Prescribing information (Summary of Product Characteristics)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

CLAVBID 228.5 (Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5mg/5ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative declaration

Each 5 ml (after reconstitution) suspension contains:
Amoxicillin Trihydrate
USP Eq. to Amoxicillin
200
mg
Clavulanate Potassium
BP
Eq. to Clavulanic Acid
28.50 mg Excipientsq.s.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Dry Powder Suspension

Visual/Physical Description of FPP: White to off white granular powder filled in white color HDPE bottle, after reconstitution with water, off white color suspension to be produced.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml is indicated for the treatment of the following infections in adults and children:

- *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.
- *Bone and joint infections*, in particular osteomyelitis.
- *Dental infections* e.g. severe dental abscess with spreading cellulitis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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.

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml bottle presentations for suspension may be supplied with a plastic dosing device.

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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml to make dosage recommendations for children under 2 months old.
The tables below give dosage guidance for children.

Children 2 years and over

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml		
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

Renal Impairment:
No adjustment in dose is required in patients with creatinine clearance greater than 30 mL/min.
Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5mg/5ml 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.

Method of administration:
For Oral administration only.
Administer at the start of a meal to minimise potential gastrointestinal intolerance and optimise absorption of amoxicillin/clavulanic acid.
Therapy can be started parenterally according to the SmPC of the IV formulation and continued with an oral preparation.

Shake to loosen powder, add water as directed, invert and shake. Shake the bottle before each dose.

4.3 Contraindications

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml is contraindicated in patients with a history of hypersensitivity to betalactams, e.g. penicillins and cephalosporins.
Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml is contraindicated in patients with a previous history of Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml associated jaundice/hepatic dysfunction.

4.4 Special warnings and precautions for use

Before initiating therapy with *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml*, 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, *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml* 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.

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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 *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml* 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml. The clinical significance of these changes is uncertain but Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml is 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.

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml
7.142 mg aspartame per 5 mL dose and therefore care should be taken in patients with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

4.6 Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml* 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 *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml* and allopurinol.

In common with other antibiotics, *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml* 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 *Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml*.

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.

4.7 Fertility, pregnancy and lactation

Pregnancy:

Reproduction studies in animals (mice and rats) with orally and parenterally administered Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP

228.5 mg/5ml 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.

Breastfeeding:

Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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.

4.8 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.

4.9 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 Amoxicillin and Clavulanate Potassium for Oral Suspension, 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)

Infection and Infestation
Common: Mucocutaneous candidosis

Blood and lymphatic System disorders:
Rare: Reversible leucopenia (including neutropenia), Thrombocytopenia
Very rare: Reversible agranulocytosis, 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
Uncommon: Indigestion
Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis, 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.

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)

Renal and urinary disorders:
Rare: Interstitial nephritis, Crystalluria

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.10 Overdose

Symptoms:
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.

Treatment:
Amoxicillin/clavulanic acid can be 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

Mechanism of action:

Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP

228.5 mg/5ml 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 Amoxicillin and Clavulanate Potassium for Oral Suspension USP

228.5 mg/5ml.

5.2 Pharmacokinetic properties

Absorption:

The two components of Amoxicillin and Clavulanate Potassium for Oral Suspension USP 228.5 mg/5ml, 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 Amoxicillin and Potassium Clavulanate is optimized when taken at the start of a meal.

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:
Approximately 40% of the dose is excreted in the urine and 42% in the faeces over a 10 day period and mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. Less than 1% of the active substance is excreted unchanged in active form, as loratadine or DL.

The mean elimination half-lives in healthy adult subjects were 8.4 hours (range = 3 to 20 hours) for loratadine and 28 hours (range = 8.8 to 92 hours) for the major active metabolite.

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 new borns) 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.

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 or its components.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sr. No.	Excipient	Grade
1	Xanthan Gum	USP
2	Hydroxy Ethyl Cellulose	IH
3	Colloidal Silicon Dioxide	USP
4	Flavour Pineapple	IH
5	Flavour Strawberry	IH
6	Micronised Silica	USP
7	Aspartame	USP
8	Succinic Acid	USP

6.2 Incompatibilities

None Known.

6.3 Shelf Life

24 Months
Use the reconstituted suspension within 7 days after opening.

6.4 Special Precautions for Storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and Contents of Container

70 ml HDPE bottle is packed in a carton along with leaflet.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

Manufacturing Authorisation Holder
Scott-Edil Advance Research Laboratories & Education Ltd.
Hill Top Industrial Area, Bhatoli
Kalan, Baddi-173205, (HP)
INDIA.

Manufacturing Site Addresses

Scott-Edil Advance Research Laboratories & Education Ltd.
Hill Top Industrial Area, Bhatoli
Kalan, Baddi-173205, (HP)
INDIA.

8. Marketing Authorisation Number

Sai Pharmaceuticals Ltd.
P.O. Box 66551 - 00800, Nairobi,
Kenya.

9. Date Of First Authorisation/Renewal Of The Authorisation

Not Applicable.

10. Date Of Revision Of The Text

23/1/26