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.

Summary of Investigation Results

Minocycline hydrochloride (oral dosage form, injections)

July 20, 2023

Non-proprietary name

Minocycline hydrochloride

Brand name (marketing authorization holder)

Minomycin Granules 2%, Minomycin Tablets 50 mg, Minomycin Capsules 50 mg, 100 mg, Minomycin Intravenous 100 mg (For Drip Use) (Pfizer Japan Inc.), and the others

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

“Exacerbation of systemic lupus erythematosus (SLE)-like symptoms” in the Clinically Significant Adverse Reactions section should be revised to “lupus-like syndrome.” In addition, a precautionary statement regarding the occurrence of this event in cases of long-term treatment should be added.

Investigation results and background of the revision

Among cases involving “lupus-like syndrome” reported in Japan, cases in which this event occurred following administration of minocycline hydrochloride and the published literature (e.g., Curr Drug Saf 2020; 16: 1-13, Arch Inter Med 1999; 159: 493-7) were evaluated. Cases for which a causal relationship between minocycline hydrochloride and lupus-like

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syndrome was reasonably possible have been reported in Japan, and there was a tendency for higher occurrence of lupus-like syndrome in long-term treatment cases. 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 lupus-like syndrome reported in Japan

A total of 5 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.

*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

Japanese market launch	Indications
Minomycin Granules 2%: February 1974	<Applicable microorganisms> Minocycline-susceptible strains of genus *Staphylococcus*, genus *Streptococcus*, *Pneumococcus,* genus *Enterococcus*, *Bacillus anthrax*, *Escherichia coli*, genus *Citrobacter*, genus *Klebsiella*, genus *Enterobacter*, genus *Rickettsia* (*Orientia tsutsugamushi*), *genus Chlamydia*, *Mycoplasma pneumonia* <Applicable conditions> Superficial skin infections, deep-seated skin infections, lymphangitis/lymphadenitis, chronic pyoderma, osteomyelitis, pharyngitis/laryngitis, tonsillitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesions, dacryocystitis, hordeolum, otitis media, sinusitis, purulent sialoadenitis, periodontal inflammation, infectious stomatitis, scarlet fever, anthrax, scrub typhus, psittacosis
Minomycin Tablets 50 mg: July 1984 Minomycin Capsules 50 mg: September 1981 Minomycin Capsules 100 mg: December 1971	<Applicable microorganisms> Minocycline-susceptible strains of genus *Staphylococcus*, genus *Streptococcus*, *Pneumococcus,* genus *Enterococcus*, *Neisseria gonorrhoeae*, *Bacillus anthrax*, *Escherichia coli*, *Shigella*, genus *Citrobacter*, genus *Klebsiella*, genus *Enterobacter*, genus *Proteus*, *Morganella morganii*, genus *Providencia*, *Pseudomonas aeruginosa*, *Treponema pallidum*, genus *Rickettsia* (*Orientia tsutsugamushi*), *genus Chlamydia*, *Mycoplasma pneumonia* <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 (including peritonsillitis), acute bronchitis, pneumonia, lung abscess, secondary

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	infection of chronic respiratory lesions, cystitis, pyelonephritis, prostatitis (acute/chronic), epididymitis, urethritis, Neisseria gonorrhoeae infection, syphilis, peritonitis, infectious enteritis, vulvitis, bacterial vaginitis, intrauterine infection, dacryocystitis, hordeolum, otitis externa, otitis media, sinusitis, purulent sialoadenitis, periodontal inflammation, pericoronitis, maxillary sinusitis, jaw inflammation, anthrax, scrub typhus, psittacosis
Minomycin Intravenous 100 mg (For Drip Use): June 1977	<Applicable microorganisms> Minocycline-susceptible strains of genus *Staphylococcus*, genus *Streptococcus*, *Pneumococcus,* genus *Enterococcus*, *Moraxella lacunata (Morax-Axenfeld diplobacilli), Bacillus anthrax, Escherichia coli*, genus *Klebsiella*, genus *Enterobacter*, *Haemophilus influenzae*, *Pseudomonas fluorescens*, *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Stenotrophomonas (Xanthomonas) maltophilia,* genus *Acinetobacter,* genus *Flavobacterium*, *Legionella pneumophila*, genus *Rickettsia* (*Orientia tsutsugamushi*), genus *Chlamydia*, *Mycoplasma pneumonia* <Applicable conditions> Sepsis, deep-seated skin infections, chronic pyoderma, tonsillitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesions, cystitis, pyelonephritis, peritonitis, anthrax, scrub typhus, psittacosis

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