

Summary of Investigation Results

Antimicrobial drugs for children with a pivoxil group

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	(1) Cefcapene pivoxil hydrochloride hydrate (2) Cefditoren pivoxil (3) Cefteram pivoxil (4) Tebipenem pivoxil	(1) FLOMOX Fine Granules for Pediatric 100 mg (Shionogi & Co., Ltd.), and others. (2) MEIACT MS FINE GRANULES 10% for Children (Meiji Seika Pharma Co., Ltd.) and others. (3) TOMIRON Fine granules 20% for pediatric (FUJIFILM Toyama Chemical Co., Ltd.) (4) ORAPENEM FINE GRANULES 10% FOR PEDIATRIC (Meiji Seika Pharma Co., Ltd.)
Japanese market launch	(1) June 1997 (2) June 1994 (Japanese market launch of “MEIACT GRANULES”) (3) February 2018 (4) August 2009	
Indications	See Attachment	
Summary of revisions	(1) to (4) In the section of "8. IMPORTANT PRECAUTIONS," it will be added as a precaution for serious hypoglycaemia associated with hypocarnitinaemia that the latest guidelines, etc. should be referred to for the selection of drugs including the necessity of administration and the duration of administration, and that family members, etc. should be instructed to visit a medical institution immediately when hypoglycaemic symptoms such as convulsions and consciousness disturbed are observed.	
Investigation results and background of the revision	Awareness of hypoglycaemia associated with hypocarnitinaemia caused by antimicrobial drugs for children with a pivoxil group has already been raised in the sections of "11.1 Clinically Significant Adverse Reactions" and "9.7 Pediatric Use" of "Precautions." However, in recent years, cases for which a causal relationship with the drug cannot be ruled out have been reported, and in the most recent reports, some cases resulted in death. Therefore, the necessity of additional safety measures was examined.	

	As a result of hearing the opinions of the expert advisors, it was considered important to disseminate specific information necessary for the proper use of the drug as described below. Therefore, it was judged appropriate to revise the Precautions as described in the "Summary of revision" for the following reasons: • In consideration of the risks of this event, it is necessary to adequately assess the necessity of administration of the drug and appropriately determine its use and duration of administration. In addition, it is necessary to refer to the latest relevant guidelines, etc. for information that contributes to these judgments. • Hypoglycaemia associated with hypocarnitinaemia has been mainly reported in infants and children. Because the symptoms may rapidly progress and become serious, appropriate instructions should be provided by healthcare professionals to family members, etc. from the viewpoint of ensuring prompt access to medical care at the onset of hypoglycemic symptoms.
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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).

Attachment

No.	Non-proprietary name	Brand name	Indications
(1)	Cefcapene pivoxil hydrochloride hydrate	FLOMOX Fine Granules for Pediatric 100 mg, and others	○ Children <Indicated microorganisms> Cefcapene susceptible strains of <i>Staphylococcus</i> sp., <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Moraxella (Branhamella) catarrhalis</i>, <i>Escherichia coli</i>, <i>Citrobacter</i> sp., <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Serratia</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., <i>Haemophilus influenzae</i>, <i>Peptostreptococcus</i> sp., <i>Bacteroides</i> sp., <i>Prevotella</i> sp. (excluding <i>Prevotella bivia</i>), and <i>Cutibacterium acnes</i> <Indications> Superficial skin infection, deep skin infection, lymphangitis/lymphadenitis, chronic pyoderma, pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, cystitis, pyelonephritis, otitis media, sinusitis, and scarlet fever ○ Adults (when it is difficult to use tablets due to swallowing difficulty, etc.) <Indicated microorganisms> Cefcapene susceptible strains of <i>Staphylococcus</i> sp., <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Neisseria gonorrhoeae</i>, <i>Moraxella (Branhamella) catarrhalis</i>, <i>Escherichia coli</i>, <i>Citrobacter</i> sp., <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Serratia</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., <i>Haemophilus influenzae</i>, <i>Peptostreptococcus</i> sp., <i>Bacteroides</i> sp., <i>Prevotella</i> sp. (excluding <i>Prevotella bivia</i>), and <i>Cutibacterium acnes</i> <Indications> Superficial skin infection, deep skin infection, lymphangitis/lymphadenitis, chronic pyoderma, secondary infection following trauma, burns, surgical wounds, etc., mastitis, perianal abscess, pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, secondary infection following chronic respiratory diseases, cystitis, pyelonephritis, urethritis, cervicitis, cholecystitis, cholangitis, Bartholinitis,

			intrauterine infection, adnexitis, dacryocystitis, hordeolum, meibomianitis, otitis externa, otitis media, sinusitis, periodontal tissue inflammation, pericoronitis, gnathitis
(2)	Cefditoren pivoxil	MEIACT MS FINE GRANULES 10% for Children and others	Children <Indicated microorganisms> Cefditoren susceptible strains of <i>Staphylococcus</i> sp., <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Moraxella</i> (<i>Branhamella</i>) <i>catarrhalis</i>, <i>Escherichia coli</i>, <i>Citrobacter</i> sp., <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Serratia</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., <i>Haemophilus influenzae</i>, <i>Bordetella pertussis</i>, <i>Peptostreptococcus</i> sp., <i>Bacteroides</i> sp., <i>Prevotella</i> sp., and <i>Cutibacterium acnes</i> <Indications> Superficial skin infection, deep skin infection, lymphangitis/lymphadenitis, chronic pyoderma, secondary infection following trauma, burns, surgical wounds, etc., perianal abscess, pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, lung abscess, secondary infection following chronic respiratory diseases, cystitis, pyelonephritis, otitis media, sinusitis, periodontal tissue inflammation, gnathitis, scarlet fever, pertussis Adults (when it is difficult to use tablets due to swallowing difficulty, etc.) <Indicated microorganisms> Cefditoren susceptible strains of <i>Staphylococcus</i> sp., <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Moraxella</i> (<i>Branhamella</i>) <i>catarrhalis</i>, <i>Escherichia coli</i>, <i>Citrobacter</i> sp., <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Serratia</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., <i>Haemophilus influenzae</i>, <i>Peptostreptococcus</i> sp., <i>Bacteroides</i> sp., <i>Prevotella</i> sp., and <i>Cutibacterium acnes</i> <Indications> Superficial skin infection, deep skin infection, lymphangitis/lymphadenitis, chronic pyoderma, secondary infection following trauma, burns, surgical wounds, etc., mastitis, perianal abscess, pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, lung abscess, secondary infection following chronic respiratory diseases, cystitis, pyelonephritis, cholecystitis, cholangitis, bartholinitis, intrauterine

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			infection, adnexitis, abscess of eyelid, dacryocystitis, hordeolum, meibomianitis, otitis media, sinusitis, periodontal tissue inflammation, pericoronitis, gnathitis
(3)	Cefteram pivoxil	TOMIRON Fine granules 20% for pediatric	○ Children <Indicated microorganisms> Cefteram susceptible strains of <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Escherichia coli</i>, <i>Klebsiella</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., and <i>Haemophilus influenzae</i> <Indications> Pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, cystitis, pyelonephritis, otitis media, sinusitis, and scarlet fever ○ Adults (when it is difficult to use tablets due to swallowing difficulty, etc.) <Indicated microorganisms> Cefteram susceptible strains of <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Neisseria gonorrhoeae</i>, <i>Escherichia coli</i>, <i>Citrobacter</i> sp., <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Serratia</i> sp., <i>Proteus</i> sp., <i>Morganella morganii</i>, <i>Providencia</i> sp., <i>Haemophilus influenzae</i>, and <i>Peptostreptococcus</i> sp. <Indications> Pharyngitis/laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, secondary infection following chronic respiratory diseases, cystitis, pyelonephritis, urethritis, Bartholinitis, intrauterine infection, adnexitis, otitis media, sinusitis, periodontal tissue inflammation, pericoronitis, gnathitis
(4)	Tebipenem pivoxil	ORAPENEM FINE GRANULES 10% FOR PEDIATRIC	<Indicated microorganisms> Tebipenem susceptible strains of <i>Staphylococcus aureus</i>, <i>Streptococcus</i> sp., <i>Streptococcus pneumoniae</i>, <i>Moraxella (Branhamella) catarrhalis</i>, and <i>Haemophilus influenzae</i> <Indications> Pneumonia, otitis media, sinusitis