MEIACT® Tablets

DESCRIPTION

White film coated tablet.

MEIACT® 200 Tablets: Cefditoren pivoxil 200 mg (potency)

INDICATIONS

Cefditoren pivoxil is indicated for the treatment of following infections which are caused by susceptible strains.

- Community acquired pneumoniae
- Acute exacerbation of chronic bronchitis
- Pharyngotonsillitis
- Acute sinusitis
- Uncomplicated skin and soft structure infections

DOSAGE AND ADMINISTRATION

- Community acquired pneumoniae 400 mg BID for 14 days
- Acute exacerbation of chronic bronchitis 400 mg BID for 10 days
- Pharyngotonsillitis 200 mg BID for 10 days
- Acute sinusitis 200 mg BID for 10 days
- Uncomplicated skin and soft structure infections 200 mg BID for 10 days

  Should be taken after meals

<Precautions>

(1) As a general rule, the duration of administration of this drug should be limited to the minimum period required for the treatment of the patient's condition, after susceptibility of the microorganism to the drug has been confirmed, in order to prevent the emergence of drug-resistant microorganisms.

(2) In patients with severely impaired renal function, the administration interval should be prolonged. (See "Careful Administration" section and "PHARMACOKINETICS" section).

CONTRAINDICATIONS (MEIACT® Tablets is contraindicated in the following patients)

(1) Patients with a history of hipersensitivity to any of the ingredients contained in this product.

(2) Patients with cow's milk allergy

(This product contains sodium caseinate as an inactive ingredient).

RELATIVE CONTRAINDICATIONS (As a general rule, MEIACT® Tablets is contraindicated in the following patients. If the use of MEIACT® Tablets is considered essential, it should be administered with care).

Patients with a history of hypersensitivity to cephalosporin antibiotics.

PRECAUTIONS

1. **Careful Administration (MEIACT® Tablets should be administered with care in the following patients)**
   (1) Patients with a history of hypersensitivity to penicillins.
   (2) Patients with a personal or familial predisposition to allergic symptoms such as bronchial asthma, exanthema or urticaria.
   (3) Patients with severely impaired renal function [Serum concentration persists. (See "PHARMACOKINETICS" section).
   (4) Elderly patients (See "Use in the Elderly" section).
   (5) Patients with poor oral food intake or who are receiving parenteral alimentation, and patients in poor general health (Patients should be observed carefully because vitamin K deficiency may develop).

2. **Important Precautions**
   The patients should be carefully interviewed to assess the risk of shock.

3. **Adverse Reaction**
   Adverse reactions occurred in 127 (4.37%) of the 2,909 patients evaluated for the safety of the product. Digestive symptoms including diarrhea, loose stools, nausea and stomach discomfort accounted for 121 patients (4.16%), followed by 16 (0.55%) patients with allergic symptoms such as exanthema.
   Changes in laboratory test values were observed in 8.17% (187/2,289). They included abnormal hepatic function such as increased AST (GOT) in 3.37% (73/2,167) and increased ALT (GPT) in 4.21% (91/2,164); and abnormal hematology, such as eosinophilia, in 2.63% (47/1,790) (at the time of approval).
   (1) Clinically significant adverse reactions
      1) Shock or anaphylaxis (<0.1%) may occur.
         Patients should be carefully monitored and if any abnormalities such as feeling unwell, oral cavity discomfort, stridor, vertigo, defecation desire, tinnitus or diaphoresis are observed, administration should be discontinued and appropriate measures should be taken.
      2) Serious colitis with bloody stool such as pseudomembranous colitis (<0.1%) may occur. Patients should be carefully monitored and if abdominal pain or frequent diarrhea occurs, administration should be discontinued immediately and appropriate measures should be taken.

3) Toxic Epidermal Necrolysis (TEN), mucocutaneo-ocular syndrome (Stevens-Johnson syndrome) (<0.1%) or erythema multiforme (incidence unknown) may occur. Patients should be carefully monitored and if any abnormality is observed, administration should be discontinued and appropriate measures should be taken.
4) Interstitial pneumonia, PIE syndrome (<0.1%), etc., with fever, cough, dyspnea, abnormal chest X-ray, eosinophilia, etc., may occur. Patients should be carefully monitored and if these symptoms occur, administration should be discontinued and appropriate measures such as administration of adrenocortical hormones should be taken.
5) Hepatic function disorder (<0.1%) with jaundice or markedly increased AST (GOT), ALT (GPT) or Al-P may occur. Patients should be carefully monitored, and periodic laboratory tests should be performed. If any abnormality is observed, administration should be discontinued and appropriate measures should be taken.
6) Serious renal disorder such as acute renal failure (<0.1%) may occur. Patients should be carefully monitored, and periodic laboratory tests should be performed. If any abnormality is observed, administration should be discontinued and appropriate measures should be taken.
7) Agranulocytosis (<0.1%) or hemolytic anemia (<0.1%) may occur. Patients should be carefully monitored, and periodic laboratory tests should be performed. If any abnormality is observed, administration should be discontinued and appropriate measures should be taken.

(2) Other adverse reactions

	≥ 0.1% to < 0.5%	< 0.1%
Hypersensitivity Note 1)	Exanthema, etc	Urticaria, erythema, pruritus, fever, lymph node swelling, arthralgia, etc.
Hematologic Note 2)	Granulocytopenia, eosinophilia, etc.	Thromocytoppenia, etc.
Hepatic Note 2)	Increased AST (GOT), ALT (GPT) and Al-P, etc.	Jaundice, etc.
Renal	Increased BUN and serum creatinine, and proteinuria	
Gastrointestinal	Diarrhea, loose stools, nausea, stomach discomfort, abdominal pain	Abdomen enlarged feeling, nausea, vomiting, etc.
Microbial substitution		Stomatitis and candidiasis
Avitaminosis		Symptoms of vitamin K deficiency (hypoprothrombinemia,

		bleeding tendency, etc.), vitamin B complex deficiency symptoms (glossitis, stomatitis, anorexia, neuritis, etc.)
Others		Headache, dizziness, edema and numbness
	Abnormal laboratory test values (increased AST (GOT)/ALT (GPT), eosinophilia, etc.), tend to appear more frequently in patients under long-term treatment with this product. Note 3)	

Note

1) If symptoms appear, administration should be discontinued and suitable measures should be taken.
2) The patients should be thoroughly monitored and if any abnormality appears, suitable measures including discontinuation of administration should be taken.
3) These patients should be monitored by performing periodical clinical tests.

4. Use in the Elderly

The incidence of adverse reactions in the elderly does not differ from that in non-elderly adult patients. However, since the physiological functions are generally reduced in the elderly, the product should be administered carefully, paying attention to the following two points: dose and dose intervals should be adjusted according to the patient's condition.

(1) Delay in excretion has been observed in patients with impaired renal function. Therefore, high serum levels of the product may persist for a longer period of time in the elderly.
(2) As for other analogous drugs, bleeding tendency due to vitamin K deficiency has been reported to occur in the elderly.

5. Use during Pregnancy, Delivery or Lactation

This product should be administered to pregnant women or women who may possibly be pregnant, only if the expected therapeutic benefits outweigh the possible risks associated with treatment. [The safety of this product during pregnancy has not been established].

6. Pediatric Use

The safety of this product in low birth-weight infants, newborns, suckling infants, infants and children has not been established (few clinical experience).

7. Effects on Laboratory Test

(1) False-positive results may occur in urine glucose tests with Benedict's solution, Fehling's solution, and Clinitests, but not with Tes-Tape.

(2) Positive results may occur in the direct Coombs test. Caution is required.

8. Precautions concerning use

Precautions regarding dispensing

In the case of press-through packages, instruct the patient to remove the drug from the package prior to use. [If the PTP sheet is swallowed, its sharp corners may penetrate the esophageal mucosa, leading to severe complications such as mediastinitis.]

9. Other Precautions

It has been reported that this product reduces serum carnitine.

PHARMACOKINETICS

1. Absorption and distribution

(1) Blood concentration

The serum concentrations (Fig.1) and pharmacokinetics (Table 1) of cefditoren after oral administration of 100 or 200 mg to healthy adults after meals demonstrated dose dependency. Absorption was better when administered after meals than when given at fasting.

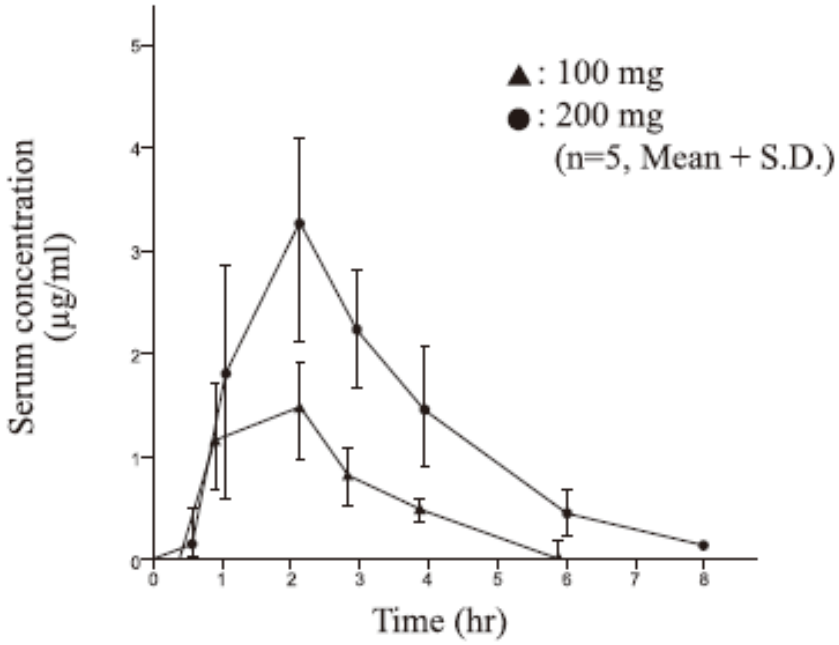


Fig. 1 Serum concentrations of Cefditoren after oral administration in healthy adults

Table1. Pharmacokinetic parameter in healthy adults

Dose (mg)	Tmax (hr)	Cmax (μg/mL)	$T_{1/2}$ (hr)	$AUC^{0\rightarrow\infty}$ (μg.hr/mL)
100	1.4	1.66	0.80	3.67
200	2.0	3.44	1.06	10.02

(2) Body fluid and tissue concentrations

The drug transferred to the sputum, tonsillar tissue, mucous membrane of maxillary sinus, skin tissue, mammary gland tissue, gallbladder tissue, vagina, uterine neck, tarsal gland tissue and wound after tooth extraction. No transfer to the milk was noted.

(3) Protein binding

In vitro binding rate to human serum protein determined by ultrafiltration method was 91.5% at concentration of 25 μg/mL.

2. Metabolism and excretion

Cefditoren pivoxil is metabolized upon absorption and becomes cefditoren which has antibacterial activity, and pivalic acid. The latter is conjugated with carnitine and excreted into urine as pivaloil carnitine. Cefditoren is hardly metabolized and is excreted mainly into urine and bile. The urinary excretion rate (0–24 hours) of cefditoren upon oral administration after meals at doses of 100 mg and 200 mg to healthy adults was about 20%.

No accumulation of the drug was observed after continuous administration (200 mg × 3 times/day, for 8 days).

3. Serum concentration and urinary excretion in patients with renal function disorder

The serum concentrations (Fig. 2) and pharmacokinetics parameters (Table 2) of cefditoren are as follows. Oral administration of 200 mg to adult patients with renal function disorder or to those receiving artificial dialysis after meals demonstrated higher levels in all the cases, showing delay in T½ in parallel with degree of renal function disorder.

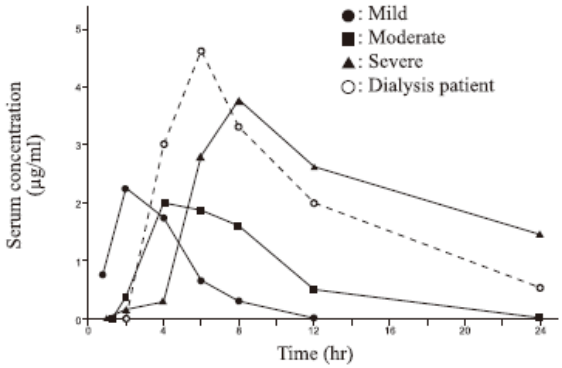


Fig. 2 Serum concentrations of cefditoren in patients with renal function disorder

Table 2 Pharmacokinetic parameter in patients with renal function disorder

Patient's condition [Ccr (mL/min)]	No. of patients	Tmax (hr)	Cmax (μg/mL)	$T_{1/2}$ (hr)	$AUC^{0\rightarrow\infty}$ (μg.hr/mL)
Mild (51 - 70)	3	2	2.32	1.13	10.2
Moderate (30 - 50)	4	4	2.17	2.06	16.4
Severe (<30)	2	8	3.70	5.68	53.5
Dialysis patient (Note 4)	1	6	4.60	5.37	50.2

Note

4) On day without dialysis
Urinary excretion rate lowered in parallel with degree of renal function disorder, showing delay in excretion.

PHARMACOLOGY

1. Antibacterial activity

(1) Cefditoren pivoxil is metabolized into cefditoren upon absorption from the intestinal wall and shows its antibacterial activity.

(2) Cefditoren exerts antibacterial activity *in vitro* against a wide spectrum of gram-positive and gram-negative bacteria. Its activity against gram-positive bacteria including *Staphylococcus sp.* and *Streptococcus sp.* such as *Streptococcus pneumoniae* as well as against gram-negative bacteria including *E. coli, B. catarrhalis, Klebsiella sp., Proteus sp.* and *H. influenzae* and anaerobic bacteria including *Peptostreptococcus sp., P. acnes* and *Bacteroides sp.*, is particularly noteworthy.

(3) *In vitro*, cefditoren demonstrated stability against β-lactamase produced by various bacteria. It also shows strong antibacterial activity against strains that produce β-lactamase.

2. Mechanism of action

Cefditoren inhibits the synthesis of bacterial cell wall. It has high affinity to penicillin binding protein (PBPs) in various bacteria, showing a bactericidal effect.

3. **Therapeutic efficacy on experimental infections**

   Cefditoren pivoxil demonstrated excellent therapeutic efficacy on experimental infections by *Staphylococcus aureus, S. pneumoniae, E. coli, Klebsiella pneumoniae* and *Proteus sp.*, in mice. Its therapeutic efficacy on the infections by β-lactamase-producing strains was equivalent or superior to similar drugs.

PHYSICOCHEMISTRY

Nonproprietary name:

Cefditoren pivoxil (JAN), Cefditoren (INN)

Chemical name:

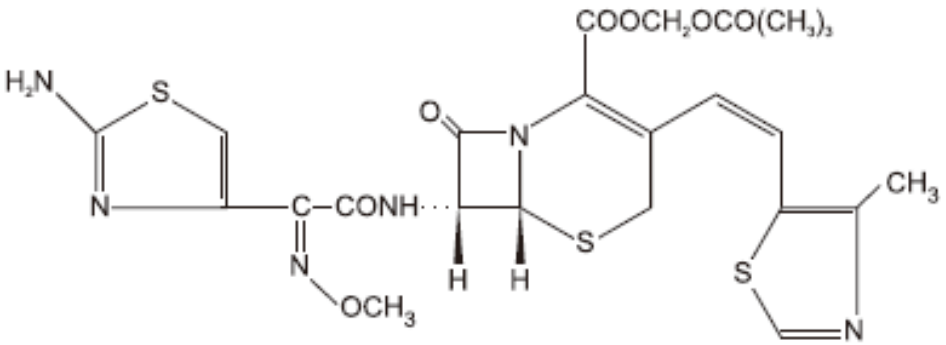
(-)-(6R,7R)-2,2-dimethylpropionyloxymethyl 7-[(Z)-2-(2-aminothiazol-4-yl)-2 methoxyiminoacetamido]-3-[(Z)-2-(4-methylthiazol-5-yl)ethenyl]-8-oxo-5-thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylate

Abbreviation: CDTR-PI

Molecular formula: $C_{25}H_{28}N_6O_7S_3$

Molecular weight: 620.72

Structural formula :



Description :

Cefditoren pivoxil, The Minimum Requirements for Antibiotic Products of Japan (MRAPJ) occurs as a light yellowish white to light yellow crystalline powder. It is freely soluble in diluted hydrochloric acid, sparingly soluble in methanol, slightly soluble in acetonitrile and in ethanol, very slightly soluble in ether and practically insoluble in water.

Melting point: 196–201°C (decomposition)

Partition coefficient: -

($\log_{10}$1 -octanol layer/water layer, 25 ± 2°C)

pH 2.0	pH 4.0 – 6.0

0.92	> 3.0

Potency:
Indicated as the weight (potency) of cefditoren ($C_{19}H_{18}N_6O_5S_3$)
1.225 mg of Cefditoren pivoxil contains 1 mg (potency) of cefditoren.

List of Excipient

Tablet Core : Mannitol, Sodium caseinate, Croscarmellose sodium, Sodium tripolyphosphate, Magnesium stearate.

Tablet Coating : Opadry Y-1-7000 white combination, Carnauba wax, Opacode S-1-20986 blue combination.

STORAGE CONDITION

Store below 30°C, protect from light and moisture.

HOW SUPPLIED

MEIACT® 200 Tablets, Box 2 blisters @ 10 tablets,
Reg. No DKI0665600217A1

HARUS DENGAN RESEP DOKTER

Manufactured by

Meiji Pharma Spain, S.A., Madrid – Spain

Imported by

meiji

PT MEIJI INDONESIAN
PHARMACEUTICAL INDUSTRIES
BANGIL - PASURUAN, JAWA TIMUR - INDONESIA

(print code)

INFORMASI PRODUK UNTUK PASIEN
MEIACT® 200 mg
Cefditoren pivoxil
FILM-COATED TABLET

Baca informasi ini secara seksama sebelum Anda mulai menggunakan obat ini karena mengandung informasi penting untuk Anda:
- Simpan informasi produk ini. Anda mungkin perlu untuk membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan memberikannya kepada orang lain.
- Jika Anda mendapatkan efek samping, laporkan kepada dokter atau apoteker Anda. Termasuk efek samping yang mungkin tidak tercantum dalam informasi produk ini.

Apa yang ada di dalam informasi produk ini

1. Apakah Meiact® 200 mg *film-coated tablets* itu dan digunakan untuk apa?

Meiact® 200 mg *film-coated tablets* merupakan tablet salut selaput berwarna putih yang mengandung *Cefditoren pivoxil* 200 mg (potensi). Antibiotik ini bekerja dengan cara menghambat pembentukan dinding sel bakteri.
Meiact® 200 mg *film-coated tablets* digunakan untuk mengobati infeksi pada:
- *Community acquired pneumonia* (pneumonia komunitas atau pneumonia yang disebabkan oleh penularan yang didapat di masyarakat).
- Eksaserbasi akut pada bronkitis kronis (gejala penyakit paru obstruktif kronik yang memburuk).
- *Pharyngotonsilitis* (peradangan pada faring dan tonsil).
- *S*inusitis akut.
- Infeksi kulit dan infeksi pada jaringan lunak.

2. Apa saja yang harus Anda ketahui sebelum menggunakan Meiact® 200 mg *film-coated tablets*?

Jangan menggunakan obat ini
- Jika Anda hipersensitivitas terhadap antibiotik, terutama antibiotik sefalosporin (jika perlu konsultasikan kepada dokter Anda) atau jika Anda hipersensitivitas terhadap salah satu bahan lain dari obat ini (tercantum di Poin 6).
- Jika Anda alergi terhadap susu sapi, perlu diperhatikan bahwa obat ini mengandung natrium kaseinat.
- Jika Anda memiliki kondisi yang disebut defisiensi karnitin primer.

Peringatan dan perhatian
Konsultasikan pada dokter Anda sebelum menggunakan Meiact® 200 mg *film-coated tablets*
- Jika Anda memiliki riwayat hipersensitivitas terhadap penisilin.
- Jika Anda memiliki gejala alergi seperti asma bronkial (batuk, sesak nafas, dada terasa berat terutama pada malam dan dini hari), eksantema atau urtikaria (terdapat ruam dan kemerahan pada kulit).
- Jika Anda memiliki gangguan fungsi ginjal berat.
- Jika Anda adalah pasien lanjut usia.
- Jika Anda adalah pasien dengan asupan makanan oral yang buruk atau yang menerima nutrisi parenteral, dan pasien yang memiliki kondisi kesehatan yang secara umum buruk (Pasien harus diamati dengan hati-hati karena defisiensi vitamin K dapat terjadi).

Konsultasikan dengan dokter Anda jika Anda mengalami salah satu dari efek berikut selama menggunakan obat ini:
- Jika Anda mengalami kondisi tidak nyaman pada mulut dan saluran pencernaan, atau kondisi tidak normal lainnya yang didapatkan setelah mengonsumsi obat ini.

Penggunaan pada kondisi kehamilan dan menyusui
Mintalah saran dokter atau apoteker Anda jika akan menggunakan Meiact® 200 mg *film-coated tablets* namun Anda sedang dalam kondisi hamil, merencanakan kehamilan atau menyusui.

Penggunaan pada pasien lanjut usia
Penyesuaian dosis tidak diperlukan untuk pasien lanjut usia, kecuali dalam kasus gangguan fungsi ginjal dan gangguan fungsi hati. Pada pasien yang mengalami defisiensi vitamin K, dapat menyebabkan perdarahan.

Penggunaan pada pasien anak-anak
Kemanan penggunaan Meiact®200 mg *Film-coated tablets* belum diteliti pada pasien di bawah 12 tahun.

Mengendarai dan menjalankan mesin
Meiact® 200 mg *film-coated tablets* dapat menyebabkan pusing, sehingga dapat mengganggu kemampuan mengendarai kendaraan dan menjalankan alat atau mesin.

3. Bagaimana cara menggunakan Meiact® 200 mg *film-coated tablets*?
Minum obat dengan cara menelan tablet secara utuh dengan segelas air putih. Obat dikonsumsi setelah makan. Selalu minum obat ini sesuai dengan anjuran dokter atau apoteker Anda. Meskipun telah merasakan perbaikan kondisi, jangan mengehentikan penggunaan obat secara tiba-tiba. Tetap gunakan sesuai dengan anjuran dokter atau apoteker Anda.
Dosis yang dianjurkan dan frekuensi pemberian obat ini adalah sebagai berikut:
- *Community-acquired pneumonia* (pneumonia komunitas atau pneumonia yang disebabkan oleh penularan yang didapat di masyarakat)
  2 tablet (400 mg Cefditoren) setiap 12 jam selama 14 hari.
- Eksaserbasi akut pada bronkitis kronis (gejala penyakit paru obstruktif kronik yang memburuk)
  2 tablet (400 mg Cefditoren) setiap 12 jam selama 10 hari.
- *Pharyngo-tonsilitis* (peradangan pada faring dan tonsil)
  1 tablet (200 mg Cefditoren) setiap 12 jam selama 10 hari.
- *S*inusitis akut
  1 tablet (200 mg Cefditoren) setiap 12 jam selama 10 hari.
- Infeksi kulit dan infeksi pada jaringan lunak
  1 tablet (200 mg Cefditoren) setiap 12 jam selama 10 hari.

<u>Pasien dengan gangguan ginjal</u>
Dosis pasien dengan gangguan ginjal dikonsultasikan terlebih dahulu dengan dokter atau apoteker Anda.

<u>Pasien dengan gangguan hati</u>
Dosis pasien dengan gangguan hati dikonsultasikan terlebih dahulu dengan dokter atau apoteker Anda.

Jika Anda lupa untuk mengonsumsi Meiact® 200 mg *Film-coated Tablet*
Jika Anda lupa meminum satu dosis, segera minum dosis berikutnya, lalu lanjutkan dengan jadwal pemberian dosis seperti biasa. Jangan mengambil dosis ganda untuk mengganti dosis yang terlupakan.

4. Apa saja efek samping yang mungkin terjadi setelah menggunakan Meiact® 200 mg *film-coated tablets*?
Semua obat-obatan, termasuk obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping yang sangat umum:
- Diare, mual, muntah dan tidak nyaman di perut.

Efek samping yang umum:
- Terjadinya reaksi alergi seperti kemerahan pada kulit.

Efek samping yang jarang terjadi:
- Terjadinya abnormalitas pada nilai laboratorium termasuk peningkatan nilai *Aspartat Transaminase* (AST) atau *Serum Glutamic-Oxaloacetic Transaminase* (SGOT), peningkatan nilai *Alanin Transaminase* (ALT) atau *Serum Glutamic-Pyruvic Transaminase* (SGPT) dan nilai abnormalitas pada hematologi seperti *eosinophilia* (kadar sel darah putih eosinophil melebihi batas normal), sakit kepala.

Efek samping yang signifikan secara klinis:
- Terjadinya shock *anaphylaxis* (reaksi alergi yang berat), diare disertai perdarahan, *Stevens Johnson Syndrome* (melepuh dan erosi pada kulit dan mukosa), pneumonia (radang paru), gangguan liver/hati, agranulositosis (penurunan jumlah sel darah).

Efek samping lainnya yang mungkin terjadi:
- Demam, arthralgia (kekakuan pada sendi), pembengkakan kelenjar getah bening, trombositopenia (kadar trombosit rendah), meningkatkan BUN (*Blood Urea Nitrogen*) dan serum kreatinin, proteinuria, candidiasis, defisiensi vitamin (K dan B kompleks), sakit kepala, edema, mati rasa dan pusing.

Pelaporan efek samping
Jika Anda mengalami efek samping, konsultasikan dengan dokter atau apoteker Anda. Termasuk kemungkinan efek samping yang tidak tercantum dalam informasi ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi tentang keamanan obat ini.

5. Bagaimana cara menyimpan Meiact® 200 mg *film-coated tablets*?
- Simpan di bawah suhu 30°C. Simpan pada tempat yang terlindung dari cahaya.
- Jauhkan obat ini dari pandangan dan jangkauan anak-anak.
- Simpan dalam kemasan aslinya.

6. Apa komposisi Meiact® 200 mg *film-coated tablets*?
Setiap tablet mengandung 200 mg Cefditoren (sebagai Cefditoren Pivoxil).
Bahan lainnya adalah *Mannitol, Sodium caseinat, Croscarmellose sodium, Sodium tripoliuphosphat, magnesium stearate, Opadry Y-1-7000 white combination, Carnauba wax, Opacode S-1-20986 blue combination.*

MEIACT® 200 mg *Film-coated Tablet* :
No.Reg. DKI0665600217A1

HARUS DENGAN RESEP DOKTER

Diproduksi oleh
Meiji Seika Pharma Spain, S.A., Madrid - Spain

Diimpor, dikemas sekunder, dan dipasarkan oleh

meiji

PT MEIJI INDONESIAN
PHARMACEUTICAL INDUSTRIES
Bangil – Pasuruan, Jawa timur – Indonesia

(print code)