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

DROXYL CLAV 500

1. Generic Name:
Cefadroxil And Potassium Clavulanate Tablets

2. Qualitative and quantitative composition:

Each film coated tablet contains:

Cefadroxil I.P. (as monohydrate)

equivalent to Cefadroxil Anhydrous…….500 mg

Potassium Clavulanate diluted I.P.

equivalent to Clavulanic acid……..125 mg

Colour : Titanium dioxide I.P.

The excipients used are Mannitol, Crospovidone, Colloidal silicon dioxide (AEROSIL)IP, Magnesium stearate IP, Hydroxy propyl methyl Celu.(metho E15)IP, Ethyl cellulose 10 CPS USP-NF, Diethyl phthalate USP/NF, Titanium dioxide IP, Methanol IP, Methylene chloride IP.

3. Dosage form and strength:

Dosage form: Film coated tablets

Strength: Cefadroxil 500 mg & Potassium Clavulanate 125 mg

4. Clinical particulars:

4.1 Therapeutic indication:

- Fixed dose combination (FDC) of Cefadroxil and Clavulanic acid is an antibiotic indicated for the adult patients with infections caused by susceptible microorganisms including *S. aureu*, Urinary tract Infection, Lower Respiratory tract infection and gonococcal urethritis.
- Urinary tract infections caused by *E. coli*; *P. mirabilis, and Klebsiella* species.
- Skin and skin structure infections caused by *staphylococci and/or streptococci*.
- Respiratory tract infections: Pharyngitis and/or tonsillitis caused by *Streptococcus pyogenes (Group A beta-hemolytic streptococci).* Bronchitis, Bronchiectasis, Pneumonia.
- ENT Infections- Chronic Maxillary Sinusitis, Chronic Otitis Media.

Note: Only penicillin by the intramuscular route of administration has been shown to be effective in the prophylaxis of rheumatic fever. Cefadroxil is generally effective in the eradication of streptococci from the oropharynx. However, data establishing the efficacy of Cefadroxil for the prophylaxis of subsequent rheumatic fever are not available.

Note : Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

4.2 Posology and method of administration:

<u>Posology</u>

Cefadroxil

Uncomplicated lower Urinary tract infection

Adults : 1-2g daily as single or 2 divided doses

Children > 6 Years : 500mg bid; 1-6 yrs : 250mg bid; < 1yr: 30 mg/kg daily in divided doses.

Skin and Skin structure infections

Adults: 1g daily as single or divided doses

Children: 30mg/kg/day in equal divided doses.

Pharyngitis

Adults: For treatment of group A β-haemolytic strep and tonsillitis: 1g/day as single or divided doses

Children: 30mg/kg/day in equal divided doses every day

Tonsilitis

Adults: For treatment of group A β-haemolytic strep and tonsillitis: 1g/day as single or divided doses

Children: 30mg/kg/day in equal divided doses every day

Renal Impairment

In patients with renal impairment, the dosage of Cefadroxil should be adjusted according to creatinine clearance rates to prevent drug accumulation. The following schedule is suggested.

In adults, the initial dose is 1000 mg of Cefadroxil and the maintenance dose (based on the creatinine clearance rate [mL/min/1.73 m^2]) is 500 mg at the time intervals listed below.

CrCl (ml/min)	25-50	10-25	0-10
Dosage Interval	12 hours	24 hours	36 hours

May be taken with or without food.

4.3 Contraindications:

Patients with known hypersensitivity to cephalosporin antibiotics.

4.4 Special warnings and precautions for use:

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with FDC of Cefadroxil/clavulanate potassium careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to Cefadroxil, cephalosporins, penicillins, or other drugs.

If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-sensitivity among beta-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 fixed dose combination (FDC) of Cefadroxil/clavulanate potassium occurs, discontinue the drug.

Serious acute hypersensitivity reactions may require treatment with Epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefadroxil, 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.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clavulanate potassium, and has ranged in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

Cefadroxil should be used with caution in the presence of markedly impaired renal function (creatinine clearance rate of less than 50 mL/min/1.73 m^2). In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy.

Prescribing Cefadroxil 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.

Prolonged use of Cefadroxil 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. Cefadroxil should be prescribed with caution in individuals with history of gastrointestinal disease particularly colitis.

Information for Patients

Patients should be counseled that antibacterial drugs including Cefadroxil should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefadroxil is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1)decrease the

effectiveness of the immediate treatment and (2)increase the likelihood that bacteria will develop resistance and will not be treatable by Cefadroxil or other antibacterial drugs in the future. Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is

discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months

after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Drug/Laboratory Test Interactions

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic 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 recognized that a positive Coombs' test may be due to the drug.

4.5 Drug-Interaction:

Contraindication of concomitant use

- Cefadroxil should not be combined with bacteriostatic antibiotics (e.g. tetracycline, erythromycin, sulfonamides, chloramphenicol) since an antagonistic effect is possible.
- Treatment with Cefadroxil in combination with aminoglycoside antibiotics, polymyxin B, colistin or high-dose loop diuretics should be avoided since such combinations can potentiate nephrotoxic effects.

Concomitant use not recommended

- Frequent checks on coagulation parameters are necessary during concomitant long term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications.

Precautions

- The concomitant administration of probenicid can produce higher and sustained concentrations of cefadroxil in the serum and in the bile.
- The occurence of diarrhoea may impair the resorption of other medicaments and therefore lead to an impairment of their efficacy.
- Forced diuresis leads to a decrease of cefadroxil blood levels.
- Cefadroxil may attenuate the effect of oral contraceptives.
- Cefadroxil binds to cholestyramine which may lead to reduced bioavailability of cefadroxil.
- The result of the direct Coombs' test can be transiently positive during or after treatment with cefadroxil. This also applies to Coombs' tests carried out in newborns whose mother received

  treatment with cephalosporins before delivery.
- Urinary sugar should be determined enzymatically (e.g. with test strips) during treatment with cefadroxil since reduction tests can furnish falsely elevated values.

4.6 Use in special populations

Carcinogenesis, Mutagenesis and Impairment of Fertility
No long-term studies have been performed to determine carcinogenic potential. No genetic toxicity tests have been performed.

Pregnancy

Pregnancy Category B Reproduction studies have been performed in mice and rats at doses up to 11 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefadroxil monohydrate. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

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

Nursing Mothers

Caution should be exercised when Cefadroxil monohydrate is administered to a nursing mother.

Geriatric Use

Of approximately 650 patients who received Cefadroxil for the treatment of urinary tract infections in three clinical trials, 28% were 60 years and older, while 16% were 70 years and older. Of approximately 1,000 patients who received Cefadroxil for the treatment of skin and skin structure infection in 14 clinical trials, 12% were 60 years and older while 4% were 70 years and over. No overall differences in safety were reported between the elderly patients in these studies and younger patients. Clinical studies of Cefadroxil for the treatment of pharyngitis or tonsillitis did not include sufficient numbers of patients 65 years and older to determine whether they respond differently from younger patients. Other reported clinical experience with cefadroxil has not identified differences in responses between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

4.7 Effects on ability to drive and use machines:

None stated.

4.8 Undesirable effects:

Gastrointestinal

Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment. Dyspepsia, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black "hairy" tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudomembranous colitis have been reported rarely. Diarrhea has also occurred.

Hypersensitivity

Allergies (in the form of rash, urticaria, angioedema, and pruritus) have been reported. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported. Skin rashes, pruritus, urticaria, angioedema, serum sickness - like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis, hypersensitivity vasculitis, and an occasional case of exfoliative dermatitis (including toxic epidermal necrolysis) have been reported. These reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Whenever such reactions occur, the drug should be discontinued, unless the opinion of the physician dictates otherwise. Serious and occasional fatal hypersensitivity (anaphylactic) reactions can occur with oral penicillin.

Other

Other reactions have included hepatic dysfunction including cholestasis and elevations in serum transaminase, genital pruritus, genital moniliasis, vaginitis, moderate transient neutropenia,

fever. Agranulocytosis, thrombocytopenia, idiosyncratic hepatic failure, erythema multiforme, Stevens - Johnson syndrome, serum sickness, and arthralgia have been rarely reported.

In addition to the adverse reactions listed above which have been reported in patients treated with Cefadroxil, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Toxic epidermal necrolysis, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, aplastic anemia, haemolytic anemia, hemorrhage, prolonged prothrombin time, positive Coombs' test, increased BUN, increased creatinine, elevated alkaline phosphatase, elevated aspartate aminotransferase (AST), elevated alanine aminotransferase (ALT), elevated bilirubin, elevated LDH, eosinophilia, pancytopenia, neutropenia.

Allergic exanthema, angioneurotic edema, leucopenia, haemolytic anaemia of immunologic origin, headache, nervousness, sleeplessness, fatigue, opportunistic infections (e.g. vaginal mycoses, thrush) have been reported with use of cefadroxil.

Renal

Interstitial nephritis and hematuria have been reported rarely. Crystalluria has also been reported. 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.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose:

There is no information on overdosage with FDC of Cefadroxil & Clavulanic acid in humans. A study of children under six years of age suggested that ingestion of less than 250 mg/kg of cephalosporins is not associated with significant outcomes. No action is required other than general support and observation. For amounts greater than 250 mg/kg, induce gastric emptying.

5. Pharmacological properties:

5.1 Mechanism of Action:

Cefadroxil is a cephalosporin for oral administration which inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins. The result is formation of a defective cell wall that is osmotically unstable, and bacterial cell lysis. Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

5.2 Pharmacodynamic properties:

Microbiology

Cefadroxil: *In vivo* test demonstrate that the cephalosporins are bactericidal because of their inhibition of cell wall synthesis.

Cefadroxil has been shown to be active against the following organisms both in vitro and in clinical infections.

Beta-hemolytic streptococci

Staphylococci, including penicillinase-producing strains, *Streptococcus (Diplococcus) pneumonia, Escherichia coli, Proteus mirabilis, Klebsiella species, Moraxella (Branhamella) catarrhalis.*

Note: Most strains of *Entervcoccus faecalis* (formerly *Streptococcus faecalis*) and *Enterococcus faecium* (formerly *Streptococcus faecium*) are resistant to Cefadroxil. It is not active against most strains of *Enter obacter* species, *Morganella morganii* (formerly Proteus morganii), and *P.vulgaris*. It has no activity against Pseudomonas species and Acinetobacter calcoaceticus (formerly Mima and Herellea species).

Clavulanic acid is an irreversible 'suicide' inhibitor of intracellular and extracellular β-lactamases, demonstrating concentration-dependent and competitive inhibition. It has a high affinity for the class A β-lactamases. This wide range of β-lactamases, which includes the plasmid-mediated TEM and SHV enzymes, is found frequently in members of the *Enterobacteriaceae, Haemophilus influenzae* and *Neisseria gonorrhoeae*. The chromosomally mediated β-lactamases of *Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Bacteroides fragilis* and *Moraxella catarrhalis* are also inhibited, as are the extended-spectrum β-lactamases. The frequency of β-lactamase mediated resistance has continued to rise over the years, but the majority of clinically significant β-lactamases are inhibited by clavulanate.

5.3 Pharmacokinetic properties:

Combining clavulanic acid with beta lactam antibiotic causes no appreciable alteration of the pharmacokinetics of either drug compared with their separate administration.

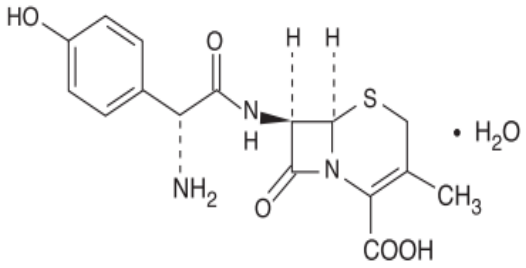
Cefadroxil is rapidly absorbed after oral administration. Following single doses of 500 mg and 1000 mg, average peak serum concentrations were approximately 16 and 28 μg/mL, respectively. Measurable levels were present 12 hours after administration. Over 90% of the drug is excreted unchanged in the urine within 24 hours. Peak urine concentrations are approximately 1800 μg/mL during the period following a single 500 mg oral dose. Increases in dosage generally produce a proportionate increase in cefadroxil monohydrate urinary concentration. The urine antibiotic concentration, following a 1g dose, was maintained well above the MIC of susceptible urinary pathogens for 20 to 22 hours.

6. Nonclinical properties:

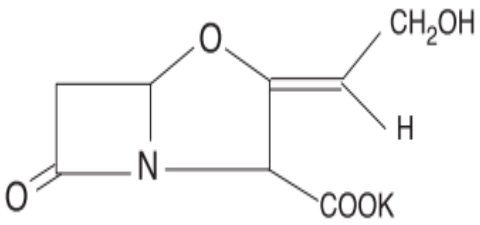
Pre-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, safety pharmacology, genotoxicity and toxicity to reproduction.

7. Description:

Cefadroxil is a semisynthetic cephalosporin antibiotic intended for oral administration. It is a white to off white, crystalline powder. It is slightly soluble in water, practically insoluble in ethanol (95%), in chloroform and in ether. It is chemically designated as 7-[(R)-2-amino-2-(4-hydroxyphenyl)acetamido]-3- methyl-3-cephem-4-carboxylic acid monhydrate. The Cefadroxil molecular formula is $C_{16}H_{17}N_3O_5S,H_2O$ and the molecular weight is 381.4. It has the following structural formula:



Clavulanic acid is produced by the fermentation of Streptomyces clavuligerus. It 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.
Clavulanic acid is particularly active against the clinically important plasmid-mediated β-lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins. Potassium Clavulanate is a white to off white, crystalline hygroscopic powder. It is freely soluble in water; slightly soluble in ethanol (95 per cent); very slightly soluble in acetone. The clavulanate potassium molecular formula is $C_8H_8KNO_5$, and the molecular weight is 237.3. Chemically, clavulanate potassium is potassium (Z) (2R,5R) -3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]- heptane-2-carboxylate, and may be represented structurally as:



Product Description:

<u>Droxyl clav 500</u>

Cefadroxil And potassium Clavulanate Tablets are white to off white capsule shape, biconvex, film coated tablets, plain on both the side.

The excipients used are Mannitol, Crospovidone, Colloidal silicon dioxide (AEROSIL)IP, Magnesium stearate IP, Hydroxy propyl methyl Celu.(metho E15)IP, Ethyl cellulose 10 CPS USP-NF, Diethyl phthalate USP/NF, Titanium dioxide IP, Methanol IP, Methylene chloride IP.

8. Pharmaceutical particulars:

8.1 Incompatibilities:

None stated.

8.2 Shelf-life:

Do not use later than the date of expiry.

8.3 Packaging information:

DROXYL CLAV 500 are available in strip pack of 10’s tablets.

8.4 Storage and handing instructions:

Store at a temperature not exceeding 25ºC, protected from light and moisture.

Keep out of reach of children.

9. Patient Counselling Information

Package leaflet: Information for the user

DROXYL CLAV 500

Cefadroxil And potassium Clavulanate Tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet?

9.1. What DROXYL CLAV 500 is and what it is used for

DROXYL CLAV 500 consists of Cefadroxil and Potassium Clavulanate. Cefadroxil is a cephalosporin for oral administration which inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins. The result is formation of a defective cell wall that is osmotically unstable, and bacterial cell lysis. Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect. It is an antibiotic indicated for the adult patients with infections caused by susceptible microorganisms. In Urinary tract Infection, Lower Respiratory tract infection and gonococcal urethritis and ENT infections.

9.2. What you need to know before you take DROXYL CLAV 500

- Patients should know that antibacterial drugs including DROXYL CLAV 500 should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold).
- When DROXYL CLAV 500 is prescribed to treat a bacterial infection, patients should know that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed.
- Skipping doses or not completing the full course of therapy may (1)decrease the effectiveness of the immediate treatment and (2)increase the likelihood that bacteria will develop resistance and will not be treatable by DROXYL CLAV 500 or other antibacterial drugs in the future.
- Diarrhea is a common problem caused by antibiotics, which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or

more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Do not take DROXYL CLAV 500

If you have known hypersensitivity to cephalosporin antibiotics.

Warnings and precautions

Talk to your doctor or pharmacist before taking DROXYL CLAV 500. Inform your doctor if you have or develop one of the following problems:

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions in patients on penicillin therapy mainly with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens.

If taken by penicillin-sensitive patients, caution should be exercised because cross-sensitivity to beta-lactam antibiotics, with a history of penicillin allergy may occur. DROXYL CLAV 500 should be taken with caution in patients with history of gastrointestinal disease particularly colitis.

Serious acute hypersensitivity reactions arises in treatment with Epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Clostridium difficile associated diarrhea (CDAD) has been reported, which may range in severity from mild diarrhea to fatal colitis.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clavulanate potassium, and has ranged in severity from mild to life-threatening.

DROXYL CLAV 500 with food and drink

You can take your tablets with or without food.

Pregnancy, breast-feeding and fertility

This drug should be used during pregnancy only if clearly needed.

Caution should be exercised when DROXYL CLAV 500 is administered to a nursing mother.

Driving and using machines

None stated.

9.3. How to take DROXYL CLAV 500

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

- Your doctor will tell you how many tablets to take and how long to take them for. This will depend on your condition, how old you are.

If you take more DROXYL CLAV 500 than you should

If you take more DROXYL CLAV than prescribed by your doctor, talk to your doctor or pharmacist straight away.

If you forget to take DROXYL CLAV 500

- If you forget to take a dose, take it as soon as you remember it. However, if it is almost time for your next dose, skip the missed dose.

- Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

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

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
If you notice any of the following serious side effects, stop taking DROXYL CLAV 500 and contact a doctor immediately:
Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment. Dyspepsia, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black "hairy" tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudomembranous colitis have been reported rarely. Diarrhea, Skin rashes, pruritus, urticaria, angioedema, serum sickness - like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis, hypersensitivity vasculitis, and an occasional case of exfoliative dermatitis (including toxic epidermal necrolysis), hepatic dysfunction including cholestasis and elevations in serum transaminase, genital pruritus, genital moniliasis, vaginitis, moderate transient neutropenia, fever. Agranulocytosis, thrombocytopenia, idiosyncratic hepatic failure, erythema multiforme, Stevens - Johnson syndrome, serum sickness, and arthralgia, Interstitial nephritis and hematuria, Crystalluria, 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.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

9.5. How to store DROXYL CLAV 500

- Keep this medicine out of the sight and reach of children.
- Store at a temperature not exceeding 25^{o}C, protected from light and moisture.
- Do not use this medicine after the expiry date, which is stated on the carton and bottle after expiry. The expiry date refers to the last day of that month.
- Store this medicine in the original package (blister) or keep the bottle tightly closed in order to protect from moisture.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

9.6. Contents of the pack and other information

What DROXYL CLAV 500 contains

The active substance is Cefadroxil and Potassium Clavulanate. DROXYL CLAV is Fixed Dose Combination of Cefadroxil and Potassium Clavulanate film coated tablets comes in strength containing 500 mg of Cefadroxil and Potassium Clavulanate 125 mg.

DROXYL CLAV 500

The other ingredients are Mannitol, Crospovidone, Colloidal silicon dioxide (AEROSIL)IP, Magnesium stearate IP, Hydroxy propyl methyl Celu.(metho E15)IP, Ethyl cellulose 10 CPS USP-NF, Diethyl phthalate USP/NF, Titanium dioxide IP, Methanol IP, Methylene chloride IP.

Colour: Titanium dioxide I.P.

DROXYL CLAV 500 are available in strip pack of 10's tablets.

10. Details of manufacturer

Manufactured by:
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist . Mehsana India
At : Block No. 10-13, Nr. M.N. Desai Petrol Pump, Sarkhej-Bavla Road, Village Changodar, Dist.: Ahmedabad 382 213
OR
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist . Mehsana India
At : Plot No. 16, Vardhman Industrial Estate, Vill. Bahadarpur Saini, N.H. 58, Haridwar 247 667 (Uttarakhand)

11. Details of permission or licence number with date

Torrent Pharmaceuticals Ltd.
Mfg lic no. G/28A/4897-A dated 21.12.2010 or Mfg lic no 24/UA/LL/SC/P-2015 dated 26.10.2020

12. Date of revision

NOV/2020

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/DROXYL CLAV 500, 125 mg/NOV-20/02/PI