PMDA Alert for Proper Use of Drugs

Pharmaceuticals and Medical Devices Agency

PMDA No. 17 June 2026

This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail

Serious hypocarnitinaemia and hypoglycaemia in children treated with antibacterials with a pivoxil group (follow-up report)

Alerts against the use of antibacterials with a pivoxil group have been provided in the electronic package inserts and "PMDA Alert for Proper Use of Drugs" (No. 8, April 2012) by presenting cases of serious hypocarnitinemia and associated serious hypoglycaemia, convulsions, and encephalopathy, etc., resulting in sequelae in children treated with antibacterials with a pivoxil group.

However, similar adverse reactions have been continuously reported even in recent years although the frequency is low. These reports include some cases that resulted in significant and irreversible outcomes. Note again that the following precautions should be taken.

- **In treatment with antibacterials with a pivoxil group in children (especially infants), refer to the latest guidelines, etc. when selecting drugs, including a process of considering the necessity of these antibacterials, and determining treatment duration.**
- **Do not administer to patients who are found to have an inborn error of metabolism that leads to decreased serum carnitine levels.**
- **Instruct the patients' families, etc. to immediately seek medical attention if serious hypoglycaemic symptoms (e.g., decreased level of consciousness and convulsions) associated with decreased blood carnitine levels occur.**
- **In some reports, serious hypoglycaemia associated with hypocarnitinaemia occurred on the day following treatment, not only in case of long-term treatment, and hypocarnitinaemia occurred in neonates of mothers treated with antibacterials with a pivoxil group during their pregnancy.**

Related information: "Alerts against hypocarnitinaemia associated with oral administration of antibacterials with a pivoxil group"
(Pharmaceutical Affairs Committee, Japan Pediatric Society, July 2019)

● **Antibacterials with a pivoxil group marketed in Japan (preparations for pediatric use)**

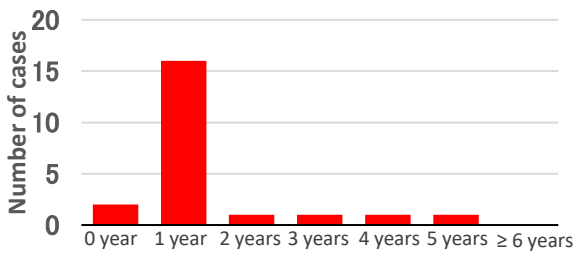
Non-proprietary name	Abbreviation	Brand name
Cefcapene pivoxil hydrochloride hydrate	CFPN-PI	FLOMOX Fine Granules for Pediatric 100 mg and others
Cefditoren pivoxil	CDTR-PI	MEIACT MS FINE GRANULES 10% for Pediatric and others
Cefteram pivoxil	CFTM-PI	TOMIRON Fine granules 20% for pediatric
Tebipenem pivoxil	TBPM-PI	ORAPENEM FINE GRANULES 10% FOR PEDIATRIC

See information on antibacterials with a pivoxil group (cefcapene pivoxil hydrochloride hydrate, cefditoren pivoxil, cefteram pivoxil, tebipenem pivoxil) in the latest package inserts at PMDA website (https://www.pmda.go.jp) > Package inserts, etc. > Prescription drug information search.

●Status of reporting

Cases reported with adverse reaction terms related to hypoglycaemia and hypocarnitinaemia that were collected in the PMDA's safety database for drugs from April 2019 to May 2026 (as of May 27, 2026)

Reporting year	2019	2020	2021	2022	2023	2024	2025	2026
Number of reports	4	2	3	2	3	3	3	3



Hypocarnitinaemia is more likely to occur in children, who have a low capacity for biosynthesis and a limited muscle mass that serves as a storage site. Antibacterials with a pivoxil group consume carnitine and can cause carnitine deficiency even in short-term use. Lack of carnitine prevents conversion of lipids into energy, thereby making it difficult to maintain blood glucose in a fasting state, which may lead to serious hypoglycaemia.

● Case summaries

Please also refer to Case 1 to 4 in the "PMDA Alert for Proper Use of Drugs" issued in April 2012 (No. 8).

Case 5

Sex/ Age	Indication	Clinical Course and Management	
Male, 1 year old	otitis media	~4 months before onset	Antibacterials, including those with a pivoxil group, had been intermittently administered.
		40 days before onset	**Cefditoren pivoxil (14 days)**
		16 days before onset	Tosufloxacin (7 days)
		8 days before onset	**Cefteram pivoxil (7 days)**
		2 days before onset	Tosufloxacin (7 days)
		1 day before onset	Food was taken at night.
		Day of onset	Repeated nocturnal crying was observed, and there was a state in which eye contact could not be established. In the morning, **convulsions** and **disturbance of consciousness** were observed, and the patient was transported to a hospital by ambulance. **Blood glucose level was 17 mg/dL**, and **hypocarnitinaemia** was confirmed. Due to central nervous system disorders, hyperthermia, etc., the patient was admitted to the intensive care unit.
		4 days after onset	In addition to severe central nervous system disorders, arrhythmia developed, and the patient **died**.
Comorbidities / Past Medical History: Asthma Special Notes: Allergies (wheat, milk, egg)			

Case 6

Sex/ Age	Indication	Clinical Course and Management	
Male, 1 year old	otitis media	~6 months before onset	Antibacterials with a pivoxil group had been intermittently administered.
		25 days before onset	**Cefditoren pivoxil (10 days)**
		7 days before onset	**Cefcapene pivoxil (5 days)**
		Day of onset	Diarrhoea was observed from the morning, and the patient visited a local clinic. After returning home, the patient **appeared lethargic**, and was transported by ambulance following an emergency request from the local clinic. **Convulsions** were observed, and **the blood glucose level was 11 mg/dL**. Glucose administration and other treatments were performed, and the patient was admitted to the pediatric intensive care unit. Laboratory tests confirmed **hypocarnitinaemia**.
		1 day after onset	The level of consciousness gradually improved.
		4 days after onset	The patient was discharged.
Comorbidities / Past Medical History: None Special Notes: None			

About this information

* "PMDA Alert for Proper Use of Drugs" communicates to healthcare providers with clear information from the perspective of promoting the proper use of drugs. The information presented here includes such cases where the reporting frequencies of similar reports have not decreased despite relevant alerts provided in package inserts, among Adverse Drug Reaction/infection cases reported in accordance with the Pharmaceutical and Medical Device Act.
* We have tried to ensure the accuracy of this information at the time of its compilation but do not guarantee its accuracy in the future.
* This information is not intended to impose constraints on the discretion of healthcare professionals or to impose obligations and responsibilities on them, but is provided to promote the proper use of drugs.

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