

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

CLAVACE 375

(Amoxicillin & Clavulanate Potassium Tablets USP 375mg)

2. Quality and Quantitative Composition

Each film coated tablet contains:

Amoxicillin Trihydrate USP

Equivalent to Amoxicillin.....250 mg

Clavulanate potassium USP

Equivalent to Clavulanic acid.....125 mg

Colour: Titanium Dioxide USP

For the full list of excipients, see section 6.1

3. Pharmaceutical Form

Tablet for oral use

4. Clinical Particulars

4.1 Therapeutic indications

Clavace is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the conditions listed below:

Lower respiratory tract infections – caused by (beta)-lactamase producing strains of *H. influenzae* and *M. catarrhalis*.

Otitis Media – caused by (beta)-lactamase producing strains of *H. influenzae* and *M. catarrhalis*.

Sinusitis – caused by (beta)-lactamase producing strains of *H. influenzae* and *M. catarrhalis*.

Skin and skin structure infections – caused by (beta)-lactamase producing strains of *S. aureus*, *E.coli* and *Klebsiella* spp.

Bone and joint infections

Other infections e.g. intra-abdominal sepsis and dental infections

While Clavace is indicated only for the conditions listed above, infections caused by ampicillin-susceptible organisms are also amenable to treatment with Clavace due to its amoxicillin content. Therefore, mixed infections caused by ampicillin-susceptible organisms and (beta)-lactamase producing organisms susceptible to Clavace should not require the addition of another antibiotic.

Because amoxicillin has greater in vitro activity against *S. pneumoniae* than does ampicillin or penicillin, the majority of *S. pneumoniae* strains with intermediate susceptibility to ampicillin or penicillin are fully susceptible to amoxicillin and Clavace.

4.2 Posology and method of administration:

Posology (Clavace Tablets)

Adults and children over 12 years.

Mild to Moderate infections: One tablet twice a day.

Dentoalveolar abscess: one Clavace tablet twice a day for five days.

Method of administration

Amoxicillin and Clavulanate Potassium Tablets is for oral use.

Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption of amoxicillin/clavulanic acid.

4.3 Contraindications

Clavace is contraindicated in patients with a history of allergic reactions to any penicillin. Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics, e.g. cephalosporins. It is also contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with amoxicillin-clavulanate.

4.4 Special warnings and precautions for use

Before initiating therapy with Clavace, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, Clavace should be discontinued and the appropriate therapy instituted. Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Clavace, and has ranged in severity from mild to life-threatening. 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.

If the parenteral administration of high doses is necessary, the sodium content must be taken into account in patients on a sodium restricted diet.

Change in liver function tests have been observed in some patients receiving amoxicillin-clavulanate. The clinical significance of these changes is uncertain but Clavace should be used with caution in patients with evidence of severe hepatic dysfunction. Cholestatic jaundice, which may be severe, but is usually reversible, has been reported rarely. Signs and symptoms may not become apparent for several weeks after treatment has ceased.

Clavace should be avoided if infectious mononucleosis is suspected since the occurrence of morbilliform rash has been associated with this condition following the use of amoxicillin. In patients with moderate or severe renal impairment Clavace Dry syrup 228 mg/5 ml is not recommended. Erythematous rashes have been associated with glandular fever in patients receiving amoxicillin. Clavace should be avoided if glandular fever is suspected. Prolonged use may also occasionally result in overgrowth of non-susceptible organisms. 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.

Acient Dry syrup 228 mg/5 ml contains 12.5 mg aspartame per 5 ml dose and therefore care should be taken in phenylketonuria.

While Clavace possess the characteristic low toxicity of the penicillin group of antibiotics, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic function, is advisable during prolonged therapy.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid: Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with Clavace may result in increased and prolonged blood levels of amoxicillin. Co-administration of probenecid cannot be recommended.

Anticoagulants: Prolongation of bleeding time and prothrombin time have been reported in some patients receiving amoxicillin/clavulanic acid. Clavace should be used with care in patients on anti-coagulation therapy.

Allopurinol: The concurrent administration of allopurinol and amoxicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving amoxicillin alone. There are no data with Clavace and allopurinol administered concurrently.

Contraceptives: In common with other broad-spectrum antibiotics, Clavace may reduce the efficacy of oral contraceptives.

Renal Impairment: Please refer dosage and administration.

Hepatic Impairment: Please refer dosage and administration.

4.6 Pregnancy and lactation

Pregnancy (Category B): There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation: Clavace may be administered during lactation. With the exception of the risk of sensitization, associated with the excretion of trace quantities in breast milk, there are no known detrimental effects for the infant.

Paediatrics: As per directions given in dosage and administration.

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

Amoxicillin-clavulanate is generally well tolerated. The majority of side effects observed in clinical trials were of a mild and transient nature and less than 3% of patients discontinued therapy because of drug-related side effects. From the original premarketing studies, where both paediatric and adult patients were enrolled, the most frequently reported adverse effects were diarrhoea/loose stools (9%), nausea (3%), skin rashes and urticaria (935), vomiting (1%) and vaginitis (1%). The overall incidence of side effects, and in particular diarrhoea, increased with the higher recommended dose. Other less frequently reported reactions include: Abdominal discomfort, flatulence, and headache.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at <https://primaryreporting.who-umc.org/ET> or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhoea. Rash, hyperactivity, or drowsiness has also been observed in a small number of patients.

In the case of overdose, discontinue Clavace, treat symptomatically, and institute supportive measures as required. If the overdosage is very recent and there is no contraindication, an attempt at emesis or other means of removal of drug from the stomach may be performed.

Interstitial nephritis resulting in oliguric renal failure use been reported in a small number of patients after overdosage with amoxicillin. Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adults and paediatric patients. In case of overdosage, adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of both amoxicillin and clavulanate. Both amoxicillin and clavulanate are removed from the circulation by haemodialysis.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: **Combinations of penicillins, incl. beta-lactamase inhibitors.**

ATC Code: **J01CR02**

Clavace is a combination of amoxicillin and clavulanic acid. Amoxicillin has a broad spectrum of bactericidal activity against many gram positive and gram-negative microorganisms. Amoxicillin is, however, susceptible to degradation by (beta⁰-lactamases, and therefore, the spectrum of activity does not include organisms which produce these enzymes. The formulation of amoxicillin and clavulanic acid in Clavace protects amoxicillin from degradation by (beta⁰-lactamase enzymes and effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other (beta)-lactam antibiotics.

Amoxicillin/clavulanic acid has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.

Gram-Positive Microorganisms:

Aerobes

Staphylococcus aureus
Coagulase-negative Staphylococci (Including Staphylococci epidermidis)
Streptococcus pyogenes
Bacillus anthracis
Corynebacterium species
Streptococcus viridans
Enterococcus faecium
Enterococcus faecalis
Listeria monocytogenes
Streptococcus agalactiae
Anaerobes:
Clostridium species
Peptococcus species
Peptostreptococcus species
Gram-Negative Microorganisms:
Aerobes
Escherichia coli
Proteus mirabilis
Proteus vulgaris
Klebsiella species
Salmonella species
Shigella species
Bordetella pertussis
Gardnerella pertussis
Gardnerella vaginalis
Legionella species
Brucella species
Neisseria gonorrhoeae
Haemophilus influenzae
Moraxella catarrhalis
Pasteurella multocida
Vibrio cholerae
Helicobacter pylori
Yersinia enterocolitica

Anaerobes

Bacteroides species including B. fragilis

Fusobacterium species

5.2 Pharmacokinetic Properties

Combining clavulanic acid with amoxicillin causes no appreciable alteration of the pharmacokinetics of either drug compared with their separate administration. After oral administration, both components achieve maximum plasma concentration in about an hour.

Absorption is unaffected by food, milk, ranitidine or pirenzepine. The tissue and body fluid distribution of both components is generally adequate to achieve antibacterial levels, although the concentrations may be somewhat low in bronchial secretions and cerebrospinal fluid. The pharmacokinetic profile of amoxicillin and clavulanic acid in children parallels that in adults.

5.3 Preclinical safety Data

Non-clinical 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 amoxicillin/clavulanic acid.

6.0 Pharmaceutical Particulars

6.1 List of excipients

Excipients

Sodium Starch Glycolate

Croscarmellose sodium

Colloidal Silicon Dioxide (Aerosil-200)

Talc

Magnesium Stearate

Micro Crystalline Cellulose (Avicel 200)

Hydroxy Propyl Methyl Cellulose E5 (HPMC-E5)

Hydroxy Propyl Methyl Cellulose E15 (HPMC-E15)

Ethyl Cellulose

Diethyl Phthalate

Isopropyl Alcohol

Dichloromethane (Methyl Chloride)

Titanium Dioxide

Polyethylene glycol 6000

6.2 Incompatibilities: Not applicable

6.3 Shelf life: 24 months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C.

Protected from light and moisture.

6.5 Nature and contents of container

Alu-Alu blister of 10 tablets is packed in unit carton along with pack insert.

6.6 Special precautions for disposal and other handling: Not Applicable**7.0 Marketing authorization holder****Cachet Pharmaceuticals Pvt. Ltd**

415, Shah Nahar Industrial Estate,
Dr. E. Moses Road, Worli, Mumbai-400 018,
Maharashtra, India.

Name and Address of Manufacturer**INDCHEMIE HEALTH SPECIALITIES PVT. LTD.**

Village – Than, Tehsil – Baddi, Dist. - Solan
Himachal Pradesh – 173 205, India

8.0 Marketing Authorization Numbers

04647/07406/NMR/2019

9.0 Date of first authorization/renewal of the authorization

Date of first authorisation: 03/10/2019

10.0 Date of revision of the text

05.07.2023