To be sold by retail on the prescription of R.M.P only

AMPOXIN CV Dry Syrup 228.5 mg/5 ml

1. Generic Name

Amoxycillin and Potassium Clavulanate Oral Suspension IP

2. Qualitative and quantitative composition

Each 5 ml after reconstitution contains:
Amoxycillin Trihydrate I.P. equivalent to Amoxycillin…. 200 mg
Potassium Clavulanate diluted I.P.
Equivalent to clavulanic acid…… 28.5 mg
Excipients……. q.s.

The excipients used are Silicon Dioxide, Xanthum Gum, Hypromellose, Colloidal Anhydrous Silica, Succinic Acid Crystals, Aspartame, Orange Flavour Dry and Raspberry Flavour Dry.

3. Dosage form and strength

Dosage form: Oral Suspension

Strength: Amoxycillin Trihydrate 200 mg and Potassium Clavulanate 28.5 mg

4. Clinical particulars

4.1 Therapeutic indication

For the treatment of LRTI infections (e.g. pneumonia, bronchitis) acute otitis media, Sinusitis, UTI, skin and soft tissue infections & bone & joint infections.

4.2 Posology and method of administration

Posology

Children < 20 kg
20 mg/2.85 mg/kg/day to 60 mg/8.5 mg/kg/day given in three divided doses.

Method of administration
Ampoxin CV is for oral use.
Ampoxin CV should be administered with a meal to minimise potential gastrointestinal intolerance.

Direction for use:
Shake the bottle to loosen powder. Slowly add water provided with this pack (about 20 ml) and shake vigorously. Adjust the volume up to mark by adding remaining water if necessary. This makes 30ml of suspension. Consume within one week after reconstitution. Store the reconstituted suspension in refrigerator when not in use.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the penicillins or to any of the excipients.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid.

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse 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 in atopic individuals. If an allergic reaction occurs, amoxicillin/clavulanic acid therapy must be discontinued and appropriate alternative therapy instituted.

In the case, that an infection is proven to be due to an amoxicillin-susceptible organisms(s) then consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance.

This presentation of Ampoxin CV is not suitable for use when there is a high risk that the presumptive pathogens have reduced susceptibility or resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. This presentation should not be used to treat penicillin-resistant S. pneumoniae.

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Amoxicillin/clavulanic acid should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.
The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction requires Ampoxin CV discontinuation and contraindicates any subsequent administration of amoxicillin.

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment.

Hepatic events have been reported very rarely reported in children. Signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and, in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects.

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening. Therefore, it is important to consider this

diagnosis in patients who present with diarrhoea during or subsequent to the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin/clavulanic acid should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin/clavulanic acid. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

In patients with renal impairment, the dose should be adjusted according to the degree of impairment.

In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained.

During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of Clavulanic acid in Ampoxin CV may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

4.5 Drugs interactions

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary.

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

Mycophenolate mofetil

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid of approximately 50% has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in pre-dose level may not

accurately represent changes in overall MPA exposure. Therefore, a change in the dose of mycophenolate mofetil should not normally be necessary in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed during the combination and shortly after antibiotic treatment.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy and Lactation
Not applicable.

Ampoxin CV is indicated in children less than 20 kg bodyweight.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines.

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.

The ADRs derived from clinical studies and post-marketing surveillance with Ampoxin CV, sorted by MedDRA System Organ Class are listed below.

The following terminologies have been used in order to classify the occurrence of undesirable effects.
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations	
Mucocutaneous candidosis	Common
Overgrowth of non-susceptible organisms	Not known
Blood and lymphatic system disorders	
Reversible leucopenia (including neutropenia)	Rare
Thrombocytopenia	Rare
Reversible agranulocytosis	Not known
Haemolytic anaemia	Not known
Prolongation of bleeding time and prothrombin time[1]	Not known
Immune system disorders[10]	
Angioneurotic oedema	Not known
Anaphylaxis	Not known
Serum sickness-like syndrome	Not known

Hypersensitivity vasculitis	Not known
Nervous system disorders	
Dizziness	Uncommon
Headache	Uncommon
Reversible hyperactivity	Not known
Convulsions[2]	Not known
Aseptic meningitis	Not known
Gastrointestinal disorders	
Diarrhoea	Common
Nausea[3]	Common
Vomiting	Common
Indigestion	Uncommon
Antibiotic-associated colitis[4]	Not known
Black hairy tongue	Not known
Tooth discolouration[11]	Not known
Hepatobiliary disorders	
Rises in AST and/or ALT[5]	Uncommon
Hepatitis[6]	Not known
Cholestatic jaundice[6]	Not known
Skin and subcutaneous tissue disorders [7]	
Skin rash	Uncommon
Pruritus	Uncommon
Urticaria	Uncommon
Erythema multiforme	Rare
Drug reaction with eosinophilia and systemic symptoms (DRESS)	Not known
Stevens-Johnson syndrome	Not known
Toxic epidermal necrolysis	Not known
Bullous exfoliative-dermatitis	Not known
Acute generalised exanthemous pustulosis (AGEP)[9]	Not known
Renal and urinary disorders	
Interstitial nephritis	Not known
Crystalluria[8]	Not known

[1] See section 4.4

[2] See section 4.4

[3] Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, they may be reduced by taking Ampoxin CV at the start of a meal.

[4] Including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)

[5] A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.

[6] These events have been noted with other penicillins and cephalosporins (see section 4.4).
[7] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).
[8] See section 4.9
[9] See section 4.4
[10] See sections 4.3 and 4.4
[11] Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

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

Symptoms and signs of overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained.

Treatment of intoxication
Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

5. Pharmacological properties

5.1 Mechanism of Action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

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

PK/PD relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The two main mechanisms of resistance to amoxicillin/clavulanic acid are:
• Inactivation by those bacterial beta-lactamases that are not themselves inhibited by clavulanic acid, including class B, C and D.
• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.
Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin/clavulanic acid are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Organism	Susceptibility Breakpoints (µg /ml)		
	Susceptible	Intermediate	Resistant
Haemophilus influenzae[1]	≤ 1	-	> 1
Moraxella catarrhalis[1]	≤ 1	-	> 1
Staphylococcus aureus [2]	≤ 2	-	> 2
Coagulase-negative staphylococci [2]	≤ 0.25		> 0.25
Enterococcus[1]	≤ 4	8	> 8
Streptococcus A, B, C, G[5]	≤ 0.25	-	> 0.25
Streptococcus pneumoniae[3]	≤ 0.5	1-2	> 2
Enterobacteriaceae[1,4]	-	-	> 8
Gram-negative Anaerobes[1]	≤ 4	8	> 8
Gram-positive Anaerobes[1]	≤ 4	8	> 8
Non-species related breakpoints[1]	≤ 2	4-8	> 8

[1] The reported values are for Amoxicillin concentrations. For susceptibility testing purposes, the concentration of Clavulanic acid is fixed at 2 mg/l.
[2] The reported values are Oxacillin concentrations.
[3] Breakpoint values in the table are based on Ampicillin breakpoints.
[4] The resistant breakpoint of R>8 mg/l ensures that all isolates with resistance mechanisms are reported resistant.
[5] Breakpoint values in the table are based on Benzylpenicillin breakpoints.

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As

necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobic Gram-positive micro-organisms *Enterococcus faecalis* *Gardnerella vaginalis* *Staphylococcus aureus (*methicillin-susceptible)£ Coagulase-negative staphylococci (methicillin-susceptible) *Streptococcus agalactiae* *Streptococcus pneumoniae*[1] *Streptococcus pyogenes* and other beta-haemolytic streptococci *Streptococcus viridans* group Aerobic Gram-negative micro-organisms *Capnocytophaga* spp. *Eikenella corrodens* *Haemophilus influenzae*[2] *Moraxella catarrhalis* *Pasteurella multocida* Anaerobic micro-organisms *Bacteroides fragilis* *Fusobacterium nucleatum* *Prevotella* spp.
Species for which acquired resistance may be a problem
Aerobic Gram-positive micro-organisms *Enterococcus faecium* $ Aerobic Gram-negative micro-organisms *Escherichia coli* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Proteus mirabilis* *Proteus vulgaris*
Inherently resistant organisms
Aerobic Gram-negative micro-organisms *Acinetobacter* sp. *Citrobacter freundii* *Enterobacter* sp. *Legionella pneumophila* *Morganella morganii* *Providencia* spp. *Pseudomonas* sp. *Serratia* sp.

Stenotrophomonas maltophilia Other micro-organisms *Chlamydophila pneumoniae* *Chlamydophila psittaci* *Coxiella burnetti* *Mycoplasma pneumoniae*
$ Natural intermediate susceptibility in the absence of acquired mechanism of resistance. £All methicillin-resistant staphylococci are resistant to amoxicillin/clavulanic acid [1]*Streptococcus pneumoniae* that are resistant to penicillin should not be treated with this presentation of amoxicillin/clavulanic acid. [2] Strains with decreased susceptibility have been reported in some countries in the EU with a frequency higher than 10%.

5.3 Pharmacokinetic properties

Absorption

Amoxicillin and clavulanic acid, are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (Tmax) in each case is approximately one hour.

The pharmacokinetic results for a study, in which amoxicillin/clavulanic acid (500 mg/125 mg tablets three times daily) was administered in the fasting state to groups of healthy volunteers are presented below.

Mean (+/- SD) pharmacokinetic parameters					
Active substance(s) administered	Dose (mg)	Cmax (µg/ml)	Tmax * (h)	AUC (0-24h) ((µg.h/ml)	T 1/2 (h)
Amoxicillin					
AMX/CA 500/125 mg	500	7.19 +/- 2.26	1.5 (1.0-2.5)	53.5 +/- 8.87	1.15 +/- 0.20
Clavulanic acid					
AMX/CA 500 mg/125 mg	125	2.40 +/- 0.83	1.5 (1.0-2.0)	15.72 +/- 3.86	0.98 +/-0.12
AMX – amoxicillin, CA – clavulanic acid * Median (range)					

Amoxicillin and clavulanic acid serum concentrations achieved with amoxicillin/clavulanic acid are similar to those produced by the oral administration of equivalent doses of amoxicillin or clavulanic acid alone.

Distribution

About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0.3-0.4 l/kg for amoxicillin and around 0.2 l/kg for clavulanic acid.
Following intravenous administration, both amoxicillin and clavulanic acid have been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.
From animal studies there is no evidence for significant tissue retention of drug-derived material for either component. Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanic acid can also be detected in breast milk.
Both amoxicillin and clavulanic acid have been shown to cross the placental barrier.

Biotransformation
Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose. Clavulanic acid is extensively metabolized in man and eliminated in urine and faeces and as carbon dioxide in expired air.

Elimination
The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms.
Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/h in healthy subjects. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of single Co-amoxiclav 250 mg/125 mg or 500 mg/125 mg tablets. Various studies have found the urinary excretion to be 50-85% for amoxicillin and between 27-60% for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.
Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid.

Age
The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. 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.

Gender
Following oral administration of amoxicillin/clavulanic acid to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of either amoxicillin or clavulanic acid.

Renal impairment
The total serum clearance of amoxicillin/clavulanic acid decreases proportionately with decreasing renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid.

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Nonclinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

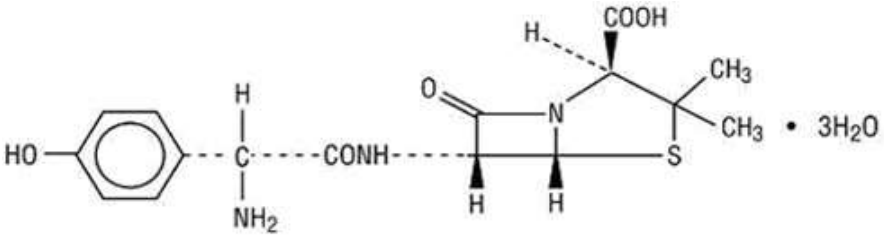
Repeat dose toxicity studies performed in dogs with amoxicillin/clavulanic acid demonstrate gastric irritancy and vomiting, and discoloured tongue.

Carcinogenicity studies have not been conducted with Ampoxin CV or its components.

7. Description

Amoxycillin Trihydrate

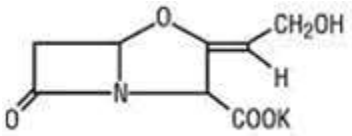
Amoxycillin Trihydrate is an analog of ampicillin, derived from the basic penicillin nucleus, 6-aminopenicillanic acid. Chemically, Amoxycillin is (6R)-6-[(α-4-hydroxyphenyl)-D-glycylamino) penicillanic acid trihydrate and may be represented structurally as:



The molecular formula is $C_{16}H_{19}N_3O_5S.3H_2O$ and molecular weight is 419.45. It is white or almost white, crystalline powder which is slightly soluble in water, in ethanol (95%) and in methanol; soluble in dilute solutions of acids and of alkali hydroxides; practically insoluble in chloroform, in ether and in fixed oils.

Potassium Clavulanate

Potassium Clavulanate molecular formula is $C_8H_8KNO_5$, and the molecular weight is 237.25. Chemically, Potassium Clavulanate 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:



Potassium Clavulanate is white to off-white, crystalline hygroscopic powder which is freely soluble in water; slightly soluble in ethanol (95%); very slightly soluble in acetone.

Amoxycillin & Potassium Clavulanate Oral Suspension is white to off white powder, which on reconstitution gives white to off white coloured suspension. The excipients used are Silicon

Dioxide, Xanthum Gum, Hypromellose, Colloidal Anhydrous Silica, Succinic Acid Crystals, Aspartame, Orange Flavour Dry and Raspberry Flavour Dry

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

AMPOXIN CV Dry Syrup is packed in 30ml glass bottle with water for reconstitution and is placed in printed carton.

8.4 Storage and handing instructions

Store in a cool and dry place. Protect from light.
Keep all medicines out of reach of children

9. Patient counselling information

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.

What is in this leaflet?

9.1 What AMPOXIN CV is and what it is used for

AMPOXIN CV Dry Syrup contains the active substance Amoxycillin and Potassium Clavulanate. Amoxicillin is semisynthetic penicillin (beta-lactam antibiotic) and Potassium Clavulanate is a salt form of clavulanic acid a beta-lactam structurally related to penicillins.

AMPOXIN CV Dry Syrup is used for the treatment of For the treatment of LRTI infections (e.g. pneumonia, bronchitis) acute otitis media, Sinusitis, UTI, skin and soft tissue infections & bone & joint infections.

9.2 What you need to know before you take AMPOXIN CV

Do not give AMPOXIN CV to your child:

– if your child is allergic to Amoxycillin & Potassium Clavulanate, or to any of the other ingredients of this medicine.

– History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam)

Warnings and precautions

Talk to your doctor before taking AMPOXIN CV if your child is suffering or have ever suffered from any of the following conditions or illnesses:

• Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy
• antibiotic-associated colitis

Talk to your doctor before taking AMPOXIN CV:

- If your child is on oral anticoagulants (for example acenocoumarol or warfarin).
- If your child is on Methotrexate, as Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity
- If your child is on Probenecid, as Probenecid decreases the renal tubular secretion of amoxicillin.

9.3 How to take AMPOXIN CV

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose will be directed by physician.

Method of administration: AMPOXIN CV is for oral use only.

Direction for use:
Shake the bottle to loosen powder. Slowly add water provided with this pack (about 20 ml) and shake vigorously. Adjust the volume up to mark by adding remaining water if necessary. This makes 30ml of suspension. Consume within one week after reconstitution. Store the reconstituted suspension in refrigerator when not in use.

If you accidentally give more AMPOXIN CV to your child than you should

Tell your doctor or pharmacist immediately. If possible take your medicine and this leaflet with you.

If you forget to give AMPOXIN CV to your child

Do not give a double dose to make up for the forgotten dose.

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

9.4 Possible side effects

The following very common, common, uncommon, rare, very rare and not known side effect has been reported. If this causes you problems, you should contact your doctor.

Frequency estimate: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), Not known (cannot be estimated from the available data).

Infections and infestations

Common: Mucocutaneous candidosis

Not known: Overgrowth of non-susceptible organisms

Blood and lymphatic system disorders

Rare: Reversible leucopenia (including neutropenia), Thrombocytopenia

Not known: Reversible agranulocytosis, Haemolytic anaemia, Prolongation of bleeding time and prothrombin time

Immune system disorders

Not known: Angioneurotic oedema, Anaphylaxis, Serum sickness-like syndrome, Hypersensitivity vasculitis

Nervous system disorders

Uncommon: Dizziness, Headache

Not known: Reversible hyperactivity, Convulsions, Aseptic meningitis

Gastrointestinal disorders

Common: Diarrhoea, Nausea, Vomiting

Uncommon: Indigestion

Not known: Antibiotic-associated colitis, Black hairy tongue, Tooth discolouration

Hepatobiliary disorders

Uncommon: Rises in AST and/or ALT

Not known: Hepatitis, Cholestatic jaundice

Skin and subcutaneous tissue disorders

Uncommon: Skin rash, Pruritus, Urticaria

Rare: Erythema multiforme

Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome, Toxic epidermal necrolysis, Bullous exfoliative-dermatitis, Acute generalised exanthemous pustulosis (AGEP)

Renal and urinary disorders

Not known: Interstitial nephritis, Crystalluria

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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. By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store AMPOXIN CV

Store in a cool and dry place. Protect from light.

9.6 Contents of the pack and other information

What **AMPOXIN CV Dry Syrup** contains

The active substances **AMPOXIN CV Dry Syrup** is Amoxycillin and Potassium Clavulanate.

The excipients used are Silicon Dioxide, Xanthum Gum, Hypromellose, Colloidal Anhydrous Silica, Succinic Acid Crystals, Aspartame, Orange Flavour Dry and Raspberry Flavour Dry.

AMPOXIN CV Dry Syrup is packed in 30ml glass bottle with water for reconstitution and is placed in printed carton.

10. Details of manufacturer

Manufactured in India by:

Torrent Pharmaceuticals Ltd.
Indrad-382721, Dist. Mehsana, INDIA.
At: Plot No. 16, Vardhman Industrial Estate,
Vill – Bahadarpur Saini, N.H. 58, Haridwar – 247667 (Uttarakhand)

11. Details of permission or licence number with date

Mfg Lic No. 24/UA/LL/SC/P/2015 issued on 01.01.2018

12. Date of revision

May 2021

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/AMPOXIN CV Dry Syrup 228.5 mg/5 ml /MAY-21/03/PI