SUMMARY OF PRODUCT CHARACTERIZATION (SMPC)

1. Name of the medicinal product

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP

2. Qualitative and quantitative composition

Composition

Each 5 ml of the reconstituted suspension contains:

Amoxicillin Trihydrate USP
Eq. to Amoxicillin ..250 mg
Diluted Potassium Clavulanate BP
Eq, to Clavulanic Acid …62.5 mg
Excipients ..QS
Flavoured Base ..QS

For the full list of excipients, see section 6.1.

Qualitative and quantitative composition

Sr. No.	Ingredients
1	Amoxicillin Trihydrate Eq. to Amoxicillin
2	Diluted Potassium Clavulanate Eq, to Clavulanic Acid
3	Colloidal Silicon Dioxide
4	Xanthan Gum
5	Aspartame
6	Silicon Dioxide
7	Hypromellose
8	Succinic Acid
9	Flavour Strawberry

3. Pharmaceutical form

White coloured Free Flowing powder.

For oral administration.

4. Clinical particulars

4.1 Therapeutic indications

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The ß- lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other _-lactam antibiotics.

4.2 Posology and method of administration

Route of Administration: Oral

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP should be used in accordance with local official antibiotic-prescribingguidelines and local susceptibility data. *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* oral presentations for three times daily dosing, are indicated for short-termtreatment 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. intra-abdominal sepsis. Susceptibility to *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* will vary with geography and time (see *Pharmacological Properties, Pharmacodynamics* for further information). Local susceptibility data shouldbe consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Infections caused by amoxicillin -susceptible organisms are amenable to *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* treatment due to its amoxicillin content. Mixed infections caused by amoxicillin - susceptible organisms in conjunction with *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* -susceptible ß-lactamase producing organisms may therefore be treated with *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* .

Usual dosages for the treatment of infection

Adults and children over 12 years:

Mild - Moderate infections	One *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL S USP* 375 mg oral suspension 3 times a day.

Severe infections	a dose of two *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 375 mg 3 times a day may be taken. Therapy can be started parenterally and continuedwith an oral preparation.

Children:

The usual recommended daily dosage is 25mg/kg/day* in divided doses every eighthours.
The table below presents guidance for children.

Under 1 year	25 mg/kg/day*, for example a 7.5 kg child wouldrequire 2 ml *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 156 mg suspension 3times a day.
1-6 years (10-18 kg)	5 ml *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 156 mg suspension 3 times a day.
Over 6 years (18-40 kg)	5 ml *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 312 mg suspension 3 times a day.

In more serious infections the dosage may be increased up to 50 mg/kg/day in divideddoses every eight hours.

***** Each 25 mg *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* provides 20 mg amoxicillin and 5 mg clavulanate.

Administration

To minimise potential gastrointestinal intolerance, administer at the start of a meal. Theabsorption of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* is optimised when taken at the start of a meal.

Treatment should not be extended beyond 14 days without review.

4.3 Contraindications

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP is contra-indicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP is contra-indicated in patients with a previous history of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* -associated jaundice/hepatic dysfunction.

4.4 Special warnings and precautions for use

Before initiating therapy with *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* , careful enquiry should be made concerningprevious 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 (see *Contraindications*). If an allergic reaction occurs, *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 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 should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following theuse 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 inseverity 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* and oral anticoagulants. Appropriate monitoring shouldbe undertaken when anticoagulants are prescribed concurrently. Adjustments in the doseof 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* . The clinical significance of these changes is uncertain but *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 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 treatmenthas ceased.

In patients with renal impairment *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* dosage should be adjusted asrecommended 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 toreduce the possibility of amoxicillin crystalluria *(*see *Overdose).*

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP suspensions contain 12.5 mg aspartame per 5 ml dose, which is a source ofphenylalanine, and therefore should be used with caution in patients with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants

Concomitant use of probenecid is not recommended. Probenecid decreases the renaltubular secretion of amoxicillin. Concomitant use with *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* may result in increased and prolonged blood levels of amoxicillin but not of clavulanate.

Concomitant use of allopurinol during treatment with amoxicillin can increase thelikelihood of allergic skin reactions. There are no data on the concomitant use of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* and allopurinol.

In common with other antibiotics, *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* may affect the gut flora, leading tolower 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 shouldbe carefully monitored with the addition or withdrawal of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* .

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid of approximately 50% has been reported followingcommencement of oral amoxicillin plus clavulanic acid. The change in pre-dose level may not accurately represent changes in overall MPA exposure.

4.6 Fertility, pregnancy and lactation

Reproduction studies in animals (mice and rats) with orally and parenterally administered *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 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* may be associated with an increased risk ofnecrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.

AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP may be administered during the period of lactation. With the exception ofthe risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no detrimental effects for the infant

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Data from large clinical trials were used to determine the frequency of very common torare 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 and <1/10 uncommon ≥1/1000 and <1/100rare ≥1/10,000 and <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 and 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

Nausea is more often associated with higher oral dosages. If gastrointestinal reactions areevident, they may be reduced by taking *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* 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 discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration asit 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 findingsis unknown.

Very rare Hepatitis and cholestatic jaundice. These events have been noted withother penicillins and cephalosporins.

Hepatic events have been reported predominantly in males and elderly patients and maybe 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 seriousunderlying disease or taking concomitant medications known to have the potential forhepatic effects
Skin and subcutaneous tissue disorders

Uncommon Skin rash, pruritus, urticariaRare

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)*

4.9 Overdose

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

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed *(*see*Warnings and Precautions).*
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP can be removed from the circulation by haemodialysis

5. Pharmacological properties

5.1 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 *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* anticipatesthis defence mechanism by blocking the ß-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 *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* it produces an antibiotic agent of broad spectrum with wideapplication 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 .

In vitro susceptibility of micro-organisms to *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* Where clinical efficacy of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* has been demonstrated in clinical trials this isindicated 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 *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* .
Commonly susceptible species

Gram-positive aerobes:
Bacillius anthracis
Enterococcus faecalis Listeria
monocytogenes Nocardia
asteroides Streptococcus
*pyogenes**† *Streptococcus*
*agalactiae**†
Streptococcus spp. (other β-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
magnusPeptostreptococcus
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.

5.2 Pharmacokinetic properties

The pharmacokinetics of the two components of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* are closely matched. Peakserum levels of both occur about 1 hour after oral administration. Absorption of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* is optimised at the start of a meal.

Doubling the dosage of *AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP* approximately doubles the serum levels achieved.

Both clavulanate and amoxicillin have low levels of serum binding; about 70% remainsfree in the serum

5.3 Preclinical safety data

No further information of relevance.

6. Pharmaceutical particulars

6.1 List of excipients

Colloidal Silicon Dioxide
Xanthan Gum
Aspartame
Silicon Dioxide
Hypromellose
Succinic Acid
Flavour Strawberry

6.2 Incompatibilities

Not known.

6.3 Shelf life

3 years

Reconstituted solution: 7 days

6.4 Special precautions for storage

Store in a well closed container at a temperature not exceeding 30ºC ± 2ºC

6.5 Nature and contents of container

100 ml HDPE bottle seals and HDPF cap with measuring cup packed in carton with literature.

6.6 Special precautions for disposal and other handling

As per regulatory country specific for disposable**.**

7. Applicant / Manufacturer

Applicant

Applicant name and address	**M/s. ALPS COMMUNICATION PVT. LTD.** Trilokpur Road, Village Johron Kala Amb, Distt. Sirmour (H.P.),173030, INDIA
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8. MARKETING AUTHORISATION NUMBER

09367/10570/NMR/2023

9. Date of authorization

Dec 29, 2023

10. Date of revision of the text

03/2024