TOWA PHARMACEUTICAL CO., LTD.

Revised: September 2020 (16th version, Section of "Precautions Concerning Indications")
Revised: March 2019 (15th version)

Oral Cephem Antibiotic

Prescription-only drug*1

Cefalexin Capsules, Japanese Pharmacopoeia
CEFALEXIN CAPSULES 250mg "TOWA"

Storage:
Store in an air-tight container at room temperature.

Expiration date:
Indicated on the package.

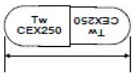
Standard Commodity Classification No. of Japan 876132	
Approval No.	21800AMX10706
Date of listing in the NHI reimbursement price	December 2006
Date of initial marketing in Japan	September 1976
Date of result of reevaluation	September 2004
Date of addition of indication	September 2004
Date of reevaluation (quality)	November 2003

*1 Caution - Use only pursuant to the prescription of a physician, etc.

CONTRAINDICATIONS (Cefalexin Capsules is contraindicated in the following patients.)
Patients with a history of hypersensitivity due to any of the ingredients in this product

RELATIVE CONTRAINDICATIONS (As a general rule, Cefalexin Capsules is contraindicated in the following patients. If use of this product is considered essential, it should be administered with care.)
Patients with a history of hypersensitivity to cephem antibiotics

DESCRIPTION

Active ingredient per capsule	Cefalexin (Potency) ····· 250 mg	
Inactive ingredients	Corn Starch, Microcrystalline Cellulose, Magnesium Stearate Capsule shell: Yellow No. 5, Blue No. 1, Titanium oxide, Sodium Lauryl Sulfate, Gelatin	
Product description	An opaque hard capsule consisting of a green cap and a whitish body, containing white to light yellowish-white powders having a characteristic odor with a bitter taste.	
Identification code	Capsule	Tw CEX250
	Package	Tw. CEX250
Appearance Length Size	 About 17.9mm (No.2 Capsule)	
Weight (mg)	About 343	

INDICATIONS

<Susceptible strains>
Cefalexin-susceptible strains of *Staphylococcus* sp., *Streptococcus* sp., *Pneumococcus*, *Enterococcus* sp., *Gonococcus*, *Escherichia coli*, *Klebsiella* sp., *Enterobacter* sp., *Proteus* sp., *Morganella morganii*, *Providencia* sp., *Haemophilus influenzae*

<Indications>
Superficial skin infection, deep skin infection, lymphangitis or lymphadenitis, chronic pyoderma, secondary infection in trauma, burn or surgical wound, etc., mastitis, osteomyelitis, myositis, pharyngitis or laryngitis, tonsillitis, acute bronchitis, pneumonia, secondary infection in chronic respiratory disease, cystitis, pyelonephritis, prostatitis (acute, chronic), epididymitis, gonococcal infection, cervicitis, bartholinitis, intrauterine infection, dacryocystitis, hordeolum, keratitis (including corneal ulcer), otitis externa, otitis media, sinusitis, purulent sialoadenitis, periodontal tissue inflammation, pericoronitis, maxillary sinusitis, jaw inflammation, secondary infection in tooth extraction or oral surgery wound

PRECAUTIONS CONCERNING INDICATIONS
For pharyngitis or laryngitis, tonsillitis, acute bronchitis, otitis media and sinusitis, this product should be administered when the administration of this product is judged to be appropriate after consideration of necessity for antimicrobial administration by referring "Guidance for Appropriate Use of Antimicrobial" 1).

DOSAGE AND ADMINISTRATION

The usual dosage for adult and children with body weight of ≥ 20 kg for oral use is 250 mg (potency) of Cefalexin every 6 hours.
The dosage for severe cases and cases whose isolated microorganisms show relatively low susceptibility for oral use is 500 mg (potency) of Cefalexin every 6 hours.
The dosage may be adjusted according to the patient's age, body weight and symptoms.

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

PRECAUTIONS

1. Careful Administration (Cefalexin Capsules should be administered with care in the following patients.)
1) Patients with a history of hypersensitivity to penicillin antibiotics
2) Patients with a personal or familial predisposition to allergic reactions such as bronchial asthma, rash and urticaria
3) Patients with severe renal dysfunction [Blood concentrations may be continuously high. The

dosage should be reduced or administration should be given with appropriate intervals.]

4) Patients of poor oral ingestion, patients receiving parenteral feeding, or patients in poor general condition [Vitamin K deficiency symptoms may occur. The patients should be carefully monitored.]
5) Elderly patients (See "Use in the Elderly".)

2. Important Precautions

Shock may occur. The patients should be carefully examined.

3. Adverse Reactions

No investigation such as a drug use investigation clearly showing the incidence of adverse reactions has been conducted.

1) Clinically significant adverse reactions (incidence unknown)

(1) **Shock, anaphylactoid reaction:** Shock or anaphylactoid reaction (including dyspnea, generalized flushing, edema, etc.) may occur. The patients should be carefully monitored, and if such symptoms are observed, administration of this product should be discontinued and appropriate measures should be taken.

(2) **Acute renal disturbance**: Serious renal disturbance such as acute renal disturbance may occur. Patients should be carefully monitored by periodically conducting laboratory tests. If any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

(3) **Hemolytic anemia:** Hemolytic anemia may occur. If any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

(4) **Pseudomembranous colitis:** Serious colitis with bloody stools such as pseudomembranous colitis may occur. If abdominal pain or frequent diarrhea occurs, appropriate measures such as discontinuation of this product should be taken.

(5) **Muco-cutaneo-ocular syndrome (Stevens-Johnson syndrome), toxic epidermal necrolysis (Lyell syndrome):** Muco-cutaneo-ocular syndrome (Stevens-Johnson syndrome) or toxic epidermal necrolysis (Lyell syndrome) may occur. Patients should be carefully monitored, and if such symptoms occur, administration of this product should be discontinued and appropriate measures should be taken.

(6) **Interstitial pneumonia, PIE syndrome:** Interstitial pneumonia, PIE syndrome, etc. accompanied with fever, cough, dyspnea, abnormal chest X-ray findings, eosinophilia, etc. may occur. If such symptoms occur, administration of this product should be discontinued and appropriate measures such as administration of adrenocortical hormone should be taken.

2) Other adverse reactions

	Incidence unknown
Hypersensitivity*2	Rash, urticaria, erythema, pruritus, fever, swollen lymph glands, arthralgia, etc.
Hematologic*2	Granulocytopenia, eosinophilia, thrombocytopenia
Hepatic*3	Jaundice, increased AST(GOT), increased ALT(GPT), increased Al-P
Gastrointestinal	Nausea, vomiting, diarrhea, soft stools, abdominal pain, anorexia, stomach discomfort, etc.
Microbial substitution	Stomatitis, candidiasis
Vitamin deficiency	Vitamin K deficiency symptoms (hypoprothrombinaemia, bleeding tendency, etc.), vitamin B complex deficiency symptoms (glossitis, stomatitis, anorexia, neuritis, etc.)
Others	Headache, dizziness, general malaise

*2: If the symptoms (abnormalities) are observed, administration of this product should be discontinued and appropriate measures should be taken.
*3: If the symptoms (abnormalities) are observed, appropriate measures such as discontinuation of this product should be taken.

4. Use in the Elderly

This product should be carefully administered to elderly patients with attention to the following points, and the dose and administration interval should be considered under a close clinical observation of the patient's conditions.

1) Since the elderly often have reduced physiological functions, adverse reactions tend to occur more frequently.
2) In elderly patients, bleeding tendency due to vitamin K deficiency may occur.

5. Use during Pregnancy, Delivery or Lactation

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

6. Effects on Laboratory Tests

1) Since false-positive results may occur in urine sugar tests with Benedict's solution, Fehling's solution and Clinitest except Tes-Tape, caution should be paid.
2) Care should be taken about positive reactions in the direct Coombs' test.

7. Precautions Concerning Use

Precautions regarding dispensing:

For drugs that are dispensed in a PTP (press-through package) sheet, instruct the patient to remove the drug from the package prior to use. (It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, resulting in severe complications such as mediastinitis.)

PHARMACOKINETICS

Bioequivalence test

<Reference data>

One capsule each of CEFALEXIN CAPSULES 250mg "TOWA" and a reference drug (as 250 mg of cefalexin) was administered orally as a single dose to male rabbits (n = 10) under fasting conditions in a crossover design to measure each unchanged drug concentration in plasma. Obtained results were statistically analyzed, which estimated that there is no significant difference between the drugs[2].

Dissolution profile

CEFALEXIN CAPSULES 250mg "TOWA" has been confirmed to conform to the dissolution standard of Cefalexin Capsules defined in the official monographs of the Japanese Pharmacopoeia[3].

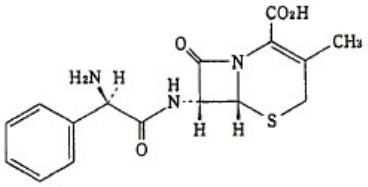
PHARMACOLOGY

Cefalexin affects gram-positive bacteria and gram-negative bacteria and does not affect acid-fast

bacteria and fungus. Cefalexin restrains the growth of *Staphylococcus aureus* and hemolytic streptococcus of gram-positive cocci, *Gonococcus* and *Neisseria meningitidis* of gram-negative cocci, and *Escherichia coli* and *Klebsiella pneumoniae* of gram-negative rod to 6.25μg/mL, and the mechanism of its effect is inhibition of cell wall synthesis and bactericidal[4].

PHYSICOCHEMISTRY

Structural formula:



Nonproprietary name:
Cefalexin
Chemical name:
(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-phenylacetylamino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid
Molecular formula:
$C_{16}H_{17}N_3O_4S$
Molecular weight:
347.39
Description:
Cefalexin occurs as a white to light yellowish white, crystals or crystalline powder. It is sparingly soluble in water, slightly soluble in methanol, and practically insoluble in ethanol (95) and in *N, N*-dimethylformamide. It is hygroscopic.

PRECAUTIONS FOR HANDLING

Stability test
In a long term stability test using final packaged products (at room temperature for 3 years), CEFALEXIN CAPSULES 250mg “TOWA” was confirmed to be stable for 3 years under normal distribution conditions[5].

PACKAGING

CEFALEXIN CAPSULES 250mg “TOWA”
Boxes of 100 capsules in press-through packages

REFERENCES

1) “Guidance for Appropriate Use of Antimicrobial” edited by Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, Ministry of Health, Labour and Welfare.
2) Internal data of Towa Pharmaceutical Co., Ltd.: Bioequivalence test
3) Internal data of Towa Pharmaceutical Co., Ltd.: Dissolution test
4) Manual of The Japanese Pharmacopoeia, fifteenth edition, C-2077, 2006
5) Internal data of Towa Pharmaceutical Co., Ltd.: Stability test

Manufacturer and Distributor
TOWA PHARMACEUTICAL CO., LTD.
2-11, Shinbashi-cho, Kadoma, Osaka 571-8580
Japan