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

℞Amoxycillin and Potassium Clavulanate Oral Suspension IP 228.5 mg and 457 mg

Moxanute® CV DUO / Moxanute® CV DDS

COMPOSITION

Moxanute® CV DUO

Each Combipack contains:

(A) Amoxycillin and Potassium Clavulanate Oral Suspension IP 228.5 mg

Each 5ml of reconstituted suspension contains:

Amoxycillin Trihydrate IP

eq. to Amoxycillin……..200 mg

Potassium Clavulanate Diluted IP

eq. to Clavulanic acid…..…….28.5 mg

Excipients…….q.s.

(B) Sterile Water for Reconstitution 30 ml

Moxanute® CV DDS

Each Combipack contains:

(A) Amoxycillin and Potassium Clavulanate Oral Suspension IP 457 mg

Each 5ml of reconstituted suspension contains:

Amoxycillin Trihydrate IP

eq. to Amoxycillin……....400 mg

Potassium Clavulanate Diluted IP

eq. to Clavulanic acid…..…….....57 mg

Excipients…….....q.s.

(B) Sterile Water for Reconstitution 30 ml

Dosage form:

Dry Powder for Oral suspension.

Therapeutic indications:

Moxanute CV should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data.

Moxanute CV suspension (228 mg/5 mL and 457 mg/5 mL), for twice daily oral dosing, is indicated for short term treatment of bacterial infections at the following sites when amoxicillin resistant beta-lactamase producing strains are suspected as the cause. In other situations, amoxicillin alone should be considered.

Upper respiratory tract infections (including ENT) e.g. recurrent tonsillitis, sinusitis, otitis media.

Lower respiratory tract infections e.g. acute exacerbations of chronic bronchitis, lobar and bronchopneumonia.

Urinary tract infections e.g. cystitis, urethritis, pyelonephritis

Skin and soft tissue infections e.g. cellulitis, animal bites.

Dental infections e.g. severe dental abscess with spreading cellulitis.

Susceptibility to Moxanute CV will vary with geography and time *(see Pharmacological Properties, Pharmacodynamics for further information).* Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Mixed infections caused by amoxicillin-susceptible organisms in conjunction with Moxanute CV susceptible beta-lactamase-producing organisms may be treated with Moxanute CV suspension 228 mg/5 ml and 457 mg/5 ml. These infections should not require the addition of another antibiotic resistant to beta-lactamases.

Posology and method of administration:

Dosage depends on the age, weight and renal function of the patient and the severity of the infection.

Dosages are expressed throughout in terms of amoxicillin/clavulanate content except when doses are stated in terms of an individual component.

To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of Moxanute CV is optimised when taken at the start of a meal.

Treatment should not exceed 14 days without review.

Therapy can be started parenterally and continued with an oral preparation.

The usual recommended daily dosage is:

- *Lower dose:* 25/3.6 to 45/6.4 mg/kg/day in two divided doses for mild to moderate infections (upper respiratory tract infections e.g. recurrent tonsillitis, lower respiratory infections and skin and soft tissue infections).
- *Higher dose:* 45/6.4 to 70/10 mg/kg/day in two divided doses for the treatment of more serious infections (upper respiratory tract infections e.g. otitis media and sinusitis, lower respiratory tract infections e.g. bronchopneumonia and urinary tract infections).

No clinical data are available on doses above 45/6.4 mg/kg/day in children under 2 years.

There are no clinical data for Moxanute CV suspension 228 mg/5 ml and 457 mg/5 ml to make dosage recommendations for children under 2 months old.

The tables below give dosage guidance for children.

Children 2 years and over

Moxanute CV suspension 228 mg/5 ml		
Body weight (kg)	**For lower dose range (ml every 12 hours)**	**For higher dose range (ml every 12 hours)**
12 to 16	5	10
17 to 26	10	15

Moxanute CV suspension 457 mg/5 ml		
Body weight (kg)	**For lower dose range (ml every 12 hours)**	**For higher dose range (ml every 12 hours)**
12 to 16	2.5	5
17 to 26	5	7.5
27 to 35	7.5	10
36 to < 40	10	12.5

Children aged 2 months to under 2 years

Moxanute CV suspension 457 mg/5 ml		
Body weight (kg)	**Lower dose at 25/3.6 mg/kg/day (ml every 12 hours)**	**Higher dose at 45/6.4 mg/kg/day (ml every 12 hours)**
2	0.3	0.6
3	0.5	0.8
4	0.6	1.1
5	0.8	1.4
6	0.9	1.7
7	1.1	2.0
8	1.3	2.3
9	1.4	2.5
10	1.6	2.8
11	1.7	3.1
12	1.9	3.4
13	2.0	3.7
14	2.2	3.9
15	2.3	4.2

Renal Impairment

No adjustment in dose is required in patients with creatinine clearance greater than 30 ml/min.

Moxanute CV suspension 228 mg/5 mL and 457 mg/5 mL are not recommended in patients with a creatinine clearance of less than 30 mL/min.

Hepatic Impairment

Dose with caution; monitor hepatic function at regular intervals. There is, as yet, insufficient evidence on which to base a dosage recommendation.

Contraindications:

Moxanute CV is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

Moxanute CV is contraindicated in patients with a previous history of Moxanute CV - associated jaundice/hepatic dysfunction.

Special Warnings and Precautions:

Before initiating therapy with Moxanute CV, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens.

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. If an allergic reaction occurs, Moxanute CV therapy must be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous (i.v.) steroids and airway management (including intubation) may also be required.

Moxanute CV 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.

Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving Moxanute CV and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Changes in liver function tests have been observed in some patients receiving Moxanute CV. The clinical significance of these changes is uncertain but Moxanute CV should be used with caution in patients with evidence of hepatic dysfunction.

Cholestatic jaundice, which may be severe, but is usually reversible, has been reported rarely. Signs and symptoms may not become apparent for up to six weeks after treatment has ceased.

In patients with renal impairment Moxanute CV suspension 228 mg/5 mL and 457 mg/5 mL are not recommended.

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.

Drug Interactions:

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

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. There are no data on the concomitant use of Moxanute CV and allopurinol.

In common with other antibiotics, Moxanute CV may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

In the literature there are rare 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 Moxanute CV.

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.

Use in special populations:

Pregnancy

Reproduction studies in animals (mice and rats) with orally and parenterally administered Moxanute CV have shown no teratogenic effects. In a single study in women with pre-term, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with Moxanute CV may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.

Lactation

Moxanute CV may be administered during the period of lactation. With the exception of the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no detrimental effects for the infant.

Effects on ability to drive and use machines:

Adverse effects on the ability to drive or operate machinery have not been observed.

Undesirable effects:

Data from large clinical trials were used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e., those occurring at < 1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

very common ≥ 1/10

common ≥ 1/100 to < 1/10

uncommon ≥ 1/1000 to < 1/100

rare ≥ 1/10,000 to < 1/1000

very rare < 1/10,000.

Infections and infestations	
Common	Mucocutaneous candidiasis
Blood and lymphatic system disorders	
Rare	Reversible leucopenia (including neutropenia) and thrombocytopenia
Very rare	Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time.
Immune system disorders	
Very rare	Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis
Nervous system disorders	
Uncommon	Dizziness, headache
Very rare	Reversible hyperactivity, aseptic meningitis, convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Gastrointestinal disorders	
Adults	
Very common	Diarrhoea
Common	Nausea, Vomiting
Children	
Common	Diarrhoea, Nausea, Vomiting

All populations

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

Uncommon	Indigestion
Very rare	Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis – see Warnings and Precautions) Black hairy tongue Superficial tooth discoloration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discoloration as it can usually be removed by brushing.
Hepatobiliary disorders	
Uncommon	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.
Very Rare	Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins.

Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been 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.

Skin and subcutaneous tissue disorders	
Uncommon	Skin rash, pruritus, urticaria
Rare	Erythema multiforme
Very rare	Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS)

If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.

Adverse Drug Reaction Reported:

Severe cutaneous adverse reactions (SCARS) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome(SJS) drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with Amoxicillin/clavulanate . Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Treatment should be discontinued.

Renal and urinary disorders	
Very rare	Interstitial nephritis, crystalluria (see Overdose)

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbpharma.com

Overdose:

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Gastrointestinal symptoms may be treated symptomatically with attention to the water electrolyte balance.

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed.

Moxanute CV can be removed from the circulation by haemodialysis.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in Moxanute CV suspension anticipates this defence mechanism by blocking the beta-lactamase enzymes, thus rendering the organisms sensitive to amoxicillin's rapid bactericidal effect at concentrations readily attainable in the body.

Clavulanate by itself has little antibacterial activity; however, in association with amoxicillin as Moxanute CV. It produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.

In the list below, organisms are categorised according to their in vitro susceptibility to Moxanute CV.

In vitro susceptibility of micro-organism to Moxanute CV

Where clinical efficacy of Moxanute CV has been demonstrated in clinical trials this is indicated with an asterisk (*).

Organisms that do not produce beta-lactamase are identified (with †). If an isolate is susceptible to amoxicillin, it can be considered susceptible to Moxanute CV.

Commonly susceptible species

Gram-positive aerobes:

Bacillius anthracis

Enterococcus faecalis

Listeria monocytogenes

Nocardia asteroids

Streptococcus pyogenes†

Streptococcus agalactiae†

Streptococcus spp. (other beta-hemolytic) †

*Staphylococcus aureus (methicillin susceptible)**

Staphylococcus saprophyticus (methicillin susceptible)

Coagulase negative staphylococcus (methicillin susceptible)

Gram-negative aerobes:

Bordetella pertussis

Haemophilus influenzae

Haemophilus parainfluenzae

Helicobacter pylori

Moraxella catarrhalis

Neisseria gonorrhoeae

Pasteurella multocida

Vibrio cholera

Other

Borrelia burgdorferi

Leptospira ictterohaemorrhagiae

Treponema pallidum

Species for which acquired resistance may be a problem

Gram positive anaerobes:

Clostridium spp.

Peptococcus niger

Peptostreptococcus magnus

Peptostreptococcus micros

Peptostreptococcus spp.

Gram-negative anaerobes:
Bacteroides fragilis
Bacteroides spp.
Capnocytophaga spp.
Eikenella corrodens
Fusobacterium nucleatum
Fusobacterium spp.
Porphyromonas spp.
Prevotella spp.

Species for which acquired resistance may be a problem

Gram-negative aerobes:
*Escherichia coli**
Klebsiella oxytoca
*Klebsiella pneumonia**
Klebsiella spp.
Proteus mirabilis
Proteus vulgaris
Proteus spp.
Salmonella spp.
Shigella spp.

Gram-positive aerobes:
Corynebacterium spp.
Enterococcus faecium
Streptococcus pneumonia*†
Viridans group streptococcus

Inherently resistant organisms

Gram-negative aerobes:
Acinetobacter spp.
Citrobacter freundii
Enterobacter spp.
Hafnia alvei
Legionella pneumophila
Morganella morganii
Providencia spp.
Pseudomonas spp.
Serratia spp.
Stenotrophomas maltophilia
Yersinia enterolitica

Others:
Chlamydia pneumonia
Chlamydia psittaci
Chlamydia spp.
Coxiella burnetti
Mycoplasma spp.

Pharmacokinetic properties

Absorption

The two components of Moxanute CV suspension 228 mg/5 ml and 457 mg/5 ml, amoxicillin and clavulanate, are each fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of Moxanute CV is optimised when taken at the start of a meal.

Distribution

The pharmacokinetics of the two components of Moxanute CV are closely matched. Both clavulanate and amoxicillin have low levels of serum binding; about 70% remains free in the serum. Doubling the dosage of Moxanute CV approximately doubles the serum levels achieved.

Pre-clinical Safety Data:

No further information of relevance.

Pharmaceutical particulars:

List of excipients

Micronised Silica, Xanthan gum, Hydroxyethyl Cellulose, colloidal silicon dioxide, Aspartame, Succinic acid

Incompatibilities

Not applicable

Shelf life

Refer Pack

Special precautions for storage

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

Nature and contents of container

60 ml Bottle + Sterile Water for reconstitution 30 ml

Special precautions for disposal and other handling

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

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Note: This prescribing information is applicable for India Market only