Summary of Investigation Results

Colistin sodium methanesulfonate

May 8, 2024

Non-proprietary name

a Colistin sodium methanesulfonate (injections)

b Colistin sodium methanesulfonate (oral dosage form)

c Erythromycin lactobionate/colistin sodium methanesulfonate

d Chloramphenicol/colistin sodium methanesulfonate

Brand name (marketing authorization holder)

a. Aldreb for Injection 150 mg (GlaxoSmithKline K.K.)

b. Colimycin Powder 2 million units/g, Methacolimycin Capsules 3 million units, Methacolimycin Granules 2 million units/g (Sun Pharma Japan Limited)

c. Ecolicin ophthalmic ointment (Santen Pharmaceutical Co., Ltd.)

d. Ophthalon Ophthalmic Solution (Wakamoto Pharmaceutical Co., Ltd.), Colinacol Ophthalmic Solution (Rohto Nitten Co., Ltd.)

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

a.

1. A statement should be added to the 8. IMPORTANT PRECAUTIONS section that hypokalaemia, hypomagnesaemia, and hypocalcaemia may occur, and periodic tests should be performed.

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

2. “Hypokalaemia, hypomagnesaemia, hypocalcaemia, metabolic alkalosis” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

b., c., d.
Revision is not necessary.

Investigation results and background of the revision

Cases involving hypokalaemia, hypomagnesaemia, hypocalcaemia, and metabolic alkalosis were evaluated. Cases for which a causal relationship between colistin sodium methanesulfonate (injections) and hypokalaemia, hypomagnesaemia, hypocalcaemia, and metabolic alkalosis was reasonably possible have been reported. 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. No cases for which a causal relationship between the other preparations containing colistin sodium methanesulfonate (oral dosage form and topical ophthalmic drugs) and hypokalaemia, hypomagnesaemia, hypocalcaemia, and metabolic alkalosis have been reported, and their systemic transferability is limited. Therefore, the MHLW/PMDA concluded that revision of PRECAUTIONS for those preparations was not necessary at present.

Reference: Number of cases* and patient mortalities involving hypokalaemia, hypomagnesaemia, hypocalcaemia, and metabolic alkalosis reported in Japan and overseas

a.
A total of 2 cases have been reported in Japan to date. (A causal relationship between the drug and event could not be established for any of these cases.)
No patient mortalities have been reported in Japan to date.

b., c., d.
No cases have been reported in Japan to date.

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

A total of 5 cases† have been reported overseas to date. (A causal relationship between the drug and event was reasonably possible for these cases.)

No patient mortalities have been reported overseas to date.

b., c., d.

No cases have been reported overseas to date.

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

†The cases for which it was determined by the MAHs that a causal relationship between the drug and event was reasonably possible.

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	Japanese market launch	Indications
a.	Colistin sodium methanesulfonate (injections)	May 2015	<Applicable microorganisms> Colistin-susceptible *Escherichia coli*, genus *Citrobacter*, genus *Klebsiella*, genus *Enterobacter*, *Pseudomonas aeruginosa*, genus *Acinetobacter* The use is limited to the bacterial strains resistant to antimicrobial drugs. <Applicable conditions> Infections
b.	Colistin sodium methanesulfonate (oral dosage form)	Colimycin Powder 2 million units/g: November 1960 (date of initial marketing of “Colimycin-S Powder”) Methacolimycin Capsules 3 million units: December 1963 (date of initial marketing of “Methacolimycin Capsules”) Methacolimycin Granules 2 million units/g: February 1974 (date of initial marketing of “Methacolimycin Granules”)	<Applicable microorganisms> Colistin-susceptible *Escherichia coli*, *Shigella* <Applicable conditions> Infectious enteritis
c.	Erythromycin lactobionate/ colistin sodium methanesulfonate	July 1970	<Applicable microorganisms> Erythromycin/colistin-susceptible bacteria <Applicable conditions> Blepharitis, dacryocystitis, hordeolum, conjunctivitis, keratitis (including corneal ulcer)
d.	Chloramphenicol/colistin sodium methanesulfonate	Ophthalon Ophthalmic Solution: September 1976 Colinacol Ophthalmic Solution: September 1981	<Applicable microorganisms> Chloramphenicol/colistin-susceptible gram-negative rod mainly consisting of *Pseudomonas aeruginosa* <Applicable conditions> Blepharitis, conjunctivitis, keratitis (including corneal ulcer), sterilization therapy during ophthalmic perioperative period

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