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For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

ALTIPOD 50

(Cefpodoxime Proxetil Oral Suspension I.P.)

COMPOSITION

ALTIPOD 50

When reconstituted as directed,
Each 5 ml of the reconstituted suspension contains :
Cefpodoxime Proxetil I.P.
equivalent to Cefpodoxime 50 mg
Colour: Sunset Yellow FCF

DESCRIPTION

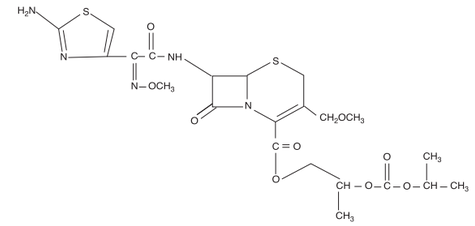
Cefpodoxime proxetil is an orally administered, extended spectrum, semi-synthetic antibiotic of the cephalosporin class. Cefpodoxime proxetil is a prodrug; its active metabolite is cefpodoxime. All doses of cefpodoxime proxetil in this insert are expressed in terms of the active cefpodoxime moiety.

Chemical Name: 1-(isopropoxycarbonyloxy)ethyl(6R,7R)-7-[2-(2-amino-4-thiazolyl)-(Z)-2-(methoxyimino)acetamido]-3-methoxymethyl-3-cephem-4-carboxylate.

Molecular Weight: 557.6

Molecular Formula: $C_{21}H_{27}N_5O_9S_2$

Structural formula :



DOSAGE FORM

Oral Suspension

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

Cefpodoxime proxetil is a beta-lactam antibiotic, a 3rd generation oral cephalosporin. It is the prodrug of cefpodoxime. Following oral administration, Cefpodoxime is taken up by the gastro-intestinal wall where it is rapidly hydrolysed to cefpodoxime, a bactericidal antibiotic, which is then absorbed systemically.

BACTERIOLOGY

The mechanism of action of cefpodoxime is based on inhibition of bacterial cell wall synthesis. It is stable to numerous beta-lactamases. Cefpodoxime has been shown to possess in vitro bactericidal activity against numerous Gram-positive and Gram-negative bacteria.

It is highly active against the Gram-positive organisms:

- *Streptococcus pneumoniae*
- Streptococci of Groups A (*S. pyogenes*),B (*S. agalactiae*), C, F and G
- Other streptococci (*S. mitis, S. sanguis* and *S. salivarius*)
- *Corynebacterium diphtheriae*

It is highly active against the Gram-negative organisms :

- *Haemophilus influenzae* (beta-lactamase and non beta-lactamase producing strains)
- *Haemophilus para-influenzae* (beta-lactamase and non beta-lactamase producing strains)
- *Branhamella catarrhalis* (beta-lactamase and non beta-lactamase producing strains)
- *Neisseria meningitidis*
- *Neisseria gonorrhoeae*
- *Escherichia coli*
- *Klebsiella Spp.* (*K. pneumoniae; K. oxytoca*)
- *Proteus mirabilis*

It is moderately active against meticillin-sensitive staphylococci, penicillinase and non-penicillinase producing strains (*S. aureus* and *S. epidermidis*).

In addition, as with many cephalosporins, the following are resistant to cefpodoxime: enterococci, meticillin-resistant staphylococci (*S. aureus* and *S. epidermidis*), *Staphylococcus saprophyticus, Pseudomonas aeruginosa* and *Pseudomonas Spp., Clostridium difficile, Bacteroides fragilis* and related species. As with all antibiotics, whenever possible, sensitivity should be confirmed by *in vitro* testing.

Pharmacokinetics

Cefpodoxime is taken up in the intestine and is hydrolysed to the active metabolite cefpodoxime. When cefpodoxime proxetil is administered orally to fasting subjects as a tablet corresponding to 100mg of cefpodoxime, 51.5% is absorbed and absorption is increased by food intake.

The volume of distribution is 32.3 l and peak levels of cefpodoxime occur 2 to 3 hrs after dosing. The maximum plasma concentration is 1.2mg/l and 2.5mg/l after doses of 100mg and 200mg respectively. Following administration of 100mg and 200mg twice daily over 14.5 days, the plasma pharmacokinetic parameters of cefpodoxime remain unchanged.

Serum protein binding of cefpodoxime, 40% principally to albumin. This binding is non saturable in type. Concentrations of cefpodoxime in excess of the minimum inhibitory levels (MIC) for common pathogens can be achieved in lung parenchyma, bronchial mucosa, pleural fluid, tonsils, interstitial fluid and prostate tissue.

As the majority of cefpodoxime is eliminated in the urine, the concentration is high. (Concentrations in 0-4, 4-8, 8-12 hr fractions after a single dose exceed MIC90 of common urinary pathogens). Good diffusion of cefpodoxime is also seen into renal tissue, with concentrations above MIC90 of the common urinary pathogens, 3-12hrs after an administration of a single 200mg dose (1.6-3.1μG/G). Concentrations of cefpodoxime in the medullary and cortical tissues is similar.

Studies in healthy volunteers show median concentrations of cefpodoxime in the total ejaculate 6-12hrs following administration of a single 200mg dose to be above the MIC90 of N. gonorrhoeae.

The main route of excretion is renal, 80% is excreted unchanged in the urine, with an elimination half life of approx 2.4 hours.

CHILDREN

In children, studies have shown the maximum plasma concentration occurs approximately 2-4 hours after dosing. A single 5mg/kg dose in 4-12 year olds produced a maximum concentration similar to that in adults given a 200mg dose.

In patients below 2 years receiving repeated doses of 5mg/kg 12 hourly, the average plasma concentrations, 2hrs post dose, are between 2.7mg/l (1-6 months) and 2.0mg/l (7 months-2 years). In patients between 1 month and 12 years receiving repeated doses of 5mg/kg 12 hourly, the residual plasma concentrations at steady state are between 0.2-0.3mg/l (1 month-2 years) and 0.1mg/l (2-12 years).

INDICATIONS

Cefpodoxime is a bactericidal cephalosporin antibiotic active against a wide range of Gram-negative and Gram-positive organisms. It is indicated for the treatment of the following infections either before the infecting organism has been identified or when caused by bacteria of established sensitivity.

Indications include:

Upper respiratory tract infections caused by organisms sensitive to cefpodoxime, including acute otitis media, sinusitis, tonsillitis and pharyngitis.

Cefpodoxime should be reserved for recurrent or chronic infections, or for infections where the causative organism is known or suspected to be resistant to commonly used antibiotics.

Lower respiratory tract infections caused by organisms sensitive to cefpodoxime. Including pneumonia, acute bronchitis and when bacterial super-infection complicates bronchiolitis.

Upper and lower urinary tract infections caused by organisms sensitive to cefpodoxime including cystitis and acute pyelonephritis.

Skin and soft tissue infections caused by organisms sensitive to cefpodoxime such as abscesses, cellulitis, infected wounds, furuncles, folliculitis, paronychia, carbuncles and ulcers.

DOSE AND METHOD OF ADMINISTRATION

Children:

The recommended mean dosage for children is 8mg/kg/day administered in two divided doses at 12 hour intervals. Cefpodoxime should not be used in infants less than 15 days old, as no experience yet exists in this age group.

The product should be taken during meals for optimal absorption.

Renal Impairment:

The dosage of Cefpodoxime does not require modification if creatinine clearance exceeds 40 ml. $min^{-1}/1.73m^2$.

Below this value, pharmacokinetic studies indicate an increase in plasma elimination half-life and the maximum plasma concentrations, and hence the dosage should be adjusted appropriately.

CREATININE CLEARANCE (ML/MIN)	
39-10	Unit dose1 administered as a single dose every 24 hours (i.e half of the usual adult dose).
< 10	Unit dose1 administered as a single dose every 48 hours (i.e quarter of the usual adult dose).
Haemodialysis Patients	Unit dose[1] administered after each dialysissession.

NOTE:

[1] The unit dose is either 100mg or 200mg, depending on the type of infection.

Hepatic Impairment:

The dosage does not require modification in cases of hepatic impairment.

DIRECTION OF USE:

Directions for reconstitution:
Slowly add boiled and cooled water up to the ring mark of the bottle.
Shake vigorously.
Adjust the volume up to the ring mark by adding more water, if necessary.
This makes 30 ml of suspension.
SHAKE WELL BEFORE EACH USE

CONTRAINDICATIONS

Hypersensitivity to cephalosporin antibiotics.

WARNINGS AND PRECAUTIONS

Preliminary enquiry about allergy to penicillin is necessary before prescribing cephalosporins since cross allergy to penicillins occurs in 5-10 % of cases.

Particular care will be needed in patients sensitive to penicillin: strict medical surveillance is necessary from the very first administration. Where there is doubt, medical assistance should be available at the initial administration, in order to treat any anaphylactic episode.

In patients who are allergic to other cephalosporins, the possibility of cross allergy to Cefpodoxime should be borne in mind. Cefpodoxime should not be given to those patients with a previous history of immediate type hypersensitivity to cephalosporins. Hypersensitivity reactions (anaphylaxis) observed with beta-lactam antibiotics can be serious and occasionally fatal.

The onset of any manifestation of hypersensitivity indicates that treatment should be stopped.

Cefpodoxime is not the preferred antibiotic for the treatment of staphylococcal pneumonia and should not be used in the treatment of atypical pneumonia caused by organisms such as Legionella, Mycoplasma and Chlamydia. In cases of severe renal insufficiency it may be necessary to reduce the dosage regimen dependent on the creatinine clearance.

Possible side effects include gastrointestinal disorders such as nausea, vomiting and abdominal pain. Antibiotics should always be prescribed with caution in patients with a history of gastrointestinal disease, particularly colitis. Cefpodoxime may induce diarrhoea, antibiotic associated colitis and pseudo-membranous colitis. These side-effects, which may occur more frequently in patients receiving higher doses for prolonged periods, should be considered as potentially serious. The presence of C. difficile should be investigated. In all potential cases of colitis, the treatment should be stopped immediately. The diagnosis should be confirmed by sigmoidoscopy and specific antibiotic therapy (vancomycin) substituted if considered clinically necessary. The administration of products which cause faecal stasis must be avoided. Although any antibiotic may cause pseudomembranous colitis, the risk may be higher with broad-spectrum drugs, such as the cephalosporins.

As with all beta-lactam antibiotics, neutropenia, and more rarely agranulocytosis may develop, particularly during extended treatment. For cases of treatment lasting longer than 10 days, blood count should therefore be monitored, and treatment discontinued if neutropenia is found.

Cephalosporins may be absorbed onto the surface of red cell membranes and react with antibodies directed against the drug. This can produce a positive Coombs' test and very rarely, haemolytic anaemia. Cross-reactivity may occur with penicillin for this reaction.

Changes in renal function have been observed with antibiotics of the same class, particularly when given concurrently with potentially nephrotoxic drugs such as aminoglycosides and/or potent diuretics. In such cases, renal function should be monitored. As with other antibiotics, the prolonged use of cefpodoxime proxetil may result in the overgrowth of non-susceptible organisms. With oral antibiotics the normal colonic flora may be altered, allowing overgrowth by clostridia with consequent pseudomembranous colitis. Repeated evaluation of the patient is essential and if superinfection occurs during therapy, appropriate measures should be taken.

DRUG INTERACTIONS

No clinically significant drug interactions have been reported during the course of clinical studies.

Histamine H2-antagonists and antacids reduce the bioavailibility of cefpodoxime. Probenecid reduces the excretion of cephalosporins. Cephalosporins potentially enhance the anticoagulant effect of coumarins and reduce the contraceptive effect of oestrogens. As with other cephalosporins, isolated cases showing development of a positive Coombs' test have been reported.

Studies have shown that bioavailability is decreased by approximately 30% when Cefpodoxime is administered with drugs which neutralise gastric pH or inhibit acid secretions. Therefore, such drugs as antacids of the mineral type and H2 blockers such as ranitidine, which can cause an increase in gastric pH, should be taken 2 to 3 hours after Cefpodoxime administration.

The bioavailability increases if the product is administered during meals.

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions.

UNDESIRABLE EFFECTS

Possible side effects include gastrointestinal disorders such as diarrhoea and rarely antibiotic- associated colitis, including pseudomembranous colitis (see Warnings and Precautions), nausea, vomiting and abdominal pain and rash, urticaria and itching. Changes in renal function have been observed with antibiotics from the same group as Cefpodoxime, particularly when co-prescribed with aminoglycosides and/or potent diuretics.

Occasional cases have been reported of headaches, dizziness, tinnitus, parethesia, asthenia and malaise. Rare cases of allergic reactions include hypersensitivity mucocutaneous reactions, skin rashes and pruritus. Occasional cases of bullous reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme have also been received. Transient moderate elevations of ASAT, ALAT and alkaline phosphatases and/or bilirubin have been reported. These laboratory abnormalities which may be explained by the infection, may rarely exceed twice the upper limit of the named range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic. Slight increases in blood urea and creatinine have also been reported. Exceptionally rare are the occurrence of liver damage and of haematological disorders such as reduction in haemoglobin, thrombocytosis, thrombocytopenia, leucopenia and eosinophilia. Haemolytic anaemia has extremely rarely been reported.

As with other β-lactam antibiotics, neutropenia and, more rarely, agranulocytosis may develop during treatment with Cefpodoxime, particularly if given over long periods.

As with other cephalosporins, there have been rare reports of anaphylactic reactions, bronchospasm, purpura and angiodema, serum-sickness-like reactions with rashes, fever and arthralgia.

OVERDOSAGE

In the event of overdosage with Cefpodoxime, supportive and symptomatic therapy is indicated. In cases of overdosage, particularly in patients with renal insufficiency, encephalopathy may occur. The encephalopathy is usually reversible once cefpodoxime plasma levels have fallen.

Expiry Date

Do not use later than the date of expiry.

Storage

Reconstituted suspension should be stored in a refrigerator and used within two weeks.

Store protected from moisture, at a temperature not exceeding 30°C.

Keep out of reach of children

Presentation

ALTIPOD 50 oral suspension is available in 30 ml bottle.

torrent

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.
at: Vill. Manakpur, PO Lodhimajra,
Nalagarh, Distt. Solan (HP)-174 101