Clamovid

VICLA19-var7 (MY)

DESCRIPTION
Clamovid 625 Tablet- White colour, oblong film-coated tablet.
Clamovid Granules - Cream white colour homogen powder mixture.

COMPOSITION
Clamovid 625 Tablet- Amoxycillin (as trihydrate) 500 mg/tablet
Clavulanic Acid (as potassium clavulanate)125 mg/tablet
Clamovid Granules - Amoxycillin (as trihydrate) 125 mg/5 ml
Clavulanic Acid (as potassium clavulanate) 31.25 mg/5 ml

PHARMACODYNAMICS
Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in CLAMOVID anticipates this defense mechanism by blocking the beta-lactamase enzymes, thus rendering the organisms susceptible 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 CLAMOVID it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.

Commonly susceptible species
Gram-positive aerobes: *Bacillius anthracis, Enterococcus faecalis, Listeria monocytogenes, Nocardia asteroides, 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 cholerae.*

Other: *Borrelia burgdorferi, Leptospira ictterohaemorrhagiae, Treponema pallidum.*

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 pneumoniae, Klebsiella spp., Proteus mirabilis, Proteus vulgaris, Proteus spp., Salmonella spp., Shigella spp.*

Gram-positive aerobes: *Corynebacterium spp., Enterococcus faecium, Streptococcus pneumoniae, 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 pneumoniae, Chlamydia psittaci, Chlamydia spp., Coxiella burnetti, Mycoplasma spp.*

PHARMACOKINETICS
The pharmacokinetics of the two components of CLAMOVID are closely matched. Peak serum levels of both occur about 1 hour after oral administration. Absorption of CLAMOVID is optimised at the start of a meal. Doubling the dosage of CLAMOVID approximately doubles the serum levels achieved. Both clavulanate and amoxicillin have low levels of serum binding; about 70% remains free in the serum.

INDICATIONS
CLAMOVID is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The beta-lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other beta-lactam antibiotics.

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

CLAMOVID oral presentations are indicated for short-term treatment of bacterial infections at the following sites:
- Upper respiratory tract infections (including ENT) e.g. tonsillitis, sinusitis, otitis media.
- Lower respiratory tract infections e.g. acute exacerbation of chronic bronchitis, lobar and bronchopneumonia.
- Genito-urinary tract infections e.g. cystitis, urethritis, pyelonephritis.
- Skin and soft tissue infections, e.g. boils, abscesses, cellulitis, wound infections.
- Bone and joint infections e.g. osteomyelitis.
- Dental infections e.g. dentoalveolar abscess
- Other infections e.g. septic abortion, puerperal sepsis, intra-abdominal sepsis.

Susceptibility to CLAMOVID will vary with geography and time. Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

CONTRAINDICATIONS
- CLAMOVID is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.
- CLAMOVID is contraindicated in patients with a previous history of CLAMOVID-associated jaundice/hepatic dysfunction.

WARNINGS AND PRECAUTIONS
Before initiating therapy with CLAMOVID 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, CLAMOVID 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. CLAMOVID 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 CLAMOVID 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 CLAMOVID. The clinical significance of these changes is uncertain. CLAMOVID 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 CLAMOVID dosage should be adjusted as recommended in the Dosage and Administration section.

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.

Effects on Ability to Drive and Use Machines
Adverse effects on the ability to drive or operate machinery have not been observed.

USE IN PREGNANCY AND LACTATION
As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.

CLAMOVID 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.

Reproduction studies in animals (mice and rats) with orally and parenterally administered amoxicillin and clavulanic acid have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin + clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates.

SIDE EFFECTS
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 CLAMOVID 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

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.

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

DRUG INTERACTIONS

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with CLAMOVID 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 CLAMOVID and allopurinol.

In common with other antibiotics, CLAMOVID 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 coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of CLAMOVID.

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.

OVERDOSAGE AND TREATMENT

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 (see Warnings and Precautions). CLAMOVID can be removed from the circulation by haemodialysis.

DOSAGE AND ADMINISTRATION

Clamovid is taken orally.

CLAMOVID 625 TABLET
Dosage depends on the age and renal function of the patient and the severity of the infection. To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of CLAMOVID is optimised when taken at the start of a meal. Treatment should not be extended beyond 14 days without review. Therapy can be started parenterally and continued with an oral preparation.

Tablets should be swallowed whole without chewing. If required, tablets may be broken in half and swallowed without chewing. CLAMOVID tablets are not recommended in children of 12 years and under.

Adults and children over 12 years; ≥ 40 kg
The usual recommended daily dosage is:

Mild – Moderate infections	One CLAMOVID 625 TABLET every 12 hours.
Severe infections	One CLAMOVID 625 TABLET every 8 hours.

Renal impairment
No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 mL/min. The CLAMOVID 1g tablet should only be used in patients with a creatinine clearance (CrCl) rate of more than 30 mL/min.

CrCl 10-30 mL/min	One CLAMOVID 625 TABLET every 12 hours.
CrCl < 10 mL/min	One CLAMOVID 625 TABLET every 24 hours.
Haemodialysis	One CLAMOVID 625 TABLET every 24 hours, plus a further one tablet during dialysis, to be repeated at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased).

Hepatic impairment
Dose with caution; monitor hepatic function at regular intervals.

CLAMOVID GRANULES
CLAMOVID GRANULES recommendations for children below the age of 12 years are based on 25-50 mg/kg body weight/day (based on amoxicillin component) depending on the severity of infection.

Children 7 – 12 years: 10 ml CLAMOVID GRANULES three times a day*

Children 2 – 7 years: 5 ml CLAMOVID GRANULES three times a day*

Children 9 months – 2 years: 2.5 ml CLAMOVID GRANULES three times a day*

Children 0 – 9 months: No suitable oral presentation is currently available for this age group

Treatment with CLAMOVID GRANULES should not be extended beyond 14 days without review.

*These doses may be doubled in severe infections.

Elderly
No dose adjustment is considered necessary. The duration of therapy should be determined by the response of the patient. Some infections (e.g. osteomyelitis) require longer periods of treatment. Treatment should not be extended beyond 14 days without review.

Renal impairment
No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 ml/min. Similar reduction in dosage should be made for children.

Hepatic impairment
Dose with caution and monitor hepatic function at regular intervals.

Storage : Store below 30°C. Protect from light and moisture.
Refrigerate and use within 7 days after reconstitution.

Presentation/Packing : Tablet 625 mg x alu-alu blisters of 3 x 5's, 2 x 5's
Granules 156.25 mg/5 ml x amber glass bottles of 100 ml

Product Registration Holder (Malaysia)/
Marketing Authorisation Holder/ Product Owner: HOVID Bhd.
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