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

8034548-805

ALTIPOD CV 100

(Cefpodoxime Proxetil And Potassium Clavulanate Dispersible Tablets)

COMPOSITION

Each uncoated dispersible tablet contains :

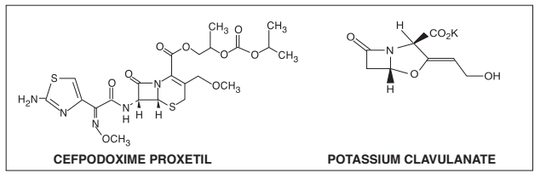
Cefpodoxime Proxetil I.P. equivalent to Cefpodoxime	100 mg
Potassium Clavulanate Diluted I.P. equivalent to Clavulanic acid	62.5 mg

DOSAGE FORM : Dispersible Tablet

DESCRIPTION

ALTIPOD CV is fixed dose combination (FDC) of cefpodoxime proxetil and potassium clavulanate. Cefpodoxime proxetil is an orally administered, extended spectrum, semi-synthetic antibiotic of the cephalosporin class and clavulanate potassium is the β-lactamase inhibitor. Clavulanic acid is a β-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of β-lactamases by blocking the active sites of these enzymes. Cefpodoxime proxetil is chemically designated as 1-(isopropoxycarbonyloxy)ethyl(6R,7R)-7-[2-(2-amino-4-thiazolyl)-(Z)-2-(methoxyimino)acetamido]-3-methoxymethyl-3-cephem-4-carboxylate. The molecular formula of cefpodoxime proxetil is $C_{21}H_{27}N_5O_9S_2$ and its molecular weight is 557.6.

Chemically, Potassium clavulanate is Potassium (Z) (2R, 5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate. Its molecular formula is $C_8H_8KNO_5$ and molecular weight is 237.3. The structural formula of cefpodoxime proxetil and potassium clavulanate are shown below:



CEFPODOXIME PROXETIL

POTASSIUM CLAVULANATE

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

Pharmacodynamics

Mechanism of Action

Cefpodoxime proxetil is a β-lactam antibiotic, a 3rd generation oral cephalosporin. It is the prodrug of cefpodoxime. Following oral administration, cefpodoxime proxetil is taken up by the gastrointestinal wall where it is rapidly hydrolyzed to cefpodoxime, a bactericidal antibiotic, which is then absorbed systemically. The mechanism of action of cefpodoxime is based on inhibition of bacterial cell wall synthesis. Cefpodoxime has been shown to possess in vitro bactericidal activity against numerous gram-positive and gram-negative bacteria. Cefpodoxime is stable in the presence of β-lactamase enzymes. As a result, many organisms resistant to penicillins and cephalosporins, due to their production of β-lactamase, may be susceptible to cefpodoxime. Cefpodoxime is inactivated by certain extended spectrum β-lactamases.

Clavulanic acid is a β-lactam, structurally related to the penicillins, which possesses the ability to inactivate a wide range of β-lactamase enzymes commonly found in microorganisms resistant to penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid-mediated β-lactamases frequently responsible for transferred drug resistance. It blocks the destructive hydrolytic activity of β-lactamases sparing cefpodoxime from hydrolysis.

The presence of clavulanic acid in the FDC of Cefpodoxime + Clavlanic Acid effectively extends the antibiotic spectrum of cefpodoxime to include many bacteria normally resistant to it and to other β-lactam antibiotics. Thus, FDC of Cefpodoxime + Clavlanic Acid possess the properties of a broad- spectrum antibiotic and a β-lactamase inhibitor.

Antibacterial spectrum

While in vitro studies of cefpodoxime have demonstrated the susceptibility of most strains of the following organisms.

Cefpodoxime + clavulanic acid is usually effective against following microorganisms.

Aerobic gram-positive microorganisms:

Staphylococcus aureus (including penicillinase-producing strains)

Note: Cefpodoxime is inactive against methicillin-resistant staphylococci.

Staphylococcus saprophyticus

Streptococcus pneumoniae (excluding penicillin-resistant strains)

Streptococcus pyogenes

Aerobic gram-negative microorganisms:

Escherichia coli

Klebsiella pneumoniae

Proteus mirabilis

Haemophilus influenzae (including β-lactamase producing strains)

Moraxella (Branhamella) catarrhalis

Neisseria gonorrhoeae (including penicillinase-producing strains)

The following in vitro data are available, but their clinical significance is unknown. Cefpodoxime exhibits *in vitro* minimum inhibitory concentrations (MICs) of ≤ 2.0 µg/mL against most (≥90%) of isolates of the following microorganisms. However, the safety and efficacy of cefpodoxime in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

Aerobic gram-positive microorganisms:

Streptococcus agalactiae

Streptococcus spp. (Groups C, F, G)

Note: Cefpodoxime is inactive against enterococci.

Aerobic gram-negative microorganisms:

Citrobacter diversus

Klebsiella oxytoca

Proteus vulgaris

Providencia rettgeri

Haemophilus parainfluenzae

Note: Cefpodoxime is inactive against most strains of Pseudomonas and Enterobacter.

Anaerobic gram-positive microorganisms:

Peptostreptococcus magnus

Pharmacokinetics

Cefpodoxime:

Cefpodoxime proxetil is a prodrug that is absorbed from the gastrointestinal tract and de-esterified to its active metabolite, cefpodoxime. Following oral administration of 100 mg of cefpodoxime proxetil to fasting subjects, approximately 50% of the administered cefpodoxime dose was absorbed systemically. Over the recommended dosing range (100 to 400 mg), approximately 29 to 33% of the administered cefpodoxime dose was excreted unchanged in the urine in 12 hours. There is minimal metabolism of cefpodoxime in vivo.The extent of absorption (mean AUC) and the mean peak plasma concentration increased when film-coated tablets were administered with food. Following a 200 mg tablet dose taken with food, the AUC was 21 to 33% higher than under fasting conditions. Time to peak concentration was not significantly different between fed and fasted subjects. Over the recommended dosing range, (100 to 400 mg), the rate and extent of cefpodoxime absorption exhibited dose dependency; dose-normalized C_{max} and AUC decreased by up to 32% with increasing dose. Over the recommended dosing range, the T_{max} was approximately 2 to 3 hours and the t□ ranged from 2.09 to 2.84 hours. In patients with normal renal function, neither accumulation nor significant changes in other pharmacokinetic parameters were noted following multiple oral doses of up to 400 mg Q 12 hours. Protein binding of cefpodoxime ranges from 22 to 33% in serum and from 21 to 29% in plasma. 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.

Skin blister: Following multiple-dose administration every 12 hours for 5 days of 200 mg or 400 mg cefpodoxime proxetil, the mean maximum cefpodoxime concentration in skin blister fluid averaged 1.6 and 2.8 µg/ml, respectively. Skin blister fluid cefpodoxime levels at 12 hours after dosing averaged 0.2 and 0.4µg/ml for the 200 mg and 400 mg multiple dose regimens, respectively.

Clavulanic acid:

Clavulanate potassium is well absorbed from the gastrointestinal tract after oral administration. Absorption of clavulanate potassium when taken with food is greater relative to the fasted state. The half-life of clavulanic acid after the oral administration is 1.0 hour. Approximately 25% to 40% of the clavulanic acid is excreted unchanged in urine during the first 6 hours after administration. Concurrent administration of probenecid does not delay renal excretion of clavulanic acid.

Clavulanic acid has been found to be approximately 25% bound to human serum. The results of experiments involving the administration of clavulanic acid to animals suggest that this compound is well distributed in body tissues. The disposition of clavulanic acid is also characterized by an initial rapid phase, indicating easy distribution to the peripheral compartment. The short t½ β (0.8 -1.5 hours in adults and children) is the consequence of the rapid elimination from the body produced by metabolisrn and renal excretion, the later occurring primarily by glomerular filtration.The metabolites are excreted via faeces, in the urine and through the lungs, with 20-60% of the dose being excreted in urine in the form of the parent drug. Plasma and renal clearance values of 14.9 and 6.3 L/h/1.73m^2, respectively, have been reported for clavulanic acid after intravenous administration to healthy subjects.

Pharmacokinetics in special population

Renal disease

Cefpodoxime: Elimination of cefpodoxime is reduced in patients with moderate to severe renal impairment (< 50 ml/min creatinine clearance). In subjects with mild impairment of renal function (50 to 80 ml/min creatinine clearance), the average plasma half-life of cefpodoxime was 3.5 hours. In subjects with moderate (30 to 49 ml/min creatinine clearance) or severe renal impairment (5 to 29 ml/min creatinine clearance), the half-life increased to 5.9 and 9.8 hours, respectively. Approximately 23% of the administered dose was cleared from the body during a standard 3 hours hemodialysis procedure.

Clavulanic acid: As this drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

Hepatic disease

Cefpodoxime: Absorption was somewhat diminished and elimination unchanged in patients with cirrhosis. The mean cefpodoxime t-half and renal clearance in cirrhotic patients were similar to those derived in studies of healthy subjects. Ascites did not appear to affect values in cirrhotic subjects. No dosage adjustment is recommended in this patient population.

Elderly patients

Cefpodoxime: Elderly subjects do not require dosage adjustments unless they have diminished renal function. In healthy geriatric subjects, cefpodoxime half-life in plasma averaged 4.2 hours (vs 3.3 in younger subjects) and urinary recovery averaged 21% after a 400 mg dose was administered every 12 hours. Other pharmacokinetic parameters (C_{max}, AUC and T_{max}) were unchanged relative to those observed in healthy young subjects.

Clavulanic acid: As this drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

INDICATIONS

FDC of Cefpodoxime + Clavlanic Acid is indicated for the treatment of infection caused by susceptible microorganisms in the following conditions :

- lower and upper respiratory infections
- urinary tract infection

DOSE AND METHOD OF ADMINISTRATION

To reduce the development of drug-resistant bacteria and maintain the effectiveness of FDC of cefpodoxime and clavulanic acid tablets and other antibacterial drugs, FDC of cefpodoxime and clavulanic acid tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria susceptible to the combination. FDC Cefpodoxime + Clavulanic Acid should be taken with food to enhance absorption. The tablets should be swallowed whole and not chewed, broken, or crushed.FDC of Cefpodoxime + Clavulanic Acid contain 1) cefpodoxime proxetil which is a prodrug and its active metabolite is cefpodoxime; and 2) clavulanic acid. Based on the cefpodoxime component, FDC Cefpodoxime + Clavulanic Acid should be dosed as follows:

Adults and Adolescents (age 12 years and older):

Type of Infection	Total Daily Dose of Cefpodoxime	Dose Frequency	Duration
Pharyngitis and/or tonsillitis	200 mg	100 mg Q 12 hours	5 to 10 days
Acute community-acquired pneumonia	400 mg	200 mg Q 12 hours	14 days
Acute bacterial exacerbations of chronic bronchitis	400 mg	200 mg Q 12 hours	10 days
Uncomplicated gonorrhea (men and women) and rectal gonococcal infections (women)	200 mg	Single dose	-
Acute maxillary sinusitis	400 mg	200 mg Q 12 hours	10 days
Uncomplicated urinary tract infection	200 mg	100 mg Q 12 hours	7 days

Infants and Pediatric Patients (age 2 months through 12 years):

Type of Infection	Total Daily Dose of Cefpodoxime	Dose Frequency	Duration
Acute otitis media	10 mg/kg/day (Max 400 mg/day)	5 mg/kg Q 12 h (Max 200 mg/dose)	5 days
Pharyngitis and/or tonsillitis	10 mg/kg/day (Max 200 mg/day)	5 mg/kg Q 12 h (Max 100 mg/dose)	5 to 10 days
Acute maxillary sinusitis	10 mg/kg/day (Max 400 mg/day)	5 mg/kg Q 12 hours (Max 200 mg/dose)	10 days

Patients with Renal Dysfunction:

For patients with severe renal impairment (< 30 mL/min creatinine clearance), the dosing intervals should be increased to Q 24 hours. In patients maintained on hemodialysis, the dose frequency should be 3 times/week after hemodialysis.

When only the serum creatinine level is available, the following formula (based on sex, weight, and age of the patient) may be used to estimate creatinine clearance (mL/min).

For this estimate to be valid, the serum creatinine level should represent a steady state of renal function.

Males (ml/min) : $\frac{\text{Weight (kg) x (140 - age)}}{\text{72 x serum creatinine (mg/100 ml)}}$

Females(ml/min) : 0.85 x above value

Patients with Cirrhosis:

Cefpodoxime pharmacokinetics in cirrhotic patients (with or without ascites) are similar to those in healthy subjects. Dose adjustment is not necessary in this population.

Direction for Use : The tablet should be dispersed in water immediately before use.

USE IN SPECIAL POPULATIONS

Pregnancy - Teratogenic Effects:

Pregnancy Category B

Cefpodoxime Proxetil was neither teratogenic nor embryocidal when administered to rats during organogenesis at doses up to 100 mg/kg/day (2 times the human dose based on mg/m^2) or to rabbits at doses up to 30 mg/kg/day (1-2 times the human dose based on mg/m^2).

Clavulanic acid: The reproductive and developmental toxicity studies on clavulanic acid are available following oral administration; one generation in rat; teratogenic effects in rat: teratogenic effects in mouse and peri- and postnatal development in the rat. Overall, a moderate reduction of female fertility and/or growth and survival of the fetuses were seen at dose levels eliciting slight systemic or maternal toxicity. 10 mg/kg body weight/day could be retained as a NOEL. There are, however, no adequate and well-controlled studies with cefpodoxime and clavulanic acid in pregnant women. Because animal reproduction studies are not always predictive of human response, FDC of Cefpodoxime + Clavlanic Acid should be used during pregnancy only if clearly needed.

Labor and Delivery:

Cefpodoxime proxetil has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

Nursing Mothers:

Cefpodoxime is excreted in human milk. In a study of 3 lactating women, levels of cefpodoxime in human milk were 0%, 2% and 6% of concomitant serum levels at 4 hours following a 200 mg oral dose of cefpodoxime proxetil. At 6 hours post-dosing, levels were 0%, 9% and 16% of concomitant serum levels. Because of the potential for serious reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and efficacy in infants less than 2 months of age have not been established.

Geriatric Use:

Of the 3338 patients in multiple-dose clinical studies of cefpodoxime proxetil film-coated tablets, 521 (16%) were 65 and over, while 214 (6%) were 75 and over. No overall differences in effectiveness or safety were observed between the elderly and younger patients. In healthy geriatric subjects with normal renal function, cefpodoxime half-life in plasma averaged 4.2 hours and urinary recovery averaged 21% after a 400 mg dose was given every 12 hours for 15 days. Other pharmacokinetic parameters were unchanged relative to those observed in healthy younger subjects.Dose adjustment in elderly patients with normal renal function is not necessary.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:

Long-term animal carcinogenesis studies of cefpodoxime proxetil have not been performed. Mutagenesis studies of cefpodoxime, including the Ames test both with and without metabolic activation, the chromosome aberration test, the unscheduled DNA synthesis assay, mitotic recombination and gene conversion, the forward gene mutation assay and the in vivo micronucleus test, were all negative. No untoward effects on fertility or reproduction were noted when 100 mg / kg/day or less (2 times the human dose based on mg/m^2) was administered orally to rats.

CONTRAINDICATIONS

FDC of Cefpodoxime + Clavlanic Acid is contraindicated in patients with a known allergy to penicillin, any other type of beta-lactam drug, cephalosporin class of antibiotics, beta-lactamase inhibitors or any other ingredients of this formulation.

WARNINGS

BEFORE THERAPY WITH CEFPODOXIME PROXETIL IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFPODOXIME, OTHER CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF CEFPODOXIME IS TO BE ADMINISTERED TO PENICILLIN SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS HYPERSENSITIVITY AMONG β-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEFPODOXIME PROXETIL OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, INTRAVENOUS FLUIDS, INTRAVENOUS ANTIHISTAMINE, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefpodoxime proxetil, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy.

CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued.

Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated. A concerted effort to monitor for C. difficile in cefpodoxime-treated patients with diarrhea was undertaken because of an increased incidence of diarrhea associated with C. difficile in early trials in normal subjects. C. difficile organisms or toxin was reported in 10% of the cefpodoxime-treated adult patients with diarrhea; however, no specific diagnosis of pseudomembranous colitis was made in these patients.

PRECAUTIONS

General

In patients with transient or persistent reduction in urinary output due to renal insufficiency, the total daily dose of cefpodoxime proxetil should be reduced because high and prolonged serum antibiotic concentrations can occur in such individuals following usual doses. Cefpodoxime, like other cephalosporins, should be administered with caution to patients receiving concurrent treatment with potent diuretics. As with other antibiotics, prolonged use of cefpodoxime proxetil may result in overgrowth of nonsusceptible organisms.

Repeated evaluation of the patient's condition is essential. If super infection occurs during therapy, appropriate measures should be taken. Prescribing cefpodoxime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria. As with all β-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 anemia. 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.

Pediatrics

Cefpodoxime proxetil: Safety and efficacy of cefpodoxime in infants less than 2 months of age have not been established.

DRUG INTERACTIONS

Antacids: Concomitant administration of high doses of antacids (sodium bicarbonate and aluminum hydroxide) or H_2 blockers reduces peak plasma levels by 24% to 42% and the extent of absorption by 27% to 32%, respectively. The rate of absorption is not altered by these concomitant medications. Oral anti-cholinergics (e.g., propantheline) delay peak plasma levels (47% increase in T_{max}), but do not affect the extent of absorption (AUC).

Probenecid : As with other β-lactam antibiotics, renal excretion of cefpodoxime was inhibited by probenecid and resulted in an approximately 31% increase in AUC and 20% increase in peak cefpodoxime plasma levels.

Nephrotoxic drugs: Although nephrotoxicity has not been noted when cefpodoxime proxetil was given alone, close monitoring of renal function is advised when cefpodoxime proxetil is administered concomitantly with compounds of known nephrotoxic potential.

Food: The bioavailability increases if the product is administered during meals.

Drug/Laboratory Test Interactions: 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

Cefpodoxime Proxetil

Clinical trials: **Tablets (multiple dose):**

In reported clinical trials using multiple doses of cefpodoxime proxetil film-coated tablets, patients were treated with the recommended dosages of cefpodoxime (100 to 400 mg Q 12 hours). There were no deaths or permanent disabilities thought related to drug toxicity. 2.7% patients discontinued medication due to adverse events thought possibly or probably related to drug toxicity. 52% of the patients who discontinued therapy (whether thought related to drug therapy or not) did so because of gastrointestinal disturbances, nausea, vomiting, or diarrhea. The percentage of cefpodoxime proxetil-treated patients who discontinued study drug because of adverse events was significantly greater at a dose of 800 mg daily than at a dose of 400 mg daily or at a dose of 200 mg daily. Adverse events thought possibly or probably related to cefpodoxime in multiple-dose clinical trials were:

Incidence Greater Than 1%:

Adverse Events	Incidence
Diarrhea*	7.0 %
Nausea	3.3 %
Vaginal Fungal Infections	1.0 %
Vulvovaginal Infections	1.3 %
Abdominal Pain	1.2 %
Headache	1.0 %

* Diarrhea or loose stools were dose-related: decreasing from 10.4% of patients receiving 800 mg per day to 5.7% for those receiving 200 mg per day. Of patients with diarrhea, 10% had C. difficile organism or toxin in the stool (see WARNINGS).

Incidence Less Than 1%:

By body system in decreasing order:

Adverse events thought possibly or probably related to cefpodoxime proxetil that occurred in less than 1% of patients

Body - fungal infections, abdominal distention, malaise, fatigue, asthenia, fever, chest pain, back pain, chills, generalized pain, abnormal microbiological tests, moniliasis, abscess, allergic reaction, facial edema, bacterial infections, parasitic infections, localized edema, localized pain.

Cardiovascular - congestive heart failure, migraine, palpitations, vasodilation, hematoma, hypertension, hypotension

Digestive- vomiting, dyspepsia, dry mouth, flatulence, decreased appetite, constipation, oral moniliasis, anorexia, eructation, gastritis, mouth ulcers, gastrointestinal disorders, rectal disorders, tongue disorders, tooth disorders, increased thirst, oral lesions, tenesmus, dry throat, toothache

Blood and Lymphatic- anemia

Metabolic and Nutritional- dehydration, gout, peripheral edema, weight increase.

Musculo-skeletal- myalgia

Nervous- dizziness, insomnia, somnolence, anxiety, shakiness, nervousness, cerebral infarction, change in dreams, impaired concentration, confusion, nightmares, paresthesia, vertigo

Respiratory - asthma, cough, epistaxis, rhinitis, wheezing, bronchitis, dyspnea, pleural effusion, pneumonia, sinusitis

Skin- urticaria, rash, pruritus non-application site, diaphoresis, maculopapular rash, fungal dermatitis, desquamation, dry skin non-application site, hair loss, vesiculobullous rash, sunburn.

Special Senses - taste alterations, eye irritation, taste loss, tinnitus

Urogenital - hematuria, urinary tract infections, metrorrhagia, dysuria, urinary frequency, nocturia, penile infection, proteinuria, vaginal pain

Tablets (single dose)

In reported clinical trials using a single dose of cefpodoxime proxetil film-coated tablets, patients were treated with the recommended dosage of cefpodoxime (200 mg). There were no deaths or permanent disabilities thought related to drug toxicity in these studies. Adverse events thought possibly or probably related to cefpodoxime in single-dose clinical trials conducted by the innovator in the United States were:

Incidence Greater Than 1%

Nausea	1.4 %
Diarrhea	1.2 %

Incidence Less Than 1%

Central Nervous System: Dizziness, headache, syncope.

Dermatologic: Rash.

Genital: Vaginitis.

Gastrointestinal: Abdominal pain.

Psychiatric: Anxiety.

Laboratory changes

Significant laboratory changes that have been reported in adult and pediatric patients in clinical trials of cefpodoxime proxetil, without regard to drug relationship, were :

Hepatic: Transient increases in AST (SGOT), ALT (SGPT), GGT, alkaline phosphatase, bilirubin, and LDH

Hematologic: Eosinophilia, leukocytosis, lymphocytosis, granulocytosis, basophilia, monocytosis, thrombocytosis, decreased hemoglobin, decreased hematocrit, leukopenia, neutropenia, lymphocytopenia, thrombocytopenia, thrombocythemia, positive Coombs' test, and prolonged PT, and PTT

Serum Chemistry: Hyperglycemia, hypoglycemia, hypoalbuminemia, hypoproteinemia, hyperkalemia, and hyponatremia

Renal: Increases in BUN and creatinine

Most of these abnormalities were transient and not clinically significant.

Post-marketing experience

The following serious adverse experiences have been reported : allergic reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme and serum sickness-like reactions, pseudomembranous colitis, bloody diarrhea with abdominal pain, ulcerative colitis, rectorrhagia with hypotension, anaphylactic shock, acute liver injury, in utero exposure with miscarriage, purpuric nephritis, pulmonary infiltrate with eosinophilia, and eyelid dermatitis. One death was attributed to pseudomembranous colitis and disseminated intra vascular coagulation.

Cephalosporin class labeling

In addition to the adverse reactions listed above which have been observed in patients treated with cefpodoxime proxetil, the following adverse reactions and altered laboratory tests have been reported for cephalosporin class antibiotics.

Adverse reactions and abnormal laboratory tests : Renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, serum sickness-like reaction, hemorrhage, agranulocytosis, and pancytopenia. Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Clavulanic Acid

Side effects include bloody diarrhea, bloody urine, painful or difficult urination, unusual weakness, easy bleeding and bruising, confusion, dry mouth, increased urination, chills, body aches, fever, sore throat, headache, seizures, chest pain and irregular heartbeat. These side effects are very rare and do not affect a large amount of users. Treatment should not normally exceed 14 days.

OVERDOSE

Cefpodoxime

In acute rodent toxicity studies, a single 5 g/kg oral dose produced no adverse effects. In the event of serious toxic reaction from overdosage, hemodialysis or peritoneal dialysis may aid in the removal of cefpodoxime from the body, particularly if renal function is compromised. The toxic symptoms following an overdose of beta-lactam antibiotics may include nausea, vomiting, epigastric distress, and diarrhea.

Clavulanic Acid

The molecular weight, degree of protein binding, and pharmacokinetic profile of clavulanic acid together with information from a single patient with renal insufficiency all suggest that this compound may also be removed by hemodialysis.

INCOMPATIBILITIES

Not applicable

EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store at a temperature not exceeding 25°C, protected from light & moisture.

Keep out of reach of children

PRESENTATION

ALTIPOD CV 100 is available in a strip of 10 tablets

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

At : Vill. Manakpur, PO Lodhimajra,
Nalagarh, Distt. Solan (HP)-174 101