
No case of meningitis aseptic has been reported.
 - c. lansoprazole/amoxicillin hydrate/clarithromycin
No case of meningitis aseptic has been reported.
 - d. lansoprazole/amoxicillin hydrate/metronidazole
No case of meningitis aseptic has been reported.
 - e. rabeprazole sodium/amoxicillin hydrate/clarithromycin
No case of meningitis aseptic has been reported.
 - f. rabeprazole sodium/amoxicillin hydrate/metronidazole
No case of meningitis aseptic has been reported.

NOTE:

* The CCDS is prepared by the marketing authorization holder and covers material relating to safety, indications, dosing, pharmacology, and other information concerning the product.



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.

Annex

Non-proprietary name	Brand Name (Marketing Authorization Holder)	Indications
amoxicillin hydrate	Sawacillin Capsules 125 mg and 250 mg, Sawacillin Tablets 250 mg, Pasetocin Capsules 125 mg and 250 mg, and Pasetocin Tablets 250 mg	Applicable microorganisms: 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> , and <i>Treponema pallidum</i> 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, <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 gastritis</i>
	Pasetocin Fine Granules 10% and Sawacillin Fine Granules 10%	Applicable microorganisms: 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> , and <i>Treponema pallidum</i> 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



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Non-proprietary name	Brand Name (Marketing Authorization Holder)	Indications
		<p>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>
potassium clavulanate/amoxicillin hydrate	Augmentin Combination Tablets 125SS and 250RS	<p>Applicable microorganisms: 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 influenza</i>, genus <i>Bacteroides</i>, genus <i>Prevotella</i> (except <i>Prevotella bivia</i>)</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, <i>Neisseria gonorrhoeae</i> infection, intrauterine infection, uterine adnexitis, and otitis media</p>
	Clavamox Combination Dry Syrup for pediatric	<p>Applicable microorganisms: amoxicillin-susceptible strains of <i>Streptococcus pneumoniae</i>, (minimum inhibitory concentration of penicillin G ≤ 2 $\mu\text{g/mL}$), <i>Moraxella (Branhamella) catarrhalis</i>, <i>Haemophilus influenza</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>Applicable conditions: Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis, acute bronchitis, cystitis, pyelonephritis, and otitis media</p>
lansoprazole/amoxicillin hydrate/clarithromycin	Lansap 400 mg and 800 mg	<p>Applicable microorganisms: amoxicillin/clarithromycin-susceptible strains of <i>Helicobacter pylori</i></p>



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		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>
lansoprazole/amoxicillin hydrate/metronidazole	Lampion Pack	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>
rabeprazole sodium/amoxicillin hydrate/clarithromycin	Rabecure Pack 400 mg and 800 mg	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>
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>