Public Assessment Report

Cefalexin 250mg Capsules
Cefalexin 500mg Capsules

Cefalexin monohydrate

PL 22805/0009-10

Orchid Europe Ltd

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Lay Summary

The MHRA granted Orchid Europe Ltd Marketing Authorisations (licences) for the medicinal products Cefalexin 250mg Capsules (PL 22805/0009) and Cefalexin 500mg Capsules (PL 22805/0010) on 12/08/2009. The products are prescription only medicines.

The products contain the active ingredient Cefalexin. Cefalexin has bactericidal activity resulting from the inhibition of bacterial cell wall synthesis ultimately leading to cell death. Cefalexin is stable to a broad range of bacterial β-lactamases and is active against both gram-positive and gram-negative species.

The proposed indications include: respiratory tract infections, otitis media, skin and soft tissue infections, bone and joint infections, genitor-urinary tract infections including acute prostatitis, and dental infections. These indications and their dosage regimens are the same as the innovator product.

The drug products were demonstrated to be generic medical products of Keflex capsules 250 mg (PL 00006/5103R) and 500 mg (PL 00006/0076R), granted 30 September 1985, and marketed by Eli Lilly.

Scientific Discussion

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal products Cefalexin 250mg Capsules (PL 22805/0009) and Cefalexin 500mg Capsules (PL 22805/0010) on 12/08/2009. The marketing authorisation holder is Orchid Europe Ltd.

These were national abridged applications submitted in accordance with article 10 (1) of Directive 2001/83/ EC as amended, so-called 'generic application'. The applicant claims the products are generic medical products of Keflex capsules 250 mg (PL 00006/5103R) and 500 mg (PL 00006/0076R), granted 30 September 1985, and marketed by Eli Lilly. The products are prescription only medicines.

The products contain the active ingredient Cefalexin. Cefalexin has bactericidal activity resulting from the inhibition of bacterial cell wall synthesis ultimately leading to cell death. Cefalexin is stable to a broad range of bacterial β-lactamases and is active against both gram-positive and gram-negative species.

The proposed indications include: respiratory tract infections, otitis media, skin and soft tissue infections, bone and joint infections, genitor-urinary tract infections including acute prostatitis, and dental infections. These indications and their dosage regimens are the same as the innovator product.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

General Information

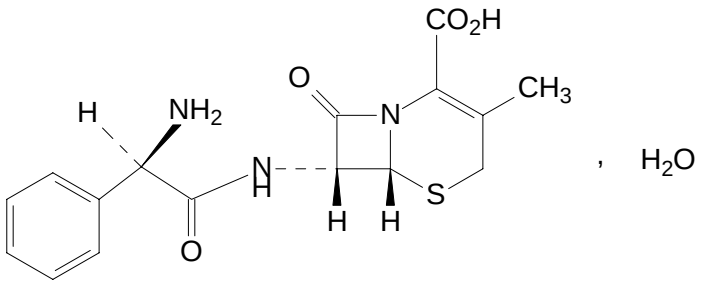
Cefalexin monohydrate has a Ph Eur monograph.

Nomenclature

INN:	Cefalexin Monohydrate
Ph. Eur./ B.P.:	Cefalexin Monohydrate
USP:	Cephalexin
Chemical name:	(6*R*,7*R*)-7-[[(2*R*)-2-Amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid monohydrate
BAN:	Cefalexin Monohydrate
CAS no:	23325-78-2

Structure

Structural formula:



Molecular formula: $C_{16}H_{17}N_3O_4S, H_2O$
Molecular weight: 365.4 g/mol

General properties

Cefalexin monohydrate is a white or almost white crystalline powder, sparingly soluble in water, practically insoluble in alcohol.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active cefalexin monohydrate is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated and support a retest period of 4 years with no specific storage conditions.

DRUG PRODUCT

Other Ingredients

The other ingredients of the drug product are

Capsule contents
Cellulose Microcrystalline
Croscarmellose Sodium
Magnesium Stearate

Capsule shell
Brilliant Blue FCF (E133)
Sunset yellow FCF (E110)
Titanium dioxide
Gelatin
Sodium lauril sulfate

Black printing ink (SW-9008 & SW-9009)

Shellac
Dehydrated Alcohol
Isopropyl Alcohol
Butyl Alcohol
Propylene Glycol
Purified Water
Strong Ammonia Solution
Potassium Hydroxide
Black Iron Oxide (E172)

All ingredients comply with relevant Ph Eur monographs except empty hard gelatin capsules which are controlled to in-house specifications. Specifications, analytical test procedures and suppliers' supporting Certificates of Analysis have been provided. Microbial limits are included in all specifications for the excipients.

Dissolution and impurity profiles

Dissolution and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

Manufacture
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
The capsules will be contained in either blister packaging or high density polyethelene (HDPE) containers. Material: blisters composed of PVC/ Aclar (titanium oxide in PVC) base film and aluminium foil coated with a heat seal lacquer on one side. All packaging has been demonstrated to meet current requirements.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life 2 years with a storage condition for the HDPE containers of “Keep container tightly closed”.

ASSESSOR’S OVERALL CONCLUSIONS ON QUALITY AND ADVICE

A Marketing Authorisation was granted.

PRE-CLINICAL ASSESSMENT

No pre-clinical data were submitted for this application and none were required.

MEDICAL ASSESSMENT

Pharmacodynamics

Mode of Action

Cefalexin is an antibacterial agent of the cephalosporin class. Like other cephalosporins cefalexin exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

Mechanisms of resistance

Bacterial resistance to cefalexin may be due to one or more of the following mechanisms:

- Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally-encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gram-negative bacterial species.
- Reduced affinity of penicillin-binding proteins.
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all other beta-lactams and/ or antibacterial drugs of other classes.

Breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the British Society of Antimicrobial Chemotherapy for beta-haemolytic Streptococci and *Streptococcus pneumoniae* are: susceptible ≤ 2mg /L, resistant ≥2.5mg /L.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobes, Gram positive:
Staphylococcus aureus (methicillin susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae

Streptococcus pyogenes

Aerobes, Gram negative:
Escherichia coli
Haemophilus influenzae
Moraxella catarrhalis

Anaerobes:
Peptostreptococcus species

Species for which resistance may be a problem

Citrobacter species
Enterobacter species
Morganella morganii.

Pharmacokinetics

Absorption
Cefalexin is almost completely absorbed from the gastrointestinal tract and produces a peak plasma concentration of about 18 micrograms/mL 1 hour after a 500mg oral dose. Absorption may be delayed if cefalexin is taken with food but the total amount absorbed is not appreciably altered. Up to 15% of a dose is bound to plasma proteins. The plasma half-life is about 1 hour. The plasma half-life increases with reduced renal function.

Distribution
Cefalexin is widely distributed in the body but does not enter the cerebrospinal fluid in significant quantities. It crosses the placenta and small quantities are found in breast milk.

Metabolism
Cefalexin is not metabolised.

Excretion
About 80% or more of a dose is excreted unchanged in the urine in the first 6 hours by glomerular filtration and tubular secretion; urinary concentrations greater than 1 mg/mL have been achieved after a dose of 500 mg. Probenecid delays urinary excretion. Therapeutically effective concentrations may be found in the bile and some may be excreted by this route.

Bioequivalence Study

Cefalexin 500mg capsules, Orchid Healthcare Ltd were compared to the reference product Keflex 500mg capsules, manufactured by Eli Lilly Ltd

Study design
Randomised, two-way, two-period, single dose crossover study in healthy fasted volunteers

24 adult, male subjects studied (26 were enrolled and 25 completed the study). There were difficulties collecting blood samples from 2 subjects and 1 subject dropped out for personal reasons.

Single oral dose of 500mg cefalexin administered for both test and reference product

Pre-defined bioequivalence acceptance criteria

The protocol defines acceptance criteria of 0.8 – 1.25 for both AUC and Cmax. This is satisfactory.

Sampling frequency was at 15min intervals for the first hour and then at 20min intervals for the second hour and then at staggered intervals up to 10hrs. The sampling around Tmax was adequate for Cmax estimation

The washout period was 7 days and this was sufficient to avoid carryover

The randomisation scheme appears balanced for sequence and appears random

Data analysis was done using Kinetica software (USA). ANOVA was performed on ln-transformed data using SAS ver 8.2 software for AUC and Cmax. This was also used to calculate 90% confidence intervals.

The protocol appears adequate

Results for main pharmacokinetic parameters:

Parent drug

	Test	**Reference**
C_{max} (microg/mL)	22.8	23.5
AUC_t (microg.h/mL)	47.4	46.2
AUC_∞ (microg.h/mL)	48.6	47.1
T_{max} (h)*	1.26	1.14

The measured PK parameters are similar to published figures.

Bioequivalence results for log-transformed test/reference ratios with 90% Confidence Intervals:

	Parent drug
C_{max}	96.3% (90 – 104)
AUC_t	102.4% (97 – 107)
AUC_∞ (ng.h/mL)	102.9% (98 – 108)

The 90% confidence intervals for test/reference lie within the acceptance criteria. Period 2 had zero baseline plasma concentrations.

Management of withdrawals and other protocol deviations were according to protocol

Appearance of individual plasma concentration – time curves – checked and appear acceptable

Assessor's Conclusion on Bioequivalence
The applicant has fulfilled the criteria for bioequivalence.

Efficacy
Efficacy is reviewed in the Clinical Expert Report. The reference product is established and the application depends upon the ability to show bioequivalence with the reference product.

Safety
Safety is reviewed in the Clinical Expert Report. The reference product is established and the application depends upon the ability to show bioequivalence with the reference product.

Expert Report
The expert report is written by a medically qualified pharmaceutical consultant and is satisfactory.

Summary Of Product Characteristics
This is satisfactory.

Patient Information Leaflet
This is satisfactory.

Conclusions
Marketing authorisations may be granted for these products.

Overall Conclusion and Risk/Benefit Analysis

Quality

The important quality characteristics of Cefalexin 250mg Capsules and Cefalexin 500mg Capsules are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

Pre-Clinical

No new preclinical data were submitted and none are required for applications of this type.

Clinical

Bioequivalence has been demonstrated between the applicant's Cefalexin 500mg Capsules the reference product. Given that linear kinetics apply between the 250mg and 500mg capsules, that proportional formulae for the capsules have been used and that similar dissolution results have been shown for the two strengths, a separate bioequivalence study using the 250mg capsules is not considered necessary.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Keflex 250mg and 500mg capsules.

Risk/Benefit Analysis

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. The risk benefit is, therefore, considered to be positive.

Steps Taken During Assessment

1	The MHRA received the application on 21/06/2006.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 14/08/2006.
3	Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 26/10/2006, 19/03/2007, 04/04/2008 and 24/02/2009 and on the clinical assessment 20/03/2007, 06/07/2007, 04/10/2007, 28/11/2007, 03/03/2008,19/10/2008 and 18/02/2009.
4	The applicant provided further information in regard to the quality assessment on 27/12/2006, 14/08/2008, 10/07/2007, 19/05/2009 and on the clinical assessment 05/04/2007, 05/09/2007, 14/11/2007,07/02/2008,19/07/2008, 9/12/2008 and 19/02/2009
5	The application was determined on 12/08/2009

Steps Taken after Assessment

No non-confidential changes have been made to the market authorisation.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefalexin 250mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains, as the active ingredient, Cefalexin monohydrate equivalent to 250mg of Cefalexin base.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard

Green coloured opaque cap and opaque white coloured body, size "2" hard gelatin capsules imprinted with black "CEF" on cap & "250" on body, filled with white to off white granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is a semi-synthetic cephalosporin antibiotic for oral administration.

Cefalexin is indicated for the treatment of the following infections when caused by susceptible organisms (see also sections 4.4 and 5.1).

Upper respiratory tract infections
Otitis media
Exacerbation of chronic bronchitis
Community-acquired pneumonia
Uncomplicated upper and lower urinary tract infections
Acute prostatitis
Skin and soft tissue infections
Bone and joint infections

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

The recommended dose for adults is 1-4 g daily in divided doses. Most infections will respond to a dosage of 500 mg every 8 hours. For skin and soft tissue infections, streptococcal pharyngitis, and mild, uncomplicated urinary tract infections, the usual dosage is 250 mg every 6 hours, or 500 mg every 12 hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of Cefalexin greater than 4 g are required, parenteral cephalosporins, in appropriate doses, should be considered.

Patients with impaired renal function

Reduce dosage if renal function is markedly impaired (see section 4.4).

Elderly patients

The recommended dose for adults should be used in elderly patients except those with impaired renal function (see section 4.4).

Children

The usual recommended daily dosage for children is 25-50 mg/kg body weight (10-20 mg/lb body weight) in divided doses. For skin and soft tissue infections, streptococcal pharyngitis, and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours. For most infections the following schedule is suggested:

Children under 5 years: 125 mg every 8 hours.

Children 5 years and over: 250 mg every 8 hours.

In severe infections, the dosage may be doubled. In the therapy of otitis media, clinical studies have shown that a dosage of 75 to 100 mg/kg/day in 4 divided doses is required.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Method of administration

Cefalexin is administered orally.

4.3 Contraindications

Cefalexin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics or to any of the excipients.

4.4 Special warnings and precautions for use

Before instituting therapy with Cefalexin, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins or other drugs. Cefalexin should be given cautiously to penicillin-sensitive patients. There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics, including macrolides, semi-synthetic penicillins, and cephalosporins. It is important, therefore, to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken.

If an allergic reaction to Cefalexin occurs, the drug should be discontinued and the patient treated with the appropriate agents.

Prolonged use of Cefalexin may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Cefalexin should be administered with caution in the presence of markedly impaired renal function. Careful clinical and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematological studies, or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side, or in Coombs' testing of newborns whose mothers have received

cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs' test may be due to the drug.

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions, or with copper sulphate test tablets.

Cefalexin capsules contains colouring agents Brilliant Blue FCF (E133) and Sunset yellow FCF (E110), which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

As with other beta-lactam drugs, renal excretion of Cefalexin is inhibited by probenecid.

In a single study of 12 healthy subjects given single 500 mg doses of Cefalexin and metformin, plasma metformin C_{max} and AUC increased by an average of 34% and 24%, respectively, and metformin renal clearance decreased by an average of 14%. No side effects were reported in 12 healthy subjects in this study. No information is available about the interaction of Cefalexin and metformin following multiple dose administration. The clinical significance of this study is unclear, particularly as no cases of "lactic acidosis" have been reported in association with concomitant metformin and Cefalexin treatment.

4.6 Pregnancy and lactation

Pregnancy

Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Lactation

The excretion of Cefalexin in human breast milk increased up to 4 hours following a 500 mg dose. The drug reached a maximum level of 4 micrograms/ml, then decreased gradually and had disappeared 8 hours after administration. Caution should be exercised when Cefalexin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

When performing these activities the possible occurrence of the adverse reactions dizziness, fatigue and confusion should be taken into account.

4.8 Undesirable effects

Adverse events that have been reported in Cefalexin trials are categorised below, according to system organ class and frequency.

Frequencies are defined as:

- very common (≥ 1/10);
- common (≥ 1/100 to <1/10);
- uncommon (≥ 1/1000 to <1/100);
- rare (≥ 1/10000 to <1/1000) and
- very rare (<1/10000).

Undesirable effects for Cefalexin occur at a frequency of 3-6%.

Infections and infestations Rare Frequency not stated	 Genital and anal pruritus, vaginitis. Vaginal candidiasis.
Blood and lymphatic disorders Uncommon Rare	 Eosinophilia. Neutropenia, thrombocytopenia, haemolytic anaemia.
Immune system disorders Rare	 Anaphylactic reaction.
Psychiatric disorders Frequency not stated	 Hallucinations, agitation, confusion.
Central and peripheral nervous system disorders Rare	 Headache, dizziness.
Gastrointestinal disorders Common Rare	 Diarrhoea, nausea. Abdominal pain, vomiting, dyspepsia, pseudomembranous colitis.
Hepatobiliary disorders Rare	 Hepatitis, cholestatic icterus.

Dermatological disorders Uncommon Rare	 Rash, urticaria, pruritus. Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis (Lyell's syndrome), angioedema.
Musculoskeletal, connective tissue and bone disorders Frequency not stated	 Arthralgia, arthritis.
Renal and urinary tract disorders Rare	 Reversible interstitial nephritis.
General symptoms and problems at site of application Rare Frequency not stated	 Tiredness. Fever.
Investigations Uncommon Frequency not stated	 Increase in AST and ALT (reversible). Positive direct Coombs test. False positive reaction for some tests of glucose in the urine (see section 4.4).

4.9 Overdose

Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea, and haematuria.

In the event of severe overdosage, general supportive care is recommended, including close clinical and laboratory monitoring of haematological, renal and hepatic functions, and coagulation status until the patient is stable. Forced diuresis, peritoneal dialysis, haemodialysis, or charcoal haemoperfusion have not been established as beneficial for an overdose of Cefalexin. It would be extremely unlikely that one of these procedures would be indicated.

Unless 5 to 10 times the normal total daily dose has been ingested, gastro-intestinal decontamination should not be necessary.

There have been reports of haematuria, without impairment of renal function, in children accidentally ingesting more than 3.5 g of Cefalexin in a day. Treatment has been supportive (fluids) and no sequelae have been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: First generation cephalosporin. **ATC code: J01DB01**

Mode of Action

Cefalexin is an antibacterial agent of the cephalosporin class. Like other cephalosporins cefalexin exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

Mechanisms of resistance

Bacterial resistance to cefalexin may be due to one or more of the following mechanisms:

- Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally-encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gram-negative bacterial species.
- Reduced affinity of pencillin-binding proteins.
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all other beta-lactams and/ or antibacterial drugs of other classes.

Breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the British Society of Antimicrobial Chemotherapy for beta-haemolytic Streptococci and *Streptococcus pneumoniae* are: susceptible ≤ 2mg /L, resistant ≥2.5mg /L.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobes, Gram positive:

Staphylococcus aureus (methicillin susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae

Streptococcus pyogenes

Aerobes, Gram negative:
Escherichia coli
Haemophilus influenzae
Moraxella catarrhalis

Anaerobes:
Peptostreptococcus species

Species for which resistance may be a problem

Citrobacter species
Enterobacter species
Morganella morganii.

5.2 Pharmacokinetic properties

Cefalexin is acid stable and may be given without regard to meals. It is rapidly absorbed after oral administration. Following doses of 250 mg, 500 mg, and 1 g, average peak serum levels of approximately 9, 18, and 32 mg/l, respectively, were obtained at 1 hour. Measurable levels were present 6 hours after administration. Cefalexin is excreted in the urine by glomerular filtration and tubular secretion. Studies showed that over 90% of the drug was excreted unchanged in the urine within 8 hours. During this period, peak urine concentrations following the 250 mg, 500 mg, and 1 g doses were approximately 1,000, 2,200, and 5,000 mg/l, respectively.

Cefalexin is almost completely absorbed from the gastro-intestinal tract, and 75-100% is rapidly excreted in active form in the urine. Absorption is slightly reduced if the drug is administered with food. The half-life is approximately

60 minutes in patients with normal renal function. Haemodialysis and peritoneal dialysis will remove cefalexin from the blood.

Peak blood levels are achieved one hour after administration, and therapeutic levels are maintained for 6-8 hours. Approximately 80% of the active drug is excreted in the urine within 6 hours. No accumulation is seen with dosages above the therapeutic maximum of 4 g/day.

The half-life may be increased in neonates due to their renal immaturity, but there is no accumulation when given at up to 50 mg/kg/day.

5.3 Preclinical safety data

The daily oral administration of Cefalexin to rats in doses of 250 or 500 mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, foetal viability, foetal weight, or litter size.

Cefalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals.

The oral LD_{50} of Cefalexin in rats is 5,000 mg/kg.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents

Cellulose Microcrystalline
Croscarmellose Sodium

Magnesium Stearate

Capsule shell
Brilliant Blue FCF (E133)
Sunset yellow FCF (E110)
Titanium dioxide
Gelatin
Sodium lauril sulfate

Black printing ink (SW-9008 & SW-9009)

Shellac
Dehydrated Alcohol
Isopropyl Alcohol
Butyl Alcohol
Propylene Glycol
Purified Water
Strong Ammonia Solution
Potassium Hydroxide
Black Iron Oxide (E172)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
24 months

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.
Keep containers tightly closed.

6.5 Nature and contents of container
The products are filled into HDPE bottles of 20 or 100 capsules, or blister packs of 28 or 100 capsules consisting of PVC/Aclar Blister film.

Not all pack sizes may be marketed

6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Orchid Europe Limited
Building 3, Chiswick Park
566, Chiswick High Road, Chiswick, London,
W4 5YA, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 22805/0009

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/08/2009

10 DATE OF REVISION OF THE TEXT

12/08/2009

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefalexin 500 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains, as the active ingredient, Cefalexin monohydrate equivalent to 500 mg of Cefalexin base.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard

Green coloured opaque cap and opaque light green coloured body, size "0" hard gelatin capsules imprinted with black "CEF" on cap & "500" on body, filled with white to off white granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is a semi-synthetic cephalosporin antibiotic for oral administration.

Cefalexin is indicated for the treatment of the following infections when caused by susceptible organisms (see also sections 4.4 and 5.1).

Upper respiratory tract infections
Otitis media
Exacerbation of chronic bronchitis
Community-acquired pneumonia
Uncomplicated upper and lower urinary tract infections
Acute prostatitis
Skin and soft tissue infections
Bone and joint infections

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

The recommended dose for adults is 1-4 g daily in divided doses. Most infections will respond to a dosage of 500 mg every 8 hours. For skin and soft tissue infections, streptococcal pharyngitis, and mild, uncomplicated urinary tract infections, the usual dosage is 250 mg every 6 hours, or 500 mg every 12 hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of Cefalexin greater than 4 g are required, parenteral cephalosporins, in appropriate doses, should be considered.

Patients with impaired renal function

Reduce dosage if renal function is markedly impaired (see section 4.4).

Elderly patients

The recommended dose for adults should be used in elderly patients except those with impaired renal function (see section 4.4).

Children

The usual recommended daily dosage for children is 25-50 mg/kg body weight (10-20 mg/lb body weight) in divided doses. For skin and soft tissue infections, streptococcal pharyngitis, and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours. For most infections the following schedule is suggested:

Children under 5 years: 125 mg every 8 hours.

Children 5 years and over: 250 mg every 8 hours.

In severe infections, the dosage may be doubled. In the therapy of otitis media, clinical studies have shown that a dosage of 75 to 100 mg/kg/day in 4 divided doses is required.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Method of administration

Cefalexin is administered orally.

4.3 Contraindications

Cefalexin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics or to any of the excipients.

4.4 Special warnings and precautions for use

Before instituting therapy with Cefalexin, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins or other drugs. Cefalexin should be given cautiously to penicillin-sensitive patients. There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics, including macrolides, semi-synthetic penicillins, and cephalosporins. It is important, therefore, to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken.

If an allergic reaction to Cefalexin occurs, the drug should be discontinued and the patient treated with the appropriate agents.

Prolonged use of Cefalexin may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Cefalexin should be administered with caution in the presence of markedly impaired renal function. Careful clinical and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematological studies, or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side, or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs' test may be due to the drug.

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions, or with copper sulphate test tablets.

Cefalexin capsules contains colouring agents Brilliant Blue FCF (E133) and Sunset yellow FCF (E110), which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

As with other beta-lactam drugs, renal excretion of Cefalexin is inhibited by probenecid.

In a single study of 12 healthy subjects given single 500 mg doses of Cefalexin and metformin, plasma metformin C_{max} and AUC increased by an average of 34% and 24%, respectively, and metformin renal clearance decreased by an average of 14%. No side effects were reported in 12 healthy subjects in this study. No information is available about the interaction of Cefalexin and metformin following multiple dose administration. The clinical significance of this study is unclear, particularly as no cases of "lactic acidosis" have been reported in association with concomitant metformin and Cefalexin treatment.

4.6 Pregnancy and lactation

Pregnancy

Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Lactation

The excretion of Cefalexin in human breast milk increased up to 4 hours following a 500 mg dose. The drug reached a maximum level of 4 micrograms/ml, then decreased gradually and had disappeared 8 hours after administration. Caution should be exercised when Cefalexin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

When performing these activities the possible occurrence of the adverse reactions dizziness, fatigue and confusion should be taken into account.

4.8 Undesirable effects

Adverse events that have been reported in Cefalexin trials are categorised

below, according to system organ class and frequency.

Frequencies are defined as:

- very common (≥ 1/10);
- common (≥ 1/100 to <1/10);
- uncommon (≥ 1/1000 to <1/100);
- rare (≥ 1/10000 to <1/1000) and
- very rare (<1/10000).

Undesirable effects for Cefalexin occur at a frequency of 3-6%.

Infections and infestations Rare Frequency not stated	 Genital and anal pruritus, vaginitis. Vaginal candidiasis.
Blood and lymphatic disorders Uncommon Rare	 Eosinophilia. Neutropenia, thrombocytopenia, haemolytic anaemia.
Immune system disorders Rare	 Anaphylactic reaction.
Psychiatric disorders Frequency not stated	 Hallucinations, agitation, confusion.
Central and peripheral nervous system disorders Rare	 Headache, dizziness.
Gastrointestinal disorders Common Rare	 Diarrhoea, nausea. Abdominal pain, vomiting, dyspepsia, pseudomembranous colitis.
Hepatobiliary disorders Rare	 Hepatitis, cholestatic icterus.
Dermatological disorders Uncommon Rare	 Rash, urticaria, pruritus. Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis (Lyell's syndrome), angioedema.
Musculoskeletal, connective tissue and bone disorders Frequency not stated	 Arthralgia, arthritis.
Renal and urinary tract disorders Rare	 Reversible interstitial nephritis.

General symptoms and problems at site of application Rare Frequency not stated	 Tiredness. Fever.
Investigations Uncommon Frequency not stated	 Increase in AST and ALT (reversible). Positive direct Coombs test. False positive reaction for some tests of glucose in the urine (see section 4.4).

4.9 Overdose

Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea, and haematuria.

In the event of severe overdosage, general supportive care is recommended, including close clinical and laboratory monitoring of haematological, renal and hepatic functions, and coagulation status until the patient is stable. Forced diuresis, peritoneal dialysis, haemodialysis, or charcoal haemoperfusion have not been established as beneficial for an overdose of Cefalexin. It would be extremely unlikely that one of these procedures would be indicated.

Unless 5 to 10 times the normal total daily dose has been ingested, gastro-intestinal decontamination should not be necessary.

There have been reports of haematuria, without impairment of renal function, in children accidentally ingesting more than 3.5 g of Cefalexin in a day. Treatment has been supportive (fluids) and no sequelae have been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: First generation cephalosporin. **ATC code: J01DB01**

Mode of Action

Cefalexin is an antibacterial agent of the cephalosporin class. Like other cephalosporins cefalexin exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

Mechanisms of resistance

Bacterial resistance to cefalexin may be due to one or more of the following mechanisms:

- Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally-encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gram-negative bacterial species.
- Reduced affinity of pencillin-binding proteins.
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all other beta-lactams and/ or antibacterial drugs of other classes.

Breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the British Society of Antimicrobial Chemotherapy for beta-haemolytic Streptococci and *Streptococcus pneumoniae* are: susceptible ≤ 2mg /L, resistant ≥2.5mg /L.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobes, Gram positive:
Staphylococcus aureus (methicillin susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae

Streptococcus pyogenes

Aerobes, Gram negative:

Escherichia coli

Haemophilus influenzae

Moraxella catarrhalis

Anaerobes:
Peptostreptococcus species

Species for which resistance may be a problem

Citrobacter species
Enterobacter species
Morganella morganii.

5.2 Pharmacokinetic properties

Cefalexin is acid stable and may be given without regard to meals. It is rapidly absorbed after oral administration. Following doses of 250 mg, 500 mg, and 1 g, average peak serum levels of approximately 9, 18, and 32 mg/l, respectively, were obtained at 1 hour. Measurable levels were present 6 hours after administration. Cefalexin is excreted in the urine by glomerular filtration and tubular secretion. Studies showed that over 90% of the drug was excreted unchanged in the urine within 8 hours. During this period, peak urine concentrations following the 250 mg, 500 mg, and 1 g doses were approximately 1,000, 2,200, and 5,000 mg/l, respectively.

Cefalexin is almost completely absorbed from the gastro-intestinal tract, and 75-100% is rapidly excreted in active form in the urine. Absorption is slightly reduced if the drug is administered with food. The half-life is approximately 60 minutes in patients with normal renal function. Haemodialysis and peritoneal dialysis will remove cefalexin from the blood.

Peak blood levels are achieved one hour after administration, and therapeutic levels are maintained for 6-8 hours. Approximately 80% of the active drug is excreted in the urine within 6 hours. No accumulation is seen with dosages above the therapeutic maximum of 4 g/day.

The half-life may be increased in neonates due to their renal immaturity, but there is no accumulation when given at up to 50 mg/kg/day.

5.3 Preclinical safety data

The daily oral administration of Cefalexin to rats in doses of 250 or 500 mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, foetal viability, foetal weight, or litter size.

Cefalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals.

The oral LD_{50} of Cefalexin in rats is 5,000 mg/kg.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents

Cellulose Microcrystalline
Croscarmellose Sodium
Magnesium Stearate

Capsule shell

Brilliant Blue FCF (E133)
Sunset yellow FCF (E110)
Titanium dioxide
Gelatin
Sodium lauril sulfate

Black printing ink (SW-9008 & SW-9009)

Shellac
Dehydrated Alcohol
Isopropyl Alcohol
Butyl Alcohol
Propylene Glycol
Purified Water
Strong Ammonia Solution
Potassium Hydroxide
Black Iron Oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
Keep containers tightly closed.

6.5 Nature and contents of container

The products are filled into HDPE bottles of 20 or 100 capsules, or blister packs of 21 or 100 capsules consisting of PVC/Aclar Blister film.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Orchid Europe Limited
Building 3, Chiswick Park
566, Chiswick High Road, Chiswick, London,
W4 5YA, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 22805/0010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/08/2009

10 DATE OF REVISION OF THE TEXT

12/08/2009

Labels and Leaflets

PACKAGE LEAFLET INFORMATION FOR THE USER

Cefalexin 500 mg Capsules
Cefalexin

The name of your medicine is Cefalexin 500 mg capsules, which will be referred to as Cefalexin throughout the rest of this document.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cefalexin is and what it is used for

Cefalexin is an antibiotic. It belongs to a group of antibiotics that are called cephalosporins. These types of antibiotics are similar to penicillin.

Cefalexin kills bacteria and it can be used against various sorts of infections. Like all antibiotics, Cefalexin is only effective against some types of bacteria. So, it is only suitable for treating some types of infection.

Cefalexin can be used to treat:

- Acute throat and ear infections
- Chest infections such as acute bronchitis and some types of pneumonia
- Kidney and bladder infections
- Acute infection of the prostate gland
- Infections in the skin and layers just under the skin
- Infections of the bones and joints

2. Before you take Cefalexin

Do not take Cefalexin if:

- you are **allergic (hypersensitive)** to **cefalexin**, or to any of the other ingredients of this medicine (see Further Information in Section 6).
- you are allergic (hypersensitive) to any other cephalosporin type of antibiotic or to any sort of penicillin antibiotic.

Not all people who are allergic (hypersensitive) to penicillins are also allergic to cephalosporins. However, you should not take this medicine if you ever had a severe allergic reaction to any penicillin. This is because you might also be allergic to this medicine.

An allergic (hypersensitive) reaction may include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue.

Take special care with Cefalexin if you:

- ever have **had an allergic (hypersensitive) reaction to any antibiotic**. Tell your doctor or pharmacist before you take this medicine.
- have ever had inflammation of your bowel, called colitis or any other severe disease affecting your gut.
- have ever been told that your kidneys do not work very well. You may take Cefalexin but you may need a lower dose.

This medicine can alter the results of some blood tests (such as cross-matching blood and the Coombs' test). It is important to tell your doctor that you are taking this medicine if you have to have these tests.

This medicine can also alter the results of urine tests for sugar (such as Benedict's or Fehling's tests or with copper sulphate test tablets). If you have diabetes and routinely test your urine, tell your doctor. This is because other tests may have to be used to monitor your diabetes while you are having this medicine.

Cefalexin is not suitable for everyone. Before treatment with Cefalexin, talk to your doctor or pharmacist if any of the above applies to you.

If you have been on Cefalexin treatment for a prolonged period, it may result in the overgrowth of organisms on which Cefalexin does not act. This may need for you to be treated by other antimicrobial agents.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken other medicines, including medicines obtained without a prescription.
In particular, tell your doctor or pharmacist if you are taking the following medicines which are known to interact with Cefalexin:

- **probenecid** (a medicine used in the treatment of gout)
- **metformin** (a medicine used in the treatment of diabetes)

It may still be all right for you to be given Cefalexin and your doctor will be able to decide what is suitable for you.

Taking Cefalexin with food and drink
Cefalexin can be taken regardless of meals.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
Before starting treatment, you must tell your doctor if you are pregnant or if you intend to become pregnant. Cefalexin is not known to harm the unborn child, but has not been deemed as safe. It will only be given to a pregnant woman if it is absolutely necessary.

Mothers who wish to breast-feed should discuss with their doctor, as small amounts of Cefalexin enters the milk. Inform your doctor if your baby develops diarrhoea or if you notice anything unusual.

Driving and using machines
Cefalexin does not usually affect your ability to drive or use machines. However, if you feel light-headed or dizzy, do not drive or use machines and check with your doctor.

Important information about some of the ingredients of Cefalexin
Cefalexin contains colouring agents including **Brilliant Blue FCF** (E133) and **Sunset yellow FCF** (E110), which **may cause allergic (hypersensitive) reactions**.

3. How to take Cefalexin

Dosage
Always take Cefalexin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose is:
Adults and the elderly with normal kidney function
The **recommended adult dosage** range for Cefalexin is 1 g to 4 g per day, given daily in divided doses. In the majority of infections, Cefalexin is given in a dose of 500 mg every 8 hours (three times a day).

For treating infections in the skin and the layers just under the skin, streptococcal pharyngitis (sore throat), and mild, uncomplicated urinary tract infections, Cefalexin is given in a dosage of 250 mg every 6 hours (four times a day) or 500 mg every 12 hours (twice daily).

For more severe infections, larger doses may be needed.

Adults (including the elderly) with impaired kidney function
In patients with impaired kidney function, the dosage of Cefalexin is usually reduced.

Children
The dose for children is based on their weight. The usual dosage range for children is 25 mg to 50 mg per kg body weight daily, given in divided doses.

For infections in the skin and the layers just under the skin, streptococcal pharyngitis, and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours.

For most infections, the following schedule is suggested:

- Children under 5 years: 125 mg every 8 hours.
- Children 5 years and over: 250 mg every 8 hours.

In severe infections, the dose may be doubled. In the therapy of otitis media (middle ear infection), a daily dose of 75 to 100 mg per kg bodyweight in 4 doses is given

Method and/or route(s) of administration
Cefalexin comes as a capsule to be taken orally. The capsules should be swallowed whole and taken with a full glass of water.

Frequency of administration
Depending on various factors, you may be asked to take Cefalexin every 6 hours (four times a day) or every 8 hours (three times a day) or every 12 hours (twice a day).

Duration of treatment
Your doctor will advise you on how long your treatment should last. The duration of therapy depends on the type and course of the disease.

In the treatment of beta-haemolytic streptococcal (a type of bacteria) infections in adults and children, treatment with Cefalexin is usually given for at least 10 days.

If you take more Cefalexin than you should
If you or your child have taken more of this medicine than you should, talk to your doctor or contact your nearest hospital emergency department immediately.

Symptoms of overdose may include nausea (feeling sick), severe vomiting, pain in the upper abdomen, diarrhoea and passing blood in the urine. In addition to treatment of the symptoms of overdose, the doctors may also try to reduce the levels of Cefalexin in the blood by dialysis.

If you forget to take Cefalexin
If you miss a dose, take it as soon as possible. However if it is nearly time for your next dose, skip the missed dose and carry on as before. Do not take a double dose to make up for a forgotten dose.

If you stop taking Cefalexin
It is important that you take this medicine until you finish the prescribed course. You should not stop the medicine just because you feel better. If you stop too soon, the infection may start up again. If the person being treated still feels unwell at the end of the prescribed course of treatment, or feels worse during treatment, tell your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Cefalexin can cause side effects, although not everybody gets them.

The following side effects are important and will require immediate action if you experience them. You should stop taking Cefalexin and see your doctor immediately if the following symptoms occur:

Rare side effects affect fewer than 1 in 1,000 patients

- swelling of the face, tongue and windpipe which can cause great difficulty in breathing
- a sudden allergic reaction with shortness of breath, rash, wheezing and drop of blood pressure
- severe, extensive, blistering skin rash
- watery and severe diarrhoea that may also be bloody

The following side-effects have also been reported:

Common side effects (affect less than 1 in 10 people) include:

- Nausea
- diarrhoea

Uncommon side effects (affect less than 1 in 100 people) include:

- Skin rash, hives, itching
- changes in blood tests that check how your liver is working

Rare side effects (affect less than 1 in 1000 people) include:

- fall in the numbers of different cells in the blood (symptoms can include susceptibility to new infections, easy bruising or bleeding, pallid appearance or shortness of breath caused by anaemia)
- headaches, dizziness
- discharge and itch of the vagina and surrounding skin
- abdominal pain, vomiting, indigestion
- liver problems that may lead to jaundice (yellowing of the skin or whites of the eyes)
- kidney problems

Other side effects (affecting an unknown number of people) include:

- tiredness, hallucinations, restlessness, confusion
- painful joints
- vaginal thrush

If you are having a blood test or a urine test for any reason, tell the person who is doing the test that you are taking this medicine as it may affect your result.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Cefalexin

Keep out of the sight and reach of children.

This medicine does not require any special storage conditions. Keep container tightly closed.

Do not use Cefalexin after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicine no longer required. These measures will help to protect the environment.

6. Further information

What Cefalexin contain:
The active substance is Cefalexin. Each capsule contains, as the active ingredient, Cefalexin monohydrate equivalent to 500 mg of Cefalexin base.

The other ingredients are- capsule contents: Cellulose Microcrystalline, Croscarmellose Sodium, Magnesium Stearate; capsule shell: Sodium laurilsulfate, Brilliant Blue FCF (E 133) and Sunset yellow FCF (E110), Titanium dioxide, gelatin and black printing ink (containing shellac, propylene glycol, potassium hydroxide and iron oxide, black (E172)).

What Cefalexin looks like and contents of the pack
Cefalexin capsules are hard gelatin capsules with a green coloured opaque cap and an opaque light green coloured body, imprinted with black ,"CEF"on cap & "500" on body, filled with white to off white granular powder.

The products are filled into plastic bottles 20 or 100 capsules, or blister packs of 21 or 100 capsules.

Not all pack sizes may be marketed.

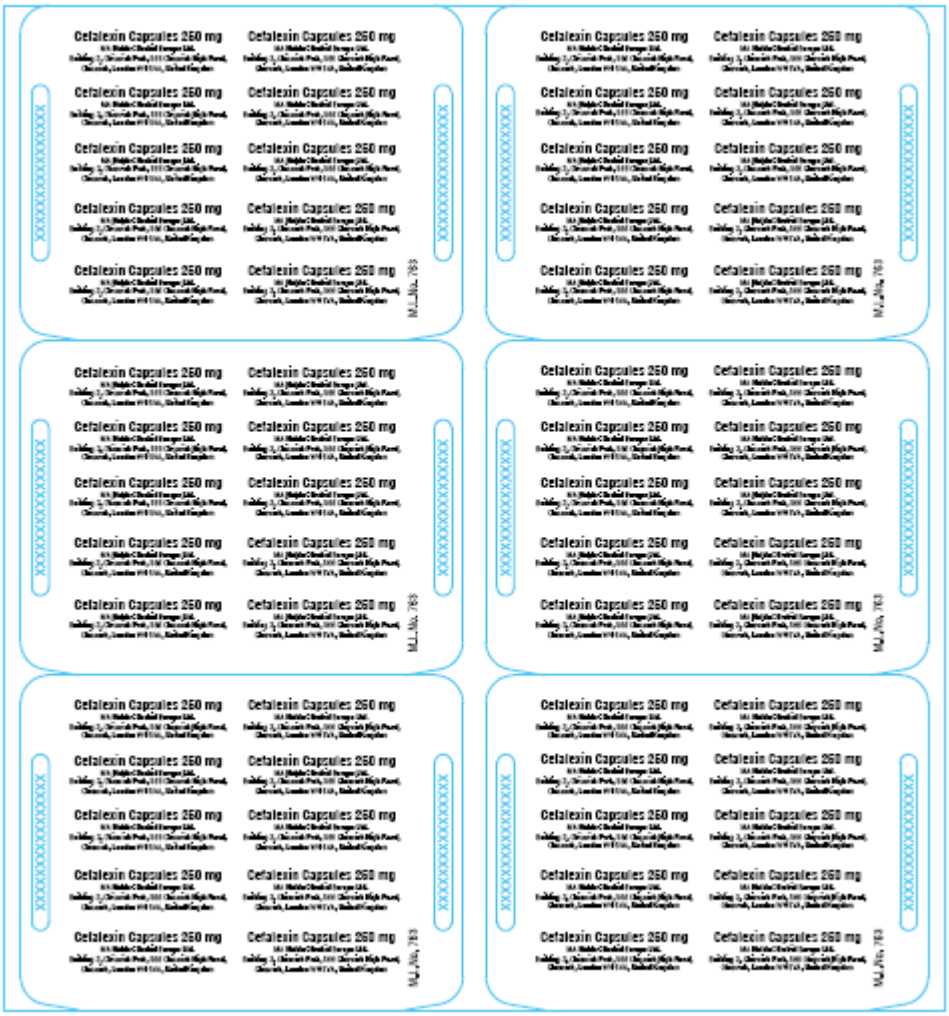
Marketing Authorisation Holder and Manufacturer

Orchid Europe Ltd.

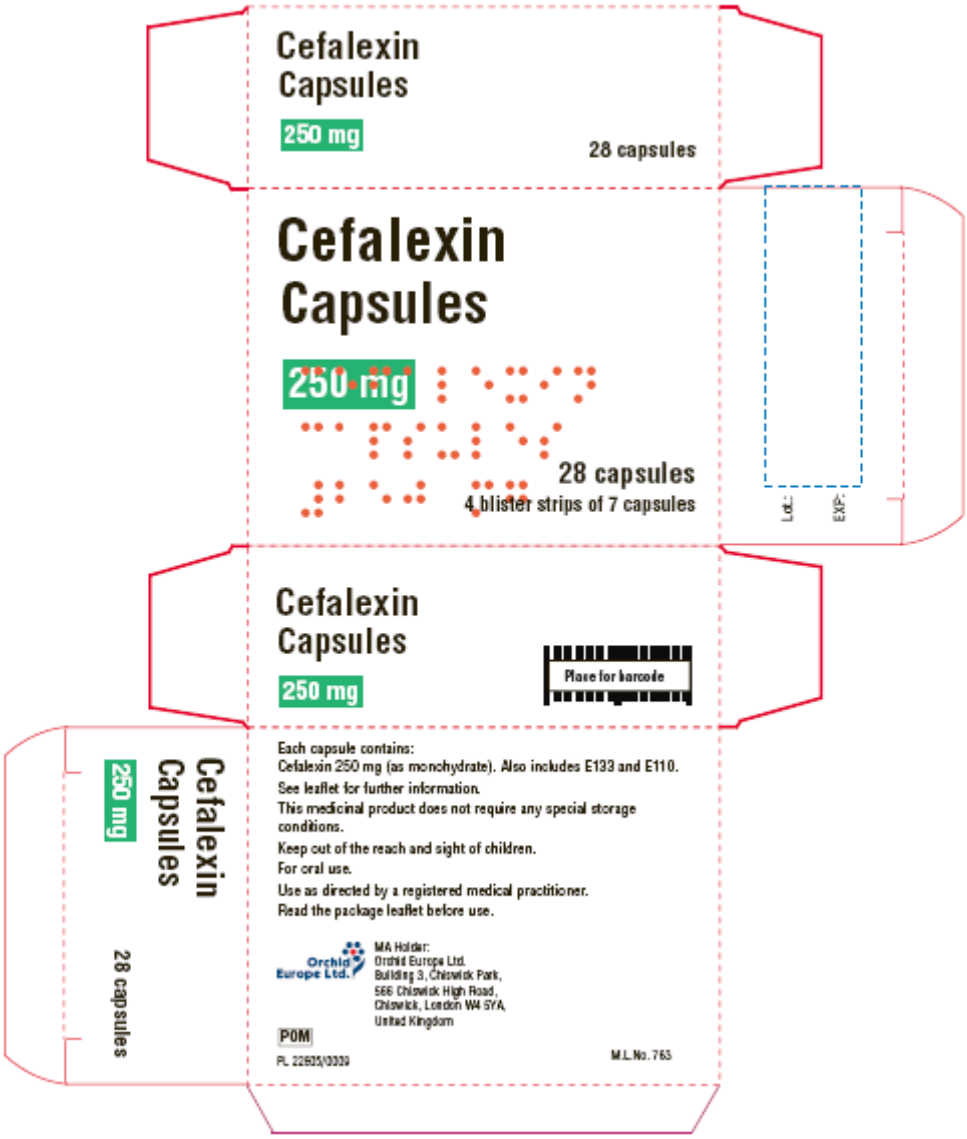
Orchid Europe Limited,
Building 3, Chiswick Park
566, Chiswick High Road, Chiswick,
London, W4 5YA, UK.

This leaflet was last revised in May 2009

Cefalexin Capsules 250 mg



Cefalexin Capsules 250 mg



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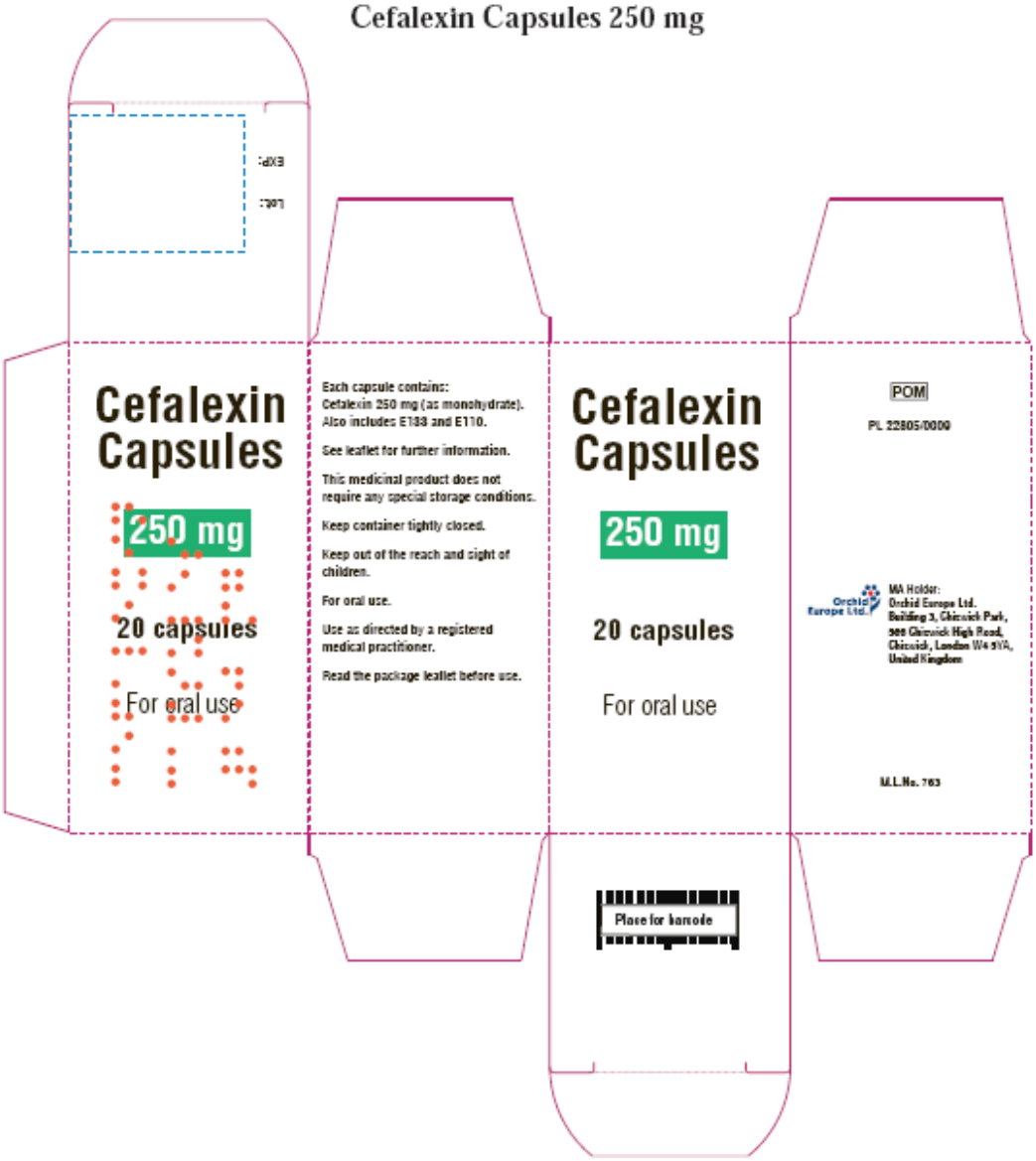
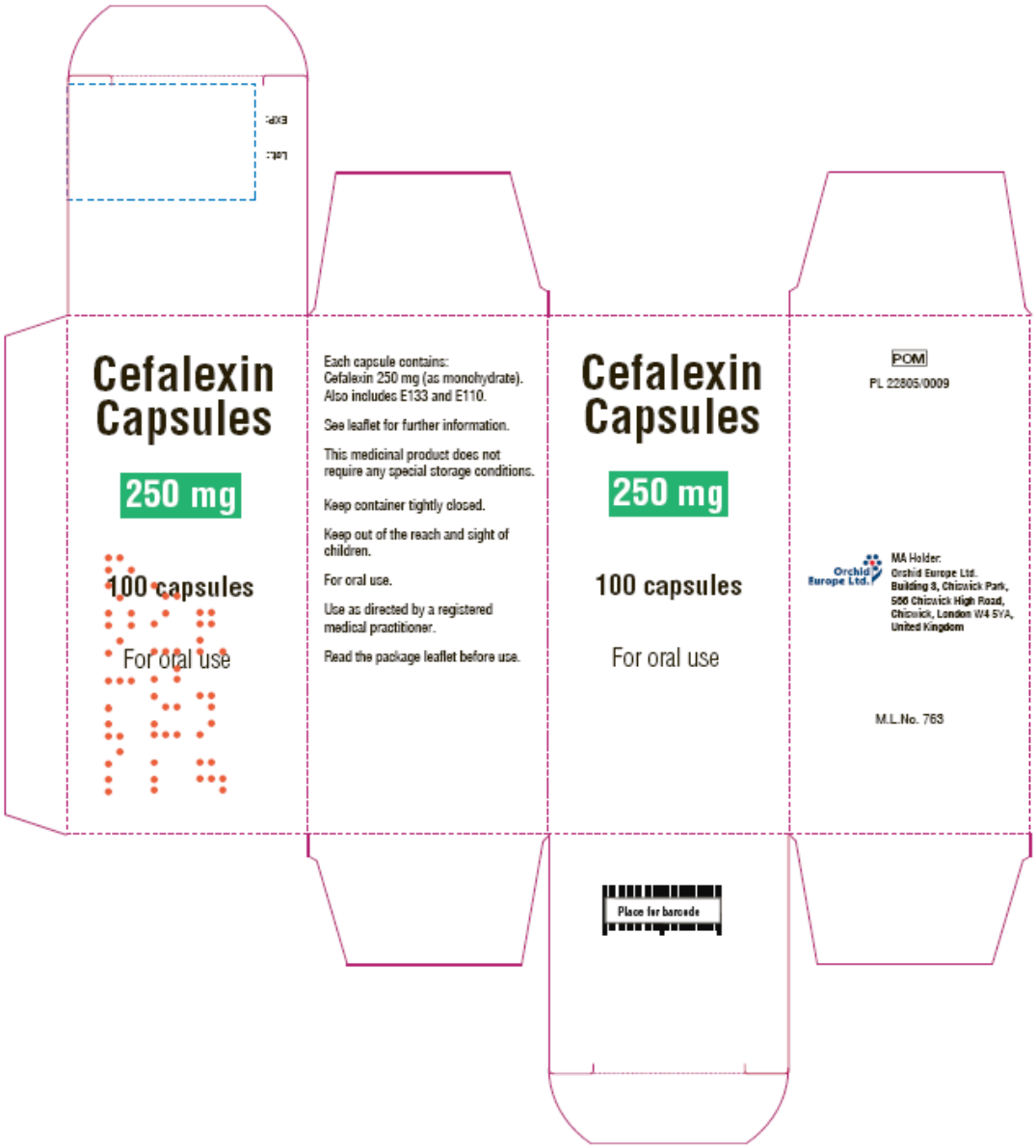
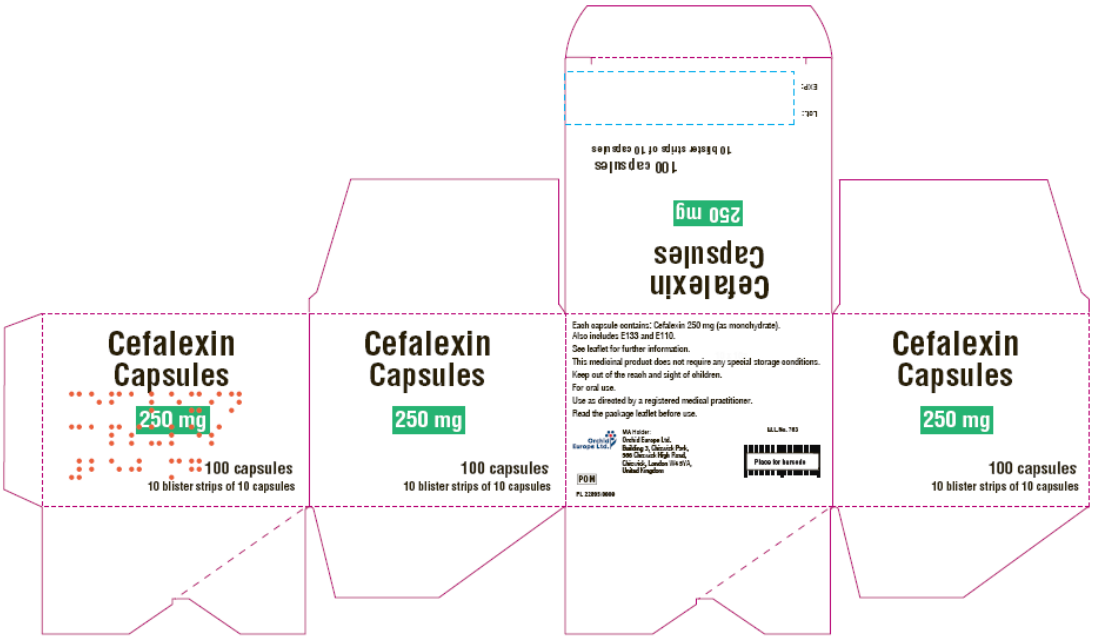
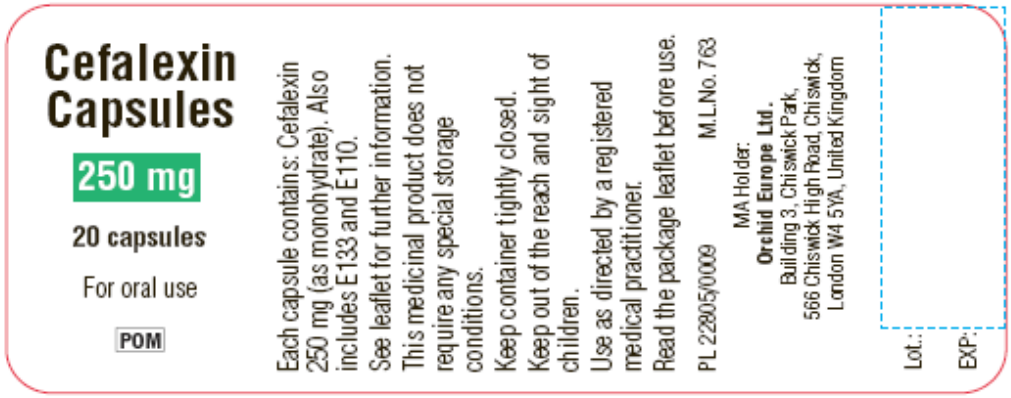


Cefalexin Capsules 250 mg




Cefalexin
Capsules
250 mg
100 capsules
10 blister strips of 10 capsules
Cefalexin
Capsules
250 mg
100 capsules
10 blister strips of 10 capsules
Each capsule contains: Cefalexin 250 mg (as monohydrate).
Also includes E133 and E110.
See leaflet for further information.
This medicinal product does not require any special storage conditions.
Keep out of the reach and sight of children.
For oral use.
Use as directed by a registered medical practitioner.
Read the package leaflet before use.
POM
Place for barcode
Cefalexin
Capsules
250 mg
100 capsules
10 blister strips of 10 capsules
Cefalexin
Capsules
250 mg
100 capsules
10 blister strips of 10 capsules


Cefalexin
Capsules
250 mg
20 capsules
For oral use
POM
Each capsule contains: Cefalexin 250 mg (as monohydrate). Also includes E133 and E110.
See leaflet for further information.
This medicinal product does not require any special storage conditions.
Keep container tightly closed.
Keep out of the reach and sight of children.
Use as directed by a registered medical practitioner.
Read the package leaflet before use.
PL 22805/0009
M.L.No. 763
MA Holder:
Orchid Europe Ltd.
Building 3, Chiswick Park,
566 Chiswick High Road, Chiswick,
London W4 5YA, United Kingdom
Lot.:
EXP:


Cefalexin
Capsules
250 mg
100 capsules
For oral use
POM
Each capsule contains: Cefalexin 250 mg (as monohydrate). Also includes E133 and E110.
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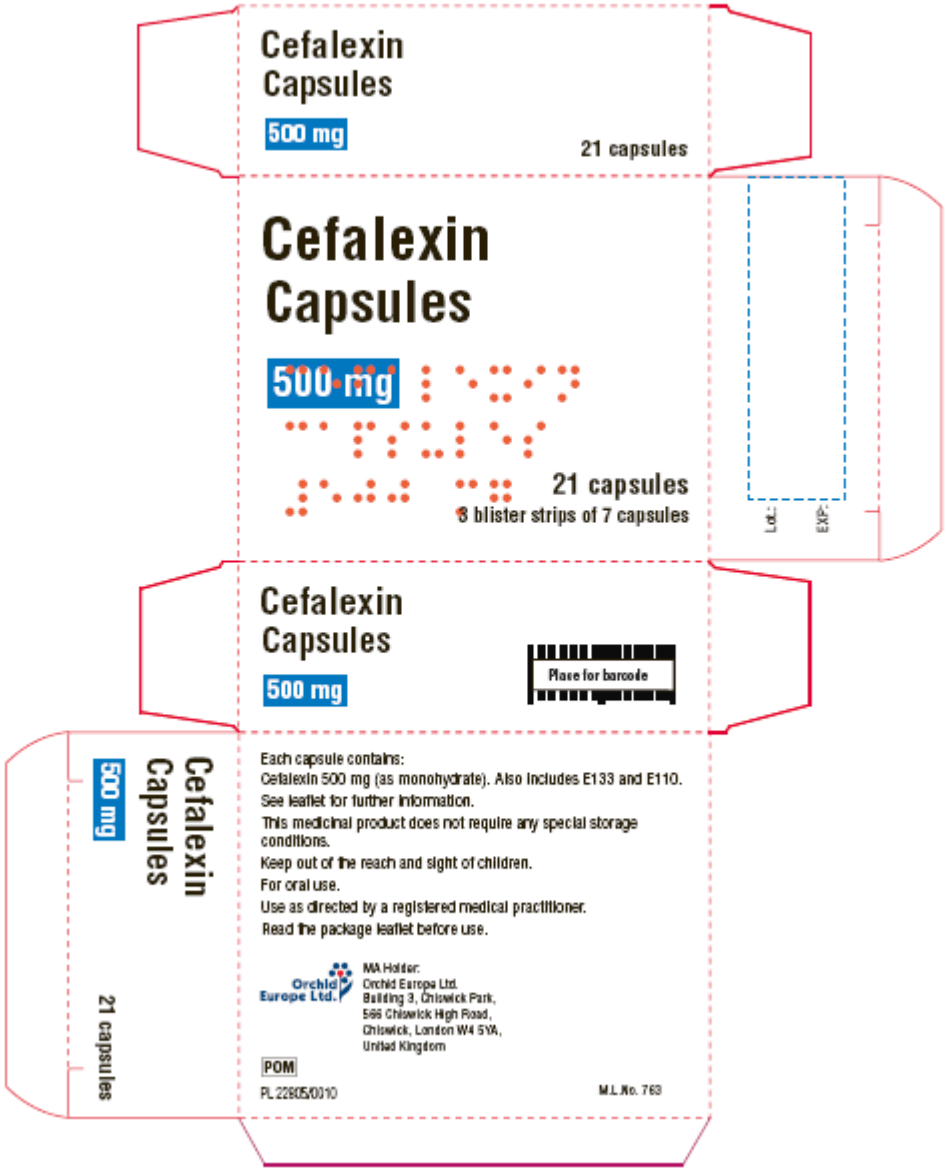
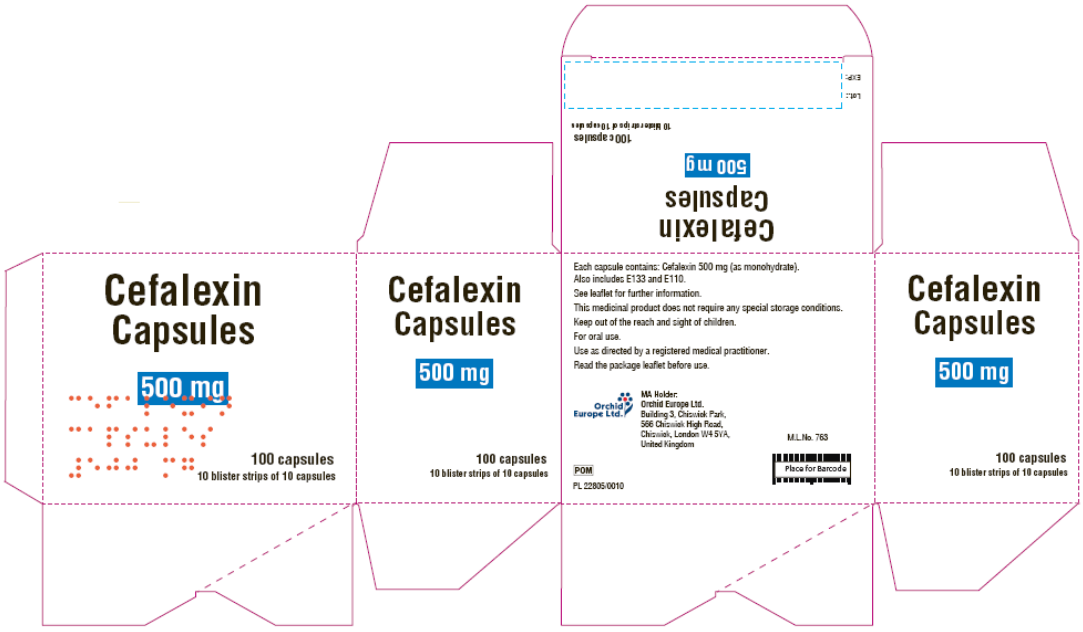
MA Holder:
Orchid Europe Ltd.
Building 3, Chiswick Park,
566 Chiswick High Road, Chiswick,
London W4 5YA, United Kingdom
Lot.:
EXP:

Cefalexin Capsules 500 mg

Cefalexin Capsules 500 mg



Cefalexin Capsules 500 mg



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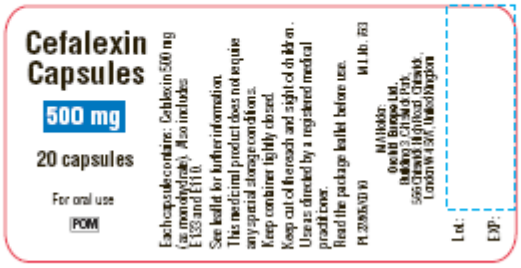
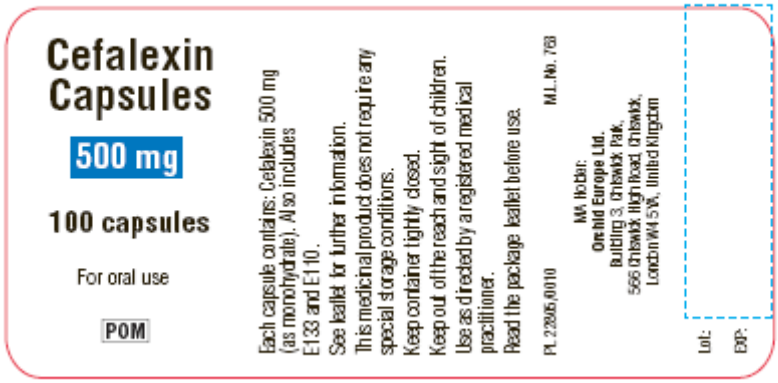
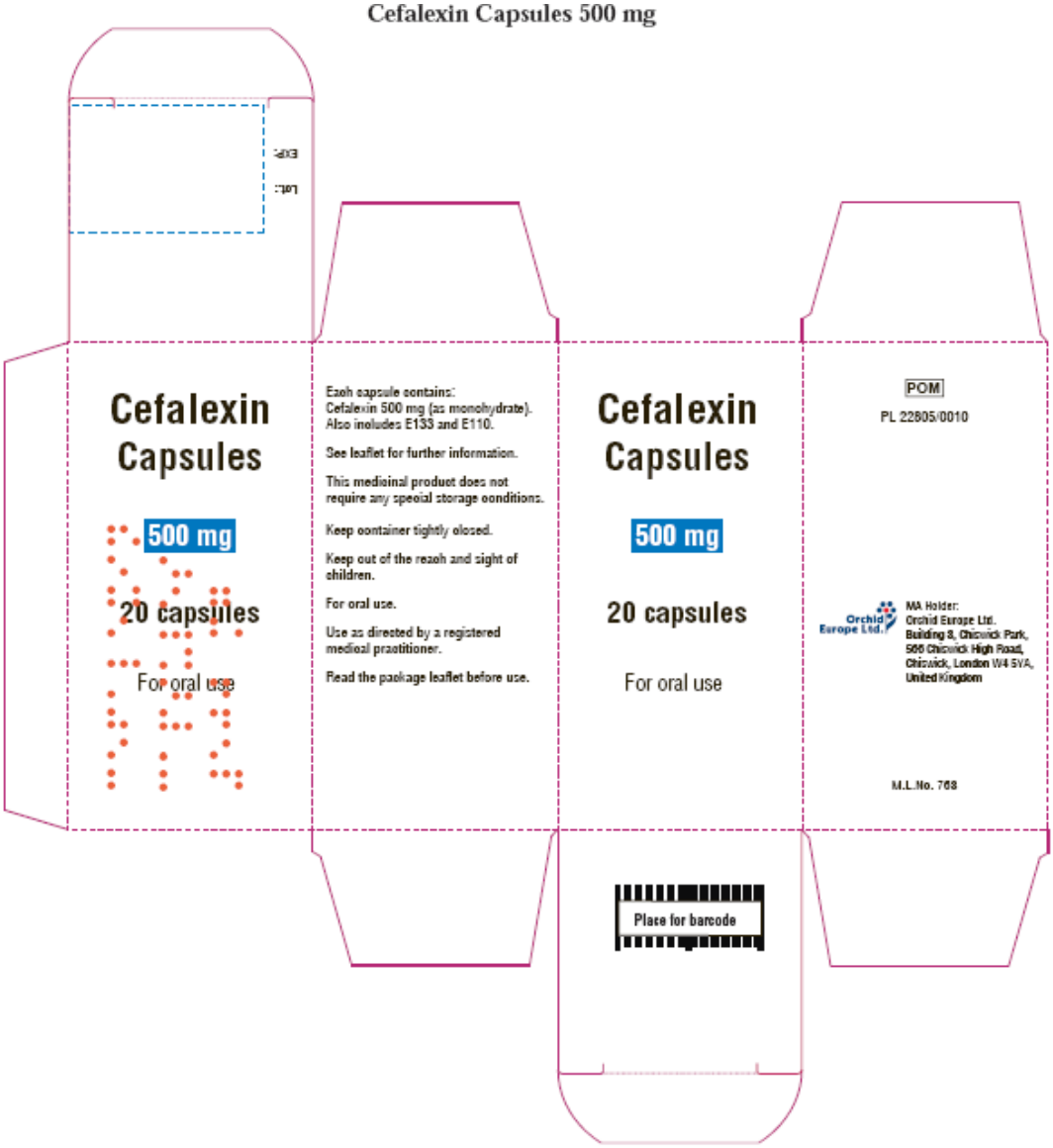
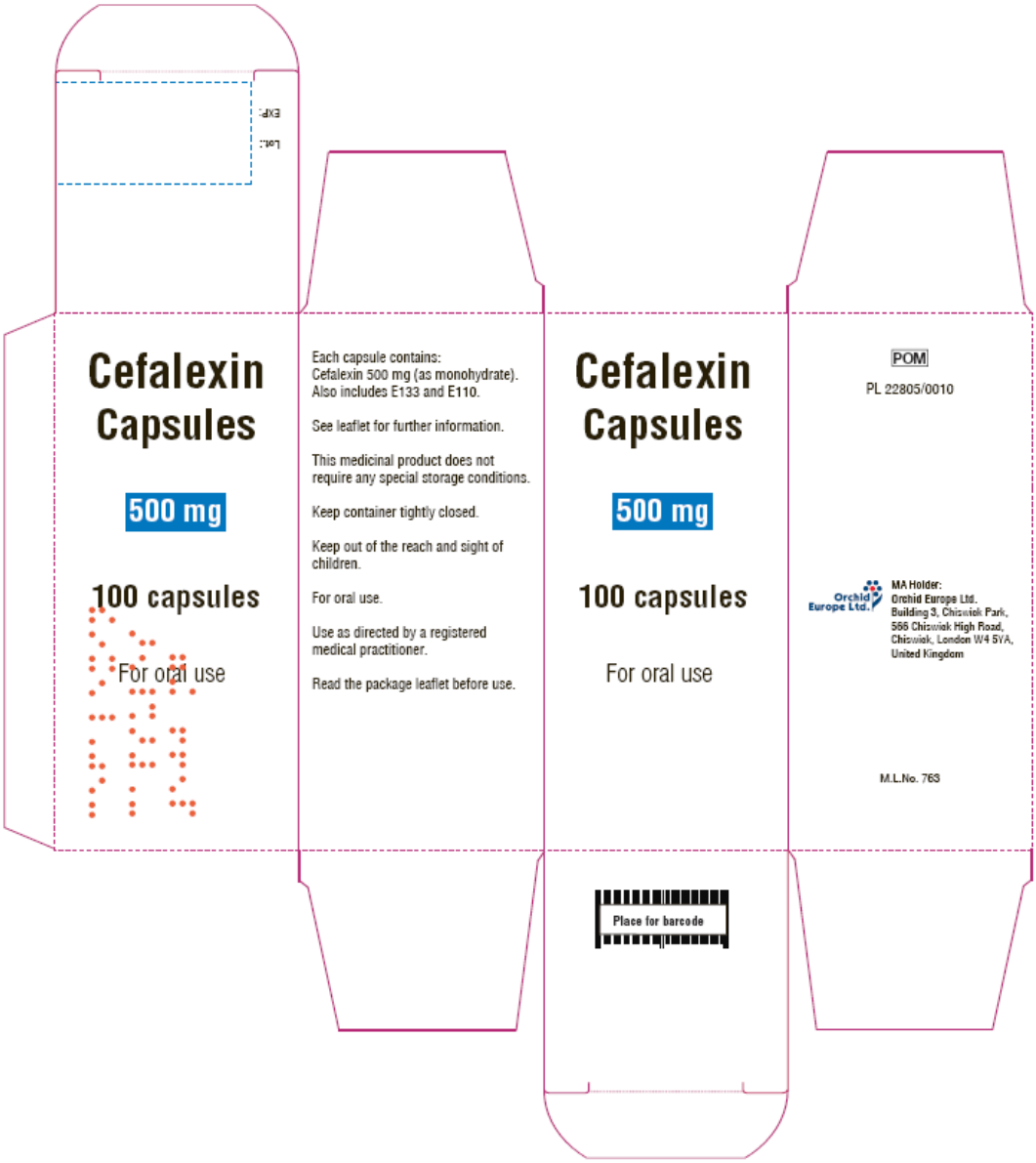




Cefalexin Capsules 500 mg




EXP:
Lot:
Cefalexin Capsules
500 mg
100 capsules
For oral use
Each capsule contains:
Cefalexin 500 mg (as monohydrate).
Also includes E133 and E110.
See leaflet for further information.
This medicinal product does not require any special storage conditions.
Keep container tightly closed.
Keep out of the reach and sight of children.
For oral use.
Use as directed by a registered medical practitioner.
Read the package leaflet before use.
Cefalexin Capsules
500 mg
100 capsules
For oral use
Place for barcode
POM
PL 22805/0010
Orchid Europe Ltd.
MA Holder:
Orchid Europe Ltd.
Building 3, Chiswick Park,
566 Chiswick High Road,
Chiswick, London W4 5YA,
United Kingdom
M.L.No. 763