SUMMARY OF PRODUCT CHARACTERISTICS
CLAVACE 625
(Amoxicillin & Clavulanate Potassium Tablets USP)

1. Name of the Medicinal Product

1.1 Product Name

CLAVACE 625
(Amoxicillin & Clavulanate Potassium Tablets USP)

1.2 Strength

Each film coated tablet contains:

Amoxicillin Trihydrate USP

Equivalent to Amoxicillin…….500 mg

Clavulanate potassium USP

Equivalent to Clavulanic acid……...125 mg

Colour: Titanium Dioxide USP

1.3 Pharmaceutical Dosage Form

Tablet for oral use

2. Quality and Quantitative Composition

Each film coated tablet contains:

Amoxicillin Trihydrate USP

Equivalent to Amoxicillin…….500 mg

Clavulanate potassium USP

Equivalent to Clavulanic acid……...125 mg

Colour: Titanium Dioxide USP

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 9beta)-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 occours, 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 usaually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and eletrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective againest C. difficille 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 tearapy. 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 phenylketonuiar.

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.

Antocoagulants: 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 alopurinol 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 brond-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 trhe 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.

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

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 Staphyloccocci 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 achive 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	Specification
Sodium Starch Glycolate	USP
Croscarmellose sodium	USP
Colloidal Silicon Dioxide (Aerosil-200)	USP
Talc	USP
Magnesium Stearate	USP
Hydroxy Propyl Methyl Cellulose E5 (HPMC-E5)	USP
Hydroxy Propyl Methyl Cellulose E15 (HPMC-E15)	USP
Ethyl Cellulose	USP
Diethyl Phthalate	USP
Isopropyl Alcohol	USP
Dichloromethane (Methyl Chloride)	USP
Titanium Dioxide	USP
Polyethylene glycol 6000	USP

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 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 holder

Cachet Pharmaceuticals Pvt. Ltd

415, Shah Nahar Industrial Estate,

Dr. E. Moses Road, Worli, Mumbai-400 018,

Maharashtra, India.

9.0 Marketing Authorization Numbers

Not Applicable.

10.0 Date of first authorization/renewal of the authorization

Not Applicable.

11.0 Date of revision of the text

Not Applicable.