CEFALEXIN 250 MG FILM-COATED TABLETS
CEFALEXIN 500 MG FILM-COATED TABLETS

(Cefalexin)

PL 21880/0080 & 0083

UK PAR

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CEFALEXIN 250 MG FILM-COATED TABLETS
CEFALEXIN 500 MG FILM-COATED TABLETS

PL 21880/0080 & 0083

LAY SUMMARY

The MHRA granted Medreich Plc, Marketing Authorisations (licences) for the medicinal products Cefalexin 250 mg and 500 mg Film-coated Tablets on 05 July 2012. These are prescription-only medicines (POM).

Cefalexin 250 mg and 500 mg Film-coated Tablets contain the active ingredient cefalexin which belongs to a class of antibiotics called 'cephalosporins'. This medicine is used to treat a variety of bacterial infections. These include infections of the airways from nose to lungs, ear, bones and joints, and urinary and reproductive systems, including inflammation of the prostate gland. It is also used to treat dental infections.

These applications are duplicates of previously granted applications for Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), which were granted to the Marketing Authorisation Holder Milpharm Limited on 19 November 2003.

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of taking Cefalexin 250 mg and 500 mg Film-coated Tablets outweigh the risks; hence Marketing Authorisations have been granted.

CEFALEXIN 250 MG FILM-COATED TABLETS
CEFALEXIN 500 MG FILM-COATED TABLETS

PL 21880/0080 & 0083

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Marketing Authorisations for the medicinal products Cefalexin 250 mg and 500 mg Film-coated Tablets (PL 21880/00080 & 0083) to Medreich Plc on 05 July 2012. These are prescription-only medicines (POM) indicated for the treatment of the following infections: respiratory tract infections; bone and joint infections; genito-urinary infections, including acute prostatitis, and dental infections.

Cefalexin 250 mg and 500 mg Film-coated Tablets contain cefalexin as the active ingredient which belongs to a class of antibiotics called first generation cephalosporins (ATC code J01DB01). Cefalexin is bactericidal and has antimicrobial activity similar to that of cephaloridine or cephalothin against both gram-positive and gram-negative organisms.

These applications were submitted as simple abridged applications according to Article 10(c) of Directive 2001/83/EC, cross-referring to Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), which were granted to the Marketing Authorisation Holder Milpharm Limited on 19 November 2003.

No new data were submitted nor were they necessary for these simple applications, as the data are identical to that of the previously granted cross-reference products.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	PL 21880/0080 PL 21880/0083
PROPRIETARY NAME:	Cefalexin 250 mg Film-coated Tablets Cefalexin 500 mg Film-coated Tablets
ACTIVE(S):	Cefalexin
COMPANY NAME:	Medreich Plc
E.C. ARTICLE:	Article 10(c) of Directive 2001/83/EC
LEGAL STATUS:	POM

1 INTRODUCTION

These are simple, informed consent applications for Cefalexin 250 mg and 500 mg Film-coated Tablets submitted under Article 10(c) of Directive 2001/83/EC. The applications cross-refer to Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), which were granted to the Marketing Authorisation Holder Milpharm Limited on 19 November 2003.

The current applications are considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)

2.1 Name(s)

The proposed names of the products are Cefalexin 250 mg and 500 mg Film-coated Tablets. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Each tablet contains cefalexin monohydrate equivalent to 250 mg or 500 mg cefalexin. The tablets are packaged in:

- a polypropylene tubular container, with a polyethylene closure and tamper evident tear strip in pack sizes of 7, 14, 20, 21, 28, 30, 50, 56, 60, 100, or 500 tablets.
- a polyvinylchloride/aluminium blister in pack sizes of 7, 14, 20, 21, 28, 30, 50, 56, 60, 100, or 500 tablets.
- a polyvinylidene chloride/polyvinylchloride/aluminium blister in pack sizes of 7, 14, 20, 21, 28, 30, 50, 56, 60, 100, or 500 tablets.

It has been stated that not all pack sizes may be marketed. However, the Marketing Authorisation Holder has committed to submitting the mock-ups for any pack size to the relevant regulatory authorities for approval before marketing.

The proposed shelf life (2 years) and storage conditions (Do not store above 25°C. Keep the container tightly closed [for bottles]. Store in the original package [for blisters]) are consistent with the details registered for the cross-referenced products.

2.3 Legal status

On approval, the products will be available by supply through pharmacies, subject to a medical prescription (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company

The proposed Marketing Authorisation Holder is Medreich Plc, 9 Royal Parade, Kew Gardens, Surrey, TW9 3QD, UK.

The Qualified Person (QP) responsible for pharmacovigilance is stated and their CV is included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the reference products and evidence of compliance with current Good Manufacturing Practice has been provided.

2.6 Qualitative and quantitative composition
The compositions are consistent with the details registered for the reference products.

2.7 Manufacturing process
The manufacturing process is consistent with the details registered for the reference products and the maximum batch sizes are stated.

2.8 Finished product/shelf-life specification
The finished product specifications are in line with the details registered for the reference products.

2.9 Drug substance specification
The drug substance specifications are consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin.

None of the excipients are sourced from genetically modified organisms.

2.11 Bioequivalence
No bioequivalence data are required to support these informed consent applications, as the proposed products are manufactured to the same formula utilising the same process as the reference products Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1).

3 EXPERT REPORT
A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert is included

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The appearance of the products is identical to that of the reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPCs are consistent with the details registered for the reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING
PILs
The patient information leaflet has been prepared in line with the details registered for the reference products.

A package leaflet has been submitted to the MHRA together with results of consultations with target patient groups ('user testing'), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

Carton and blister

The proposed artwork complies with the relevant statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with these applications is acceptable. The grant of Marketing Authorisations is recommended.

NON-CLINICAL ASSESSMENT

As these applications are identical to the reference products Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), no new non-clinical data have been supplied with these applications and none are required. A non-clinical expert report has been written by a suitably qualified person and is satisfactory.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As these applications are for identical versions of already authorised reference products, it is not expected that the environmental exposure to cefalexin will increase following the marketing approval of the proposed products.

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CLINICAL ASSESSMENT

As these applications are identical to the reference products Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), no new clinical data have been supplied with these applications and none are required. A clinical expert report has been written by a suitably qualified person and is satisfactory.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for these products.

OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with that previously assessed for the reference products and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
These applications are identical to the previously granted applications for Cefalexin 250mg and 500mg Film-coated Tablets BP (PL 16363/0120-1), granted to Milpharm Limited on 19 November 2003.

SAFETY
No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with that for the reference products.

Colour mock-ups of the labelling have been provided and are satisfactory. The approved labelling artwork complies with statutory requirements. The name of the product in Braille appears on the outer packaging.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the reference products. Extensive clinical experience with cefalexin is considered to have demonstrated the therapeutic values of the compound. The benefit/risk is therefore considered to be positive.

CEFALEXIN 250 MG FILM-COATED TABLETS
CEFALEXIN 500 MG FILM-COATED TABLETS

PL 21880/0080 & 0083

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the Marketing Authorisation Applications on 24 June 2010.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 13 July 2010.
3	Following assessment of the applications the MHRA requested further information on 08 November 2010 and 05 July 2011.
4	The applicant responded to the MHRA's request, providing further information on 22 February 2011 and 06 September 2011.
5	The applications were determined on 05 July 2012.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefalexin 250 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Cefalexin monohydrate equivalent to 250mg Cefalexin.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets
Round, pink film-coated tablets embossed 'CHX 250' on one side

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is indicated in the treatment of the following infections: Respiratory tract infections; bone and joint infections; genito urinary infections, including acute prostatitis and dental infections.
Cefalexin is active against the following organisms: Beta-haemolytic streptococci; staphylococci, including coagulasepositive, coagulase-negative and penicillinase-producing strains; streptococcus pneumoniae; escherichia coli; proteus mirabilis; klebsiella species, haemophilus influenzae; branhamella catarrhalis.

Most strains of enterococci (streptococcus faecalis) and a few strains of staphylococci are resistant to cefalexin. Cefalexin is not active against most strains of enterobacter species, morganella morganii, pseudomonas or herellea species.

4.2 Posology and method of administration

Adults
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.

More severe infections, or those caused by less susceptible organisms may need larger doses. If daily doses greater than 4g are required other parenteral cephalosporins, in appropriate doses, should be considered.

Elderly
As for adults although dosage should be reduced to a daily maximum of 500mg if renal function is severely impaired (glomerular filtration rate < 10ml/min).

Children
The recommended daily dosage for children is 25-50 mg/kg in divided doses.
In the case of skin, 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: Not recommended
Children 5 years and over: 250 mg every 8 hours.
In severe infections, the dosage may be doubled.

Clinical studies have shown that for otitis media a dosage of 75-100 mg/kg/day is required, in divided doses. In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Route of administration
Oral

4.3 Contraindications

Cefalexin is contraindicated in patients with known allergy to the cephalosporins group of antibiotics.
Cefalexin is contra-indicated in patients with porphyria.

4.4 Special warnings and precautions for use

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 during therapy is essential and appropriate action should be taken should superinfection occur.

Pseudomembranous colitis (ranging in severity from mild to life-threatening) has been reported in association with use of virtually all broad -spectrum antibiotics, including macrolides, semi-synthetic penicillins and cephalosporins. Therefore, it is essential to take this into account during diagnosis of patients who develop diarrhoea during antibiotic therapy. Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone whilst in more severe cases, 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.

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets. Positive direct Coombs' tests have been reported during treatment with cephalosporin antibiotics. In haematological studies, or in transfusion cross-matching procedures when anti globulin tests are performed on the minor side, or in Coombs' testing of newborn babies whose mothers have received cephalosporin antibiotics before parturition, it should be noted that a positive Coombs' test may be due to the drug.

4.5 Interaction with other medicinal products and other forms of interaction

Cefalexin should be given cautiously to patients who have shown hypersensitivity to other drugs.

Cephalosporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

Probenecid causes reduced excretion of cefalexin leading to increased plasma concentrations. Cephalosporins may have an increased risk of nephrotoxicity in the presence of amphotericin, loop diuretics, aminoglycosides, capreomycin or vancomycin.

4.6 Fertility, pregnancy and lactation

Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient. Caution should be exercised in administration to a nursing mother. Following a 500mg dose, levels of 4 micrograms/ml have been detected in breast milk.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Gastro-intestinal - nausea, vomiting, dyspepsia, and abdominal pain have occurred. Diarrhoea has been reported most frequently. It is rarely severe enough to warrant cessation of therapy. Colitis, including rare symptoms of pseudomembranous colitis, may occur during or after treatment.

Hypersensitivity - allergies (in the form of rash, urticaria and angio-oedema) have been observed. Also erythema multiforme, Stevens-Johnson syndrome usually subside upon discontinuation of the drug, although supportive therapy may be needed in some cases. Serum sickness-like reactions with rashes and fever have been reported.

Anaphylaxis has also been reported.

Haematological - eosinophilia, neutropenia, thrombocytopenia leucopenia, agranulocytosis, aplastic anaemia and haemolytic anaemia have been reported. Slight elevations of AST and ALT have been observed.

Hepatic - transient hepatitis and cholestatic jaundice have been reported rarely.

Miscellaneous - other reactions have included genital and anal pruritus, genital candidiasis, vaginitis and vaginal discharge, dizziness, fatigue and headache. Agitation, confusion, hallucinations, arthralgia, arthritis and joint disorder. Hyperactivity, nervousness, sleep disturbances and hypertonia have also been reported.

Reversible interstitial nephritis has been reported rarely and toxic epidermal necrolysis have been observed rarely.

4.9 Overdose

Symptoms reported include nausea, vomiting, diarrhoea, epigastric distress and haematuria. In instances where children have accidentally ingested more than 3.5g cefalexin in a day, there have been associated reports of haematuria, without impairment of renal function. Treatment has been supportive (fluids) and no sequelae have been reported.

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.

The following clinical measures are extremely unlikely to be indicated in the event of cefalexin overdose and have not been established as beneficial in this situation: forced diuresis, peritoneal dialysis, haemodialysis or charcoal haemoperfusion.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cefalexin is bactericidal and has antimicrobial activity similar to that of cephaloridine or cephalothin against both grampositive and gram-negative organisms.

5.2 Pharmacokinetic properties

Cefalexin is almost completely absorbed from the gastro-intestinal tract and produces peak plasma concentrations about 1 hour after administration. A dose of 500 mg produces a mean peak plasma concentration of about 18 micrograms per ml, about the same as the concentration produced by an equal dose of cephaloridine given intramuscularly and greater than that produced by cephalothin. If cefalexin is taken with food there is delayed and slightly reduced absorption and there may be delayed elimination from the plasma. About 10 to 15% of a dose is bound to plasma proteins.

The biological half-life has been reported to range from 0.6 to at least 1.2 hours and this increases with reduced renal function. 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 per ml have been achieved after a dose of 500 mg. Probenecid delays urinary excretion and has been reported to increase biliary excretion.

Cefalexin is widely distributed in the body but does not enter the cerebrospinal fluid in significant quantities unless the meninges are inflamed. It diffuses across the placenta and small quantities are found in the milk of nursing mothers. Therapeutically effective concentrations may be found in the bile.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised Starch
Colloidal Anhydrous Silica
Magnesium Stearate E 572

Microcrystalline Cellulose E460

Coating
Hydroxypropyl Methylcellulose E 469
Polyethylene Glycol E 1521
Titanium Dioxide (E171)
Erythrosine Lake (E127)
Purified Water

6.2 Incompatibilities
None known

6.3 Shelf life
2 years

6.4 Special precautions for storage
Do not store above 25°C.
Keep the container tightly closed.
Store in the original package (for blisters).

6.5 Nature and contents of container
Polypropylene tubular container with an open end equipped to accept a polyethylene closure, with a tamper evident tear strip containing 7, 14, 20, 21, 28, 30, 50, 56, 60,100 or 500 tablets.
Or

PVC/Aluminium blisters or PVdC coated PVC/Aluminium blisters (60g/m2PVdC on 250µm PVC/20µm Al) containing 7, 14, 20, 21, 28, 30, 50, 56, 60,100 or 500 tablets.

They come in bulk packs of 30, 50, 100 and 500 as well as blisters of 21 and 28 tablets. Not all pack sizes are marketed.

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
Medreich Plc,
9 Royal Parade,
Kew Gardens,
Surrey,
TW9 3QD
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 21880/0080

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
05/07/2012

10 DATE OF REVISION OF THE TEXT
05/07/2012

1 NAME OF THE MEDICINAL PRODUCT

Cefalexin 500 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Cefalexin monohydrate equivalent to 500mg Cefalexin.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets
Round pink film coated tablets embossed 'CHX 500' on one side

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is indicated in the treatment of the following infections: Respiratory tract infections; bone and joint infections; genito-urinary infections, including acute prostatitis and dental infections.
Cefalexin is active against the following organisms: Beta-haemolytic streptococci; staphylococci, including coagulasepositive, coagulase-negative and penicillinase-producing strains; streptococcus pneumoniae; Escherichia coli; Proteus mirabilis; Klebsiella species, Haemophilus influenzae; Branhamella catarrhalis.

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Adults
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More severe infections, or those caused by less susceptible organisms may need larger doses. If daily doses greater than 4g are required other parenteral cephalosporins, in appropriate doses, should be considered.

Elderly
As for adults although dosage should be reduced to a daily maximum of 500mg if renal function is severely impaired (glomerular filtration rate < 10ml/min).

Children
The recommended daily dosage for children is 25-50 mg/kg in divided doses.
In the case of skin, soft tissue infections, streptococcal pharyngitis and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours.
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Route of administration
Oral

4.3 Contraindications

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Probenecid causes reduced excretion of cefalexin leading to increased plasma concentrations. Cephalosporins may have an increased risk of nephrotoxicity in the presence of amphotericin, loop diuretics, aminoglycosides, capreomycin or vancomycin.

4.6 Fertility, pregnancy and lactation

Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient. Caution should be exercised in administration to a nursing mother.

Following a 500mg dose, levels of 4 micrograms/ml have been detected in breast milk.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Gastro-intestinal - nausea, vomiting, dyspepsia, and abdominal pain have occurred. Diarrhoea has been reported most frequently. It is rarely severe enough to warrant cessation of therapy. Colitis, including are symptoms of pseudomembranous colitis, may occur during or after treatment.
Hypersensitivity - allergies (in the form of rash, urticaria and angio-oedema) have been observed. Also erythema multiforme, Stevens-Johnson syndrome usually subside upon discontinuation of the drug, although supportive therapy may be needed in some cases. Serum sickness-like reactions with rashes and fever have been reported.

Anaphylaxis has also been reported.

Haematological - eosinophilia, neutropenia, thrombocytopenia leucopenia, agranulocytosis, aplastic anaemia and haemolytic anaemia have been reported. Slight elevations of AST and ALT have been observed.

Hepatic - transient hepatitis and cholestatic jaundice have been reported rarely.

Miscellaneous - other reactions have included genital and anal pruritus, genital candidiasis, vaginitis and vaginal discharge, dizziness, fatigue and headache. Agitation, confusion, hallucinations, arthralgia, arthritis and joint disorder. Hyperactivity, nervousness, sleep disturbances and hypertonia have also been reported.

Reversible interstitial nephritis has been reported rarely and toxic epidermal necrolysis have been observed rarely.

4.9 Overdose

Symptoms reported include nausea, vomiting, diarrhoea, epigastric distress and haematuria. In instances where children have accidentally ingested more than 3.5g cefalexin in a day, there have been associated reports of haematuria, without impairment of renal function. Treatment has been supportive (fluids) and no sequelae have been reported.

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.

The following clinical measures are extremely unlikely to be indicated in the event of cefalexin overdose and have not been established as beneficial in this situation: forced diuresis, peritoneal dialysis, haemodialysis or charcoal haemoperfusion.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cefalexin is bactericidal and has antimicrobial activity similar to that of cephaloridine or cephalothin against both grampositive and gram-negative organisms.

5.2 Pharmacokinetic properties

Cefalexin is almost completely absorbed from the gastro-intestinal tract and produces peak plasma concentrations about 1 hour after administration. A dose of 500 mg produces a mean peak plasma concentration of about 18 micrograms per ml, about the same as the concentration produced by an equal dose of cephaloridine given intramuscularly and greater than that produced by cephalothin. If cefalexin is taken with food there is delayed and slightly reduced absorption and there may be delayed elimination from the plasma. About 10 to 15% of a dose is bound to plasma proteins.

The biological half-life has been reported to range from 0.6 to at least 1.2 hours and this increases with reduced renal function. 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 per ml have been achieved after a dose of 500 mg. Probenecid delays urinary excretion and has been reported to increase biliary excretion. Cefalexin is widely distributed in the body but does not enter the cerebrospinal fluid in significant quantities unless the meninges are inflamed. It diffuses across the placenta and small quantities are found in the milk of nursing mothers. Therapeutically effective concentrations may be found in the bile.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised Starch
Colloidal Anhydrous Silica
Magnesium Stearate E 572
Microcrystalline Cellulose E460

Coating
Hydroxypropyl Methylcellulose E 469
Polyethylene Glycol E1521
Titanium Dioxide (E171)

Erythrosine Lake (E127)
Purified Water

6.2 Incompatibilities
None known

6.3 SHELF LIFE
2 years

6.4 Special precautions for storage
Do not store above 25°C.
Keep the container tightly closed (for bottles).
Store in the original package (for blisters).

6.5 Nature and contents of container
Polypropylene tubular container with an open end equipped to accept a polyethylene closure, with tamper evident strip containing 7, 14, 20, 21, 28, 30, 50,56, 60, 100 or 500 tablets or PVC/Aluminium blisters or

PVdC coated PVC/Aluminium blisters (60g/m²PVdC on 250µm PVC/20µm Al) containing 7, 14, 20, 21, 28, 30, 50, 56, 60, 100 or 500 tablets. They come in bulk packs of 30, 50, 100 and 500 as well as blisters of 21 and 28 tablets. Not all packs are marketed.

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
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9 Royal Parade,
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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
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10 DATE OF REVISION OF THE TEXT
05/07/2012

PATIENT INFORMATION LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cefalexin Tablets 250 mg
Cefalexin Tablets 500 mg
(cefalexin)

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.

In this leaflet:

1. WHAT CEFALEXIN TABLETS ARE AND WHAT THEY ARE USED FOR

Cefalexin Tablets contain cefalexin as the active ingredient, which belongs to a class of antibiotics called 'cephalosporins'. The tablets are used to treat a variety of bacterial infections. These include infections of the airways from nose to lungs ear, bones and joints, and urine or reproduction systems, incuding inflammation of the prostate gland. They are also used to treat dental infections.

2. BEFORE YOU TAKE CEFALEXIN TABLETS

Do not take Cefalexin Tablets if you have:
- an allergy (hypersensitivity) to the cephalosporin or penicillin group of antibiotics, or to any of the ingredients in the product *(see Section 6).*
- porphyria, a hereditary metabolic disorder.

Take special care with Cefalexin Tablets if you have:
- kidney problems.
- inflammation of the large intestine, symptoms include: diarrhoea, pain and fever.

You should be aware that Cefalexin Tablets may give a false result for:
- certain blood tests
- tests for glucose in the urine.

Taking other medicines

Please inform your doctor if you are taking or have recently taken any other medicines, including those obtained without a prescription.

In particular, tell your doctor if you are taking any of the following:
- other antibiotics, especially amphotericin, capreomycin, vancomycin, or an aminoglycoside -a broad spectrum antibiotic (for example, gentamicin or neomycin)
- diuretics (water tablets) such as furosemide, bumetanide or probenecid for gout.

Taking Cefalexin Tablets with food and drink

These tablets may be taken before, during or after your meals.

Pregnancy and breast-feeding

Ask your doctor for advice before taking any medicine if you are pregnant or planning to become pregnant.

Cefalexin passes into breast milk, so tell your doctor if you are breast-feeding.

Driving and using machines

Cefalexin Tablets are not expected to affect your ability to drive or operate machinery.

3. HOW TO TAKE CEFALEXIN TABLETS

The doctor will decide on the most appropriate dose for you, based on the nature and severity of your infection. The label will tell you how many tablets you need to take as well as how often to take them.

Swallow the tablets whole with water.

Adults: The usual dose is 500 mg every 8 hours, although your doctor may tell you to take 1g to 4g a day, split up into smaller doses.

Elderly: You should take the normal adult dose, unless you have severe kidney problems, when the maximum daily dose will be 500 mg.

Children over 5 years: Your doctor will calculate the correct dose, depending on the child's weight. The usual daily dose is 250 mg to 500 mg for each kilogram of their weight, and is usually split up into smaller amounts taken every 8 or 12 hours. If your child is taking Cefalexin Tablets for ear infections, he or she may have to take 75 mg to 100 mg for each kilogram of their weight, split up into smaller doses throughout the day.

This medicine is not recommended for use in children under 5 years of age.

Use all the tablets your doctor has given you. **Do not stop taking** them, even if you feel better

If you take more Cefalexin Tablets than you should
Contact your doctor or nearest hospital casualty department immediately for advice if you or a child have swallowed too many tablets. Take this leaflet, the pack or any tablets with you, if you can.

If you forget to take Cefalexin Tablets
If you miss a dose, take it as soon as you remember. If it is almost time to take the 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 have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cefalexin Tablets can cause side effects, although not everyone gets them.
Tell your doctor at once if you notice any of these rare side effects:

- rash, fever, itchy skin, swelling of the lips, eyes, tongue, or difficulty in breathing normally are signs of an **allergic reaction. Stop taking the tablets immediately.**
- flaky skin, red or purple inflamed skin patches; pus in your eyes; blisters in your nose or mouth.
- blood disorders (if you bruise more easily, have a sore throat, fever or a chill).
- lower gut pain, nausea, vomiting, severe diarrhoea containing blood or mucus. Colitis (inflammation of the colon) can also occur during or after treatment.
- liver damage, for example jaundice (yellowing of the skin and whites of eyes).
- nephritis (inflamed kidneys).

Tell your doctor if you suffer from any of the following for more than a few days:

- feeling or being sick, heartburn, stomach pain, diarrhoea
- skin rashes
- dizziness, tiredness, headache, sleep disorders, nervousness
- feeling confused or agitated, hallucinations, extreme restlessness
- painful or swollen joints, extreme muscle tension
- itching around the anus or genitals, inflamed vagina, discharge from the vagina.

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

5. HOW TO STORE CEFALEXIN TABLETS

Keep out of the reach and sight of children.

Do not store above 25 °C.

Store Cefalexin Tablets in their original package and keep containers tightly closed.

Do not use the tablets after the expiry 'EXP' date which is printed on the carton (the expiry date refers to the last day of the month stated).

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

6. FURTHER INFORMATION

What Cefalexin Tablets contain
The **active** ingredient is cefalexin, 250 mg or 500 mg.

The **other** ingredients are pregelatinised starch, colloidal anhydrous silica, magnesium stearate (E572) and microcrystalline cellulose (E460). The coating contains hydroxypropyl methylcellulose (E464), polyethylene glycol (E1521), titanium dioxide (E171) and erythrosine lake (E127).

What Cefalexin Tablets look like and contents of the pack
Cefalexin Tablets are round, pink and film-coated, embossed with 'CHX 250' (250mg) or 'CHX 500' (500mg) on one face.
They are available in tubular container with a temper evident tear strip or in blisters containing 7, 14, 20, 21, 28, 30, 50, 56, 60, 100 or 500 tablets. They are available in bulk packs of 30, 50, 100 and 500 tablets (Not all pack sizes may be marketed).

Cefalexin 250mg Tablets : PL 21880/0080
Cefalexin 500mg Tablets : PL 21880/0083

This leaflet was last revised in 26/09/2011

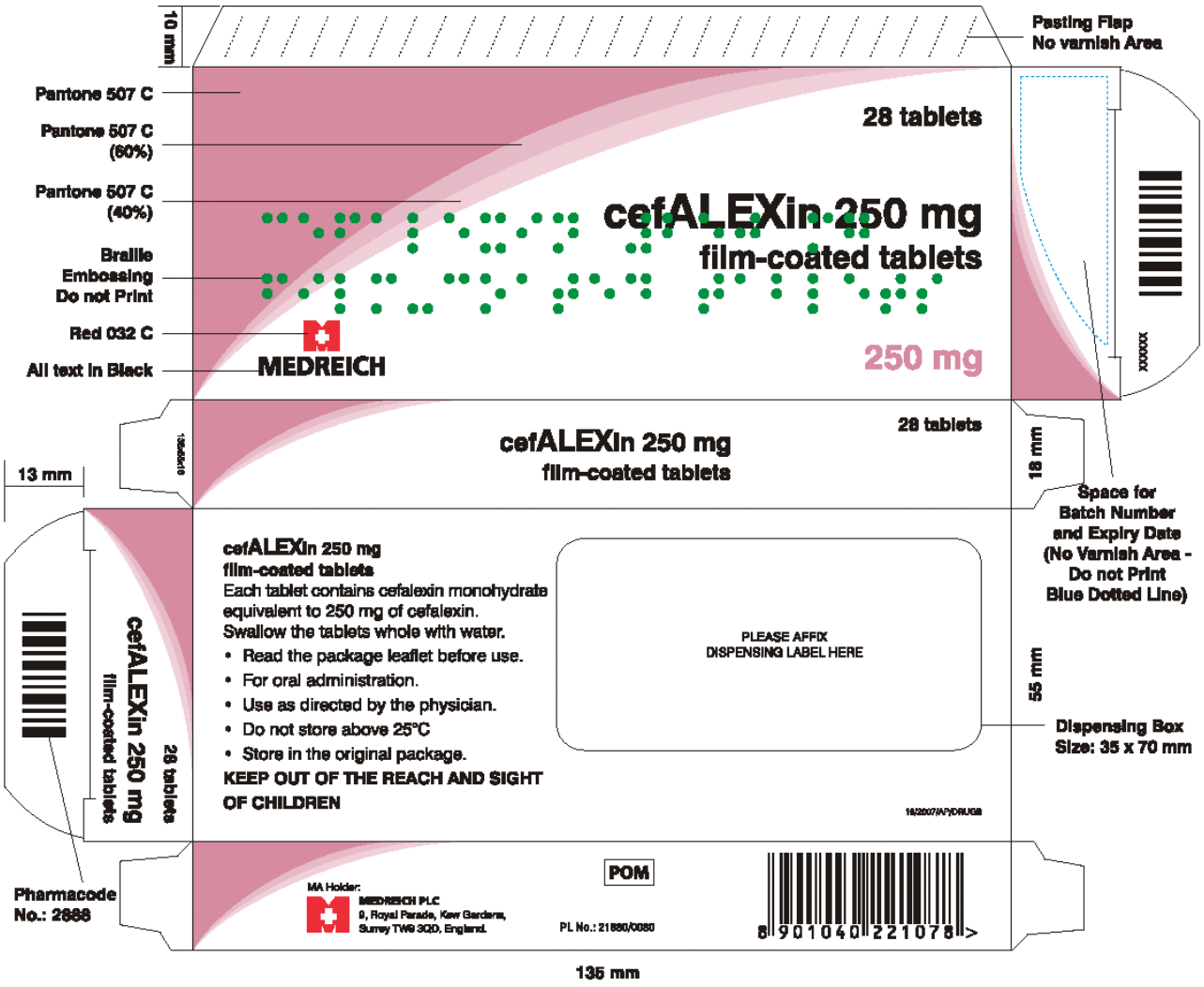
Batch Release site
Milpharm Limited
Ares, Odyssey Business Park
West End Road
South Ruislip, HA46QD
United Kingdom

MA Holder:
MEDREICH PLC
9, Royal Parade, Kew Gardens,
Surrey TW9 3QD, England

xxxxx

LABELLING

Carton:



Braille Reads:
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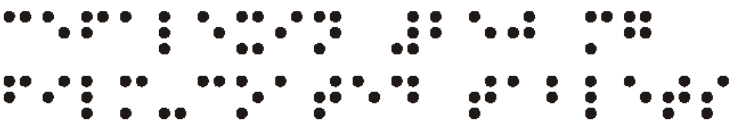
film-coated tablets



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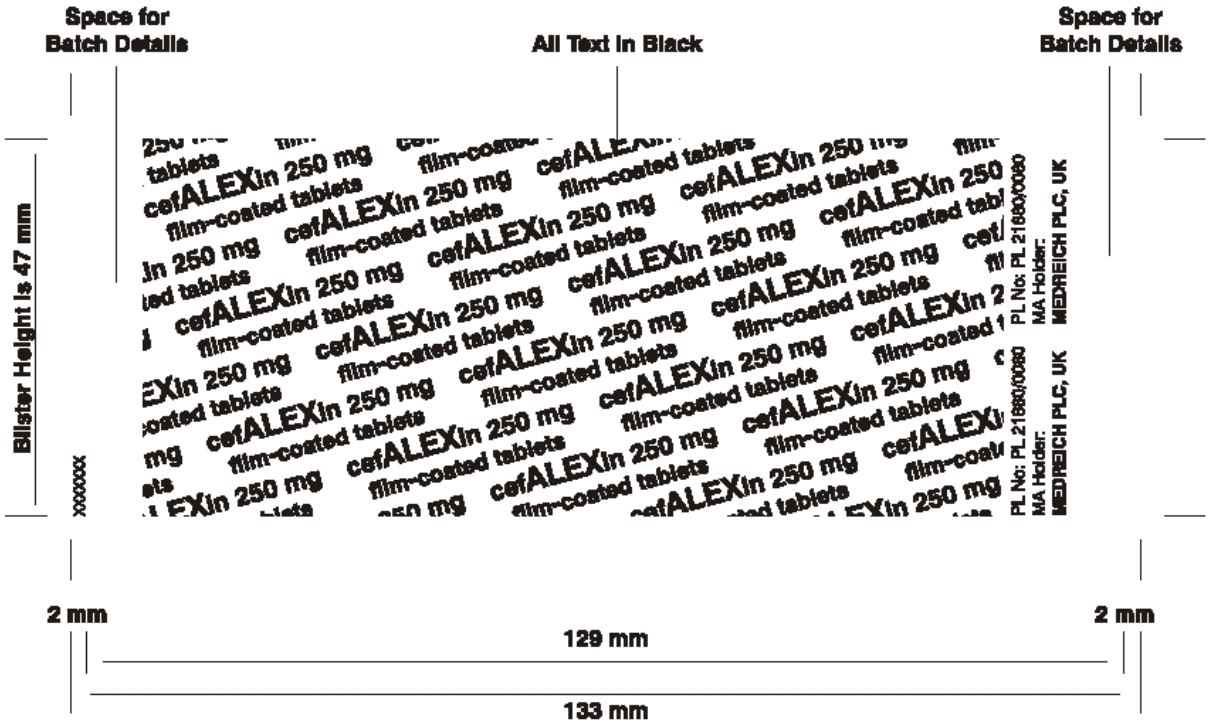
Space for Batch Details
All Text In Black
Space for Batch Details
Blister Height is 47 mm
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PL No: PL 21680/0080
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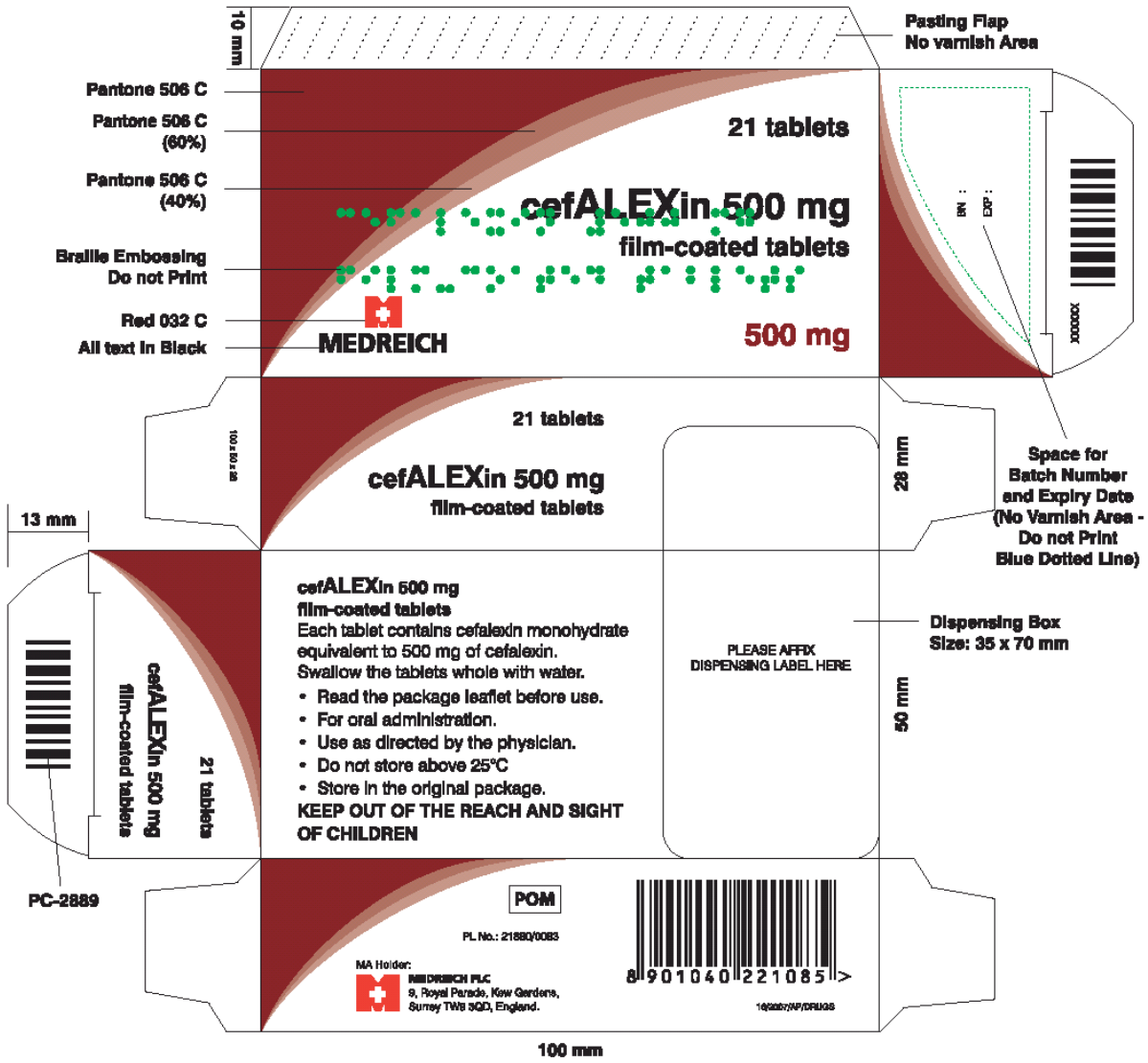
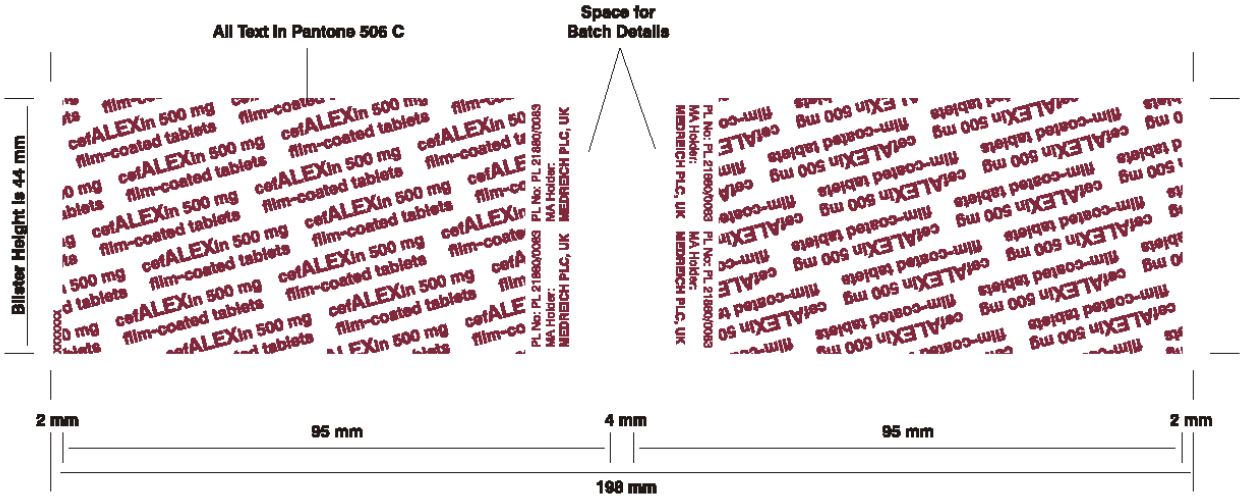
2 mm
129 mm
2 mm
133 mm

Carton:



Braille Reads:
cefALEXin #500 mg
film-coated tablets

Blister:


All Text in Pantone 506 C
Space for Batch Details
Blister Height is 44 mm
2 mm
95 mm
4 mm
95 mm
2 mm
198 mm