



Summary of Investigation Results

Preparations containing ampicillin hydrate

Preparations containing ampicillin sodium

(excluding ampicillin sodium/sulbactam sodium)

May 9, 2023

Non-proprietary name

- a. Ampicillin hydrate
- b. Ampicillin sodium
- c. Ampicillin hydrate/cloxacillin sodium hydrate
- d. Ampicillin sodium/cloxacillin sodium hydrate

Brand name (marketing authorization holder)

- a. Viccillin Capsules 250 mg, Viccillin Dry Syrup 10% (Meiji Seika Pharma Co., Ltd.)
- b. Viccillin For Injection 0.25 g, 0.5 g, 1 g, 2 g (Meiji Seika Pharma Co., Ltd.)
- c. Viccillin-S Combination Tablets (Meiji Seika Pharma Co., Ltd.)
- d. Viccillin-S100 For Injection, Viccillin-S500 For Injection, Viccillin-S1000 For Injection (Meiji Seika Pharma Co., Ltd.)

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

1. A statement that periodic liver function tests should be performed should be added to the IMPORTANT PRECAUTIONS section (new instructions) or the Clinically Significant

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Adverse Reactions section (old instructions).

2. "Hepatic impairment" should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases involving hepatic impairment in which the worst liver function test value after administration of the relevant preparations was grade 3 or higher by Common Terminology Criteria for Adverse Events (CTCAE v5.0) reported in Japan were evaluated. Cases for which a causal relationship between the relevant preparations and hepatic impairment was reasonably possible have been reported in Japan. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of Precautions, the MHLW/PMDA concluded that revision of Precautions was necessary.

Reference: Number of cases* and patient mortalities involving hepatic impairment reported in Japan

a.

A total of 3 cases have been reported to date. (A causal relationship between the drug and event could not be established for these cases.)

No patient mortalities have been reported to date.

b.

A total of 18 cases have been reported to date (including 3 cases for which a causal relationship between the drug and event was reasonably possible).

No patient mortalities have been reported to date.

c., d.

No cases have been reported to date.

*Cases collected in the PMDA's database for adverse drug reactions, etc. reports

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

No.	Non-proprietary name	Japanese market launch	Indications
a.	Ampicillin hydrate	June 1963 (Japanese market launch of Viccillin Capsules)	<p><Applicable microorganisms> Ampicillin hydrate-susceptible strains of genus <i>Staphylococcus</i>, genus <i>Streptococcus</i>, <i>Pneumococcus</i>, genus <i>Enterococcus</i>, <i>Neisseria gonorrhoeae</i>, <i>Bacillus anthrax</i>, <i>Actinomyce</i>te, <i>Escherichia coli</i>, <i>Shigella</i>, <i>Proteus mirabilis</i>, <i>Haemophilus influenzae</i>, <i>Treponema pallidum</i></p> <p><Applicable conditions> Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, secondary infections following trauma, thermal burn, and surgical wound, mastitis, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, lung abscess, pyothorax, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, <i>Neisseria gonorrhoeae</i> infection, syphilis, peritonitis, liver abscess, infectious enteritis, intrauterine infection, abscess of eyelid, hordeolum, keratitis (including corneal ulcer), otitis media, sinusitis, periodontal inflammation, pericoronitis, jaw inflammation, secondary infections following tooth extraction wound and oral surgery wound, scarlet fever, anthrax, actinomycosis</p>
		November 1966 (Japanese market launch of Viccillin Dry Syrup)	<p><Applicable microorganisms> Ampicillin hydrate-susceptible strains of genus <i>Staphylococcus</i>, genus <i>Streptococcus</i>, <i>Pneumococcus</i>, genus <i>Enterococcus</i>, <i>Neisseria gonorrhoeae</i>, <i>Bacillus anthrax</i>, <i>Actinomyce</i>te, <i>Escherichia coli</i>, <i>Shigella</i>, <i>Proteus mirabilis</i>, <i>Haemophilus influenzae</i></p> <p><Applicable conditions> Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, secondary infections</p>

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No.	Non-proprietary name	Japanese market launch	Indications
			following trauma, thermal burn, and surgical wound, mastitis, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, lung abscess, pyothorax, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, <i>Neisseria gonorrhoeae</i> infection, peritonitis, liver abscess, infectious enteritis, intrauterine infection, abscess of eyelid, hordeolum, keratitis (including corneal ulcer), otitis media, sinusitis, periodontal inflammation, pericoronitis, jaw inflammation, secondary infections following tooth extraction wound and oral surgery wound, scarlet fever, anthrax, actinomycosis
b.	Ampicillin sodium	October 1965 (Japanese market launch of Viccillin For Injection (250 mg)) January 1969 (Japanese market launch of Viccillin For Injection (500 mg, 1 g)) September 1976 (Japanese market launch of Viccillin For Injection (2 g))	<Applicable microorganisms> Ampicillin-susceptible strains of genus <i>Staphylococcus</i> , genus <i>Streptococcus</i> , <i>Pneumococcus</i> , genus <i>Enterococcus</i> , <i>Neisseria gonorrhoeae</i> , <i>Neisseria meningitidis</i> , <i>Bacillus anthrax</i> , <i>Actinomycete</i> , <i>Escherichia coli</i> , <i>Shigella</i> , <i>Proteus mirabilis</i> , <i>Haemophilus influenzae</i> , <i>Listeria monocytogenes</i> <Applicable conditions> Sepsis, infective endocarditis, superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, secondary infections following trauma, thermal burn, and surgical wound, mastitis, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, lung abscess, pyothorax, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, <i>Neisseria gonorrhoeae</i> infection, peritonitis, liver abscess, infectious enteritis, intrauterine infection, pyogenic meningitis, abscess of eyelid, keratitis (including corneal ulcer), otitis media, sinusitis, periodontal inflammation, pericoronitis, jaw inflammation, secondary infections following tooth extraction wound and oral surgery wound, scarlet fever, anthrax, actinomycosis

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c.	Ampicillin hydrate/ cloxacillin sodium hydrate	June 1970 (Japanese market launch of Viccillin- S Tablets)	<Applicable microorganisms> Ampicillin/cloxacillin-susceptible strain of genus <i>Staphylococcus</i> , genus <i>Streptococcus</i> , <i>Pneumococcus</i> , genus <i>Enterococcus</i> , <i>Escherichia coli</i> , <i>Proteus mirabilis</i> , <i>Haemophilus influenzae</i> <Applicable conditions> Pneumonia, lung abscess, secondary infection of chronic respiratory lesions
d.	Ampicillin sodium/ cloxacillin sodium hydrate	January 1969 (Japanese market launch of Viccillin- S (100) For Injection)	1. Prevention of neonatal infections 2. Others <Applicable microorganisms> Ampicillin/cloxacillin-susceptible strain of genus <i>Staphylococcus</i> , genus <i>Streptococcus</i> , <i>Pneumococcus</i> , genus <i>Enterococcus</i> , <i>Escherichia coli</i> , <i>Proteus mirabilis</i> , <i>Haemophilus influenzae</i> <Applicable conditions> Chronic pyoderma, pharyngitis/laryngitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesions, otitis externa
		Viccillin-S500 For Injection: August 1970 Viccillin-S1000 For Injection: September 1976	<Applicable microorganisms> Ampicillin/cloxacillin-susceptible strain of genus <i>Staphylococcus</i> , genus <i>Streptococcus</i> , <i>Pneumococcus</i> , genus <i>Enterococcus</i> , <i>Escherichia coli</i> , <i>Proteus mirabilis</i> , <i>Haemophilus influenzae</i> <Applicable conditions> Sepsis, pneumonia, lung abscess, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis

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