SUMMARY OF PRODUCT CHARACTERISTICS

1. Product name:

KLAMOKS ® 312.5 mg Fort Dry Powder for Oral Suspension

2. Qualitative and Quantitative Composition:

Active substance:

Each 5 ml suspension contains:

Amoxicillin (as Amoxicillin Trihydrate).....250 mg

Clavulanic acid (as Potassium Clavulanate).....62.5 mg

Excipients:

Each 5 ml suspension contains:

Sodium citrate dihydrate.....8.35 mg
Sodium benzoate (E211) .....2.1 mg
Microcrystalline cellulose +Sodium carboxymethyl cellulose.....25 mg
Granule powder sugar (sucrose) ..... q.s.*
*It changes by depending on potency of active substance.

Please see section 6.1. for other excipients.

3. Pharmaceutical Form:

Dry Powder for Oral Suspension.

Creamy-white colored raspberry odorous, homogeny powder. It is formed of creamy-white colored suspension with raspberry odorous when it is reconstituted.

4. Clinical Information:

4.1 Therapeutic Indications:

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

Klamoks is indicated for short term treatment of bacterial infections at the following sites when amoxicillin resistant beta-lactamase producing strains are suspected as the cause. In other situations, amoxicillin alone should be considered.

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
Dental infections: e.g. severe dental abscess along with creeping cellulitis.

Susceptibility to Klamoks will vary with geography and time (see Pharmacological Properties, Pharmacodynamics for further information). Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Mixed infections caused by amoxicillin-susceptible organisms in conjunction with Klamoks susceptible beta-lactamase-producing organisms may be treated with Klamoks 312.5 mg Fort Dry Powder for Oral Suspension. These infections should not require the addition of another antibiotic resistant to beta-lactamases.

4.2. Posology and method of administration:

Posology:

The usual recommended daily dosage is:

• 20/5 mg/kg/day (given in three divided doses per day) in mild to moderate infections (upper respiratory tract infections e.g. recurrent tonsillitis, lower respiratory infections and skin and soft tissue infections)

• 40/10 mg/kg/day (given in three divided doses per day) 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)

• 60/15 mg/kg/day (given in three divided doses per day) for the treatment of some infections (e.g. otitis media sinusitis and lower respiratory tract infections) for children over 2 years of age (4:1 formulation of Klamoks) may be evaluated.

Children over 2 years;

20/5 mg/kg/day	2 - 6 years (13 - 21 kg)	2.5 ml Klamoks 312.5 mg Fort Dry Powder for Oral Suspension three times daily
	7 - 12 years (22 - 40 kg)	5.0 ml Klamoks 312.5 mg Fort Dry Powder for Oral Suspension three times daily
40/10 mg/kg/day	2 - 6 years (13 - 21 kg)	5.0 ml Klamoks 312.5 mg Fort Dry Powder for Oral Suspension three times daily
	7 - 12 years (22 - 40 kg)	10.0 ml Klamoks 312.5 mg Fort Dry Powder for Oral Suspension three times daily

Children aged 2 months to 2 years

Children under 2 years should be dosed according to body weight.

Weight (kg)	**Dose (ml) to be administrated every 8 hours in Mild/Moderate infection**	**Dose (ml) to be administrated every 8 hours in severe infection**
2	0.5	1.1
3	0.8	1.6
4	1.1	2.1
5	1.3	2.7
6	1.6	3.2
7	1.9	3.7
8	2.1	4.3
9	2.4	4.8
10	2.7	5.3
11	2.9	5.9
12	3.2	6.4
13	3.5	6.9
14	3.7	7.5
15	4.0	8.0

There is insufficient experience with KLAMOKS 312.5 mg suspension to make dosage recommendations for children under 2 months old.

Method of administration:

Daily dose is given in three divided doses. To minimize potential gastrointestinal intolerance, administer at the start of a meal. The absorption of KLAMOKS is optimised when taken at the start of a meal. Duration of therapy should be appropriate to the indication and should not exceed 14 days without review.

Preparation of suspension:

Add boiled and cooled water approximately up to half of the bottle and shake well. Wait for 5 minutes for homogeneous dispersion. Then, add the water up to the marked level on the label and again shake.

An amount of drug recommended by doctor is given to patient by 5 mL measuring spoon.

Powder not reconstituted should keep at room temperature below 30°C, and dry place.
Reconstituted suspension should keep in refrigerator (2-8°C) and be used within 7 days.

Should not be frozen.

Special populations:

Renal Impairment

For children with a GFR of >30 ml/min no adjustment in dosage is required. For children with a GFR of <30 ml/min KLAMOKS 312.5 mg suspension is not recommended.

Infants with immature kidney function

For infants with immature renal function KLAMOKS 312.5 mg suspension is not recommended.

Hepatic Impairment

Dose with caution; monitor hepatic function at regular intervals. There is, as yet, insufficient evidence on which to base a dosage recommendation.

4.3 Contraindication:

KLAMOKS is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

KLAMOKS is contraindicated in patients with a previous history of KLAMOKS-associated jaundice/hepatic dysfunction.

4.4 Warnings and Precautions:

Before initiating therapy with KLAMOKS, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens.

Serious and occasionally fatal hypersensitivity (anaphylactoid) 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).

In the case that an infection is proven to be due to an amoxicillin-susceptible organisms(s) then consideration should be given to switching from amoxicillin/clavulanic acid to amoxicillin in accordance with official guidance.

This presentation of Klamoks is not suitable for use when there is a high risk that the presumptive pathogens have reduced susceptibility or resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid. This presentation should not be used to treat penicillin-resistant S. pneumoniae.

KLAMOKS 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.

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see section 4.8).

Amoxicillin/clavulanic acid 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.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP) (see Section 4.8). This reaction requires Augmentin discontinuation and contra-indicates any subsequent administration of amoxicillin.

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment (see section 4.2).

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. In all populations, 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 (see section 4.8).

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin/clavulanic acid should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin/clavulanic acid. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5 and 4.8).

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

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. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.9).

During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of Clavulanic acid in Augmentin may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

KLAMOKS contains sodium less than 1mmol (23 mg) in each dose; any side effect is not expected.

This medicinal product contains powder sugar (sucrose). Patients with rare glucose-galactose malabsorption or sucrase-isomaltase deficiency should not take this medicine.

4.5 Drug and other Interactions:

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are 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 should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

4.6 Pregnancy and Lactation:

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). Limited data on the use of amoxicillin/clavulanic acid during pregnancy in humans do not indicate an increased risk of congenital malformations. In a single study in women with preterm, premature rupture of the foetal membrane it was reported that prophylactic treatment with amoxicillin/clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates. Use should be avoided during pregnancy, unless considered essential by the physician.

Lactation

Both substances are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breast-fed infant). Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. The possibility of sensitisation should be taken into account. Amoxicillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

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 (see section 4.8).

4.8 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 KLAMOKS, 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)

Infections and infestations	
Mucocutaneous candidosis	Common
Overgrowth of non-susceptible organisms	Not known
Blood and lymphatic system disorders	
Reversible leucopenia (including neutropenia)	Rare
Thrombocytopenia	Rare
Reversible agranulocytosis	Not known
Haemolytic anaemia	Not known
Prolongation of bleeding time and prothrombin time[1]	Not known
Immune system disorders[10]	
Angioneurotic oedema	Not known
Anaphylaxis	Not known
Serum sickness-like syndrome	Not known
Hypersensitivity vasculitis	Not known
Nervous system disorders	
Dizziness	Uncommon

Headache	Uncommon
Reversible hyperactivity	Not known
Convulsions[2]	Not known
Aeseptic meningitis	Not known
Gastrointestinal disorders	
Diarrhoea	Common
Nausea[3]	Common
Vomiting	Common
Indigestion	Uncommon
Antibiotic-associated colitis[4]	Not known
Black hairy tongue	Not known
Tooth discolouration[11]	Not known
Hepatobiliary disorders	
Rises in AST and/or ALT[5]	Uncommon
Hepatitis[6]	Not known
Cholestatic jaundice[6]	Not known
Skin and subcutaneous tissue disorders[7]	
Skin rash	Uncommon
Pruritus	Uncommon
Urticaria	Uncommon
Erythema multiforme	Rare
Stevens-Johnson syndrome	Not known
Toxic epidermal necrolysis	Not known
Bullous exfoliative-dermatitis	Not known
Acute generalised exanthemous pustulosis (AGEP)[9]	Not known
Renal and urinary disorders	
Interstitial nephritis	Not known
Crystalluria[8]	Not known

[1] See section 4.4
[2] See section 4.4
[3] Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, they may be reduced by taking amoxicillin/clavulanic acid with a meal.
[4] Including pseudomembranous colitis and haemorrhagic colitis (see section 4.4)
[5] 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.
[6] These events have been noted with other penicillins and cephalosporins (see section 4.4).
[7] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).
[8] See section 4.9
[9] See section 4.4
[10] See sections 4.3 and 4.4

[11] Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

4.9 Overdosage:

Symptoms and signs of overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained (see section 4.4).

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

5. Pharmacological Properties:

5.1 Pharmacodynamics:

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

ATC code: J01CR02.

Mode of action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect

PK/PD relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The two main mechanisms of resistance to amoxicillin/clavulanic acid are:

- Inactivation by those bacterial beta-lactamases that are not themselves inhibited by clavulanic acid, including class B, C and D.
- Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin/clavulanic acid are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)

Organism	Susceptibility Breakpoints (g/ml)		
	Susceptible	Intermediate	Resistant
Haemophilus influenzae[1]	≤ 1	-	> 1
Moraxella catarrhalis[1]	≤ 1	-	> 1
Staphylococcus aureus [2]	≤ 2	-	> 2
Coagulase-negative staphylococci [2]	≤ 0.25		> 0.25
Enterococcus[1]	≤ 4	8	> 8
Streptococcus A, B, C, G[5]	≤ 0.25	-	> 0.25
Streptococcus pneumoniae[3]	≤ 0.5	1-2	> 2

Enterobacteriaceae[1,4]	-	-	> 8
Gram-negative Anaerobes[1]	≤ 4	8	> 8
Gram-positive Anaerobes[1]	≤ 4	8	> 8
Non-species related breakpoints[1]	≤ 2	4-8	> 8

1 The reported values are for Amoxicillin concentrations. For susceptibility testing purposes, the concentration of Clavulanic acid is fixed at 2 mg/l.

2 The reported values are Oxacillin concentrations.

3 Breakpoint values in the table are based on Ampicillin breakpoints.

4 The resistant breakpoint of R>8 mg/l ensures that all isolates with resistance mechanisms are reported resistant.

5 Breakpoint values in the table are based on Benzylpenicillin breakpoints.

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobic Gram-positive micro-organisms

Enterococcus faecalis

Gardnerella vaginalis

Staphylococcus aureus (methicillin-susceptible)£

Coagulase-negative staphylococci (methicillin-susceptible)

Streptococcus agalactiae

Streptococcus pneumoniae[1]

Streptococcus pyogenes and other beta-haemolytic streptococci

Streptococcus viridans group

Aerobic Gram-negative micro-organisms

Capnocytophaga spp.

Eikenella corrodens

Haemophilus influenzae[2]

Moraxella catarrhalis

Pasteurella multocida

Anaerobic micro-organisms

Bacteroides fragilis

Fusobacterium nucleatum

Prevotella spp.

Species for which acquired resistance may be a problem

Aerobic Gram-positive micro-organisms

Enterococcus faecium $

Aerobic Gram-negative micro-organisms

Escherichia coli

Klebsiella oxytoca

Klebsiella pneumoniae

Proteus mirabilis

Proteus vulgaris

Inherently resistant organisms

Aerobic Gram-negative micro-organisms

Acinetobacter sp.

Citrobacter freundii

Enterobacter sp.

Legionella pneumophila

Morganella morganii

Providencia spp.

Pseudomonas sp.

Serratia sp.

Stenotrophomonas maltophilia

Other micro-organisms

Chlamydophila pneumoniae

Chlamydophila psittaci

Coxiella burnetti

Mycoplasma pneumoniae

$ Natural intermediate susceptibility in the absence of acquired mechanism of resistance.

£ All methicillin-resistant staphylococci are resistant to amoxicillin/clavulanic acid

[1]Streptococcus pneumoniae that are resistant to penicillin should not be treated with this presentation of amoxicillin/clavulanic acid (see sections 4.2 and 4.4).

[2]Strains with decreased susceptibility have been reported in some countries in the EU with a frequency higher than 10%.

5.2 Pharmacokinetics properties:

Absorption

Amoxicillin and clavulanic acid, are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (Tmax) in each case is approximately one hour.

The pharmacokinetic results for a study, in which amoxicillin/clavulanic acid (500 mg/125 mg tablets three times daily) was administered in the fasting state to groups of healthy volunteers are presented below.

Mean (±SD) Pharmacokinetic Parameters					
Drug Administration	Dose	C_{maks}	T_{maks}*	AUC $_{(0-24h)}$	T $_{1/2}$
	(mg)	(µg/mL)	(hours)	(mg.h/L)	(hours)
Co-amoxilav 1 g					
Amoxicillin					
AMX/CA 500/125 mg	500	7.19 ± 2.26	1.5 (1.0-2.5)	53.5 ± 8.87	1.15 ± 0.20
Clavulanic Acid					
AMX/CA 500 mg/125 mg	125	2.40 ± 0.83	1.5 (1.0-2.0)	15.72 ± 3.86	0.98 ± 0.12

Amoxicillin and clavulanic acid serum concentrations achieved with amoxicillin/clavulanic acid are similar to those produced by the oral administration of equivalent doses of amoxicillin or clavulanic acid alone.

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 (see section 4.6).

Both amoxicillin and clavulanic acid have been shown to cross the placental barrier (see section 4.6).

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

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms.

Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/h in healthy subjects. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of single KLAMOKS 250 mg/125 mg or 500

mg/125 mg tablets. Various studies have found the urinary excretion to be 50-85% for amoxicillin and between 27-60% for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.

Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid (see section 4.5)

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 newborns) 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 (see section 4.2).

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:

Citric Acid (Anhydrous)
Sodium Citrate Dihydrate
Sodium Benzoate
Microcrystalline cellulose / Sodium Carboxy methyl cellulose
Xanthan Gum
Colloidal Anhydrous Silica
Silicon Dioxide
Essence Raspberry
Powdered Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life:

36 months

6.4 Special precautions for storage:

Store below 30 ^{0}C, in a dry place.

After reconstitution, suspension can be kept in a refrigerator (2-8ºC) for 7 days. Do not freeze.

Due to the hygroscopic, bottles should be well closed.

6.5 Nature and contents of container:

Our product is presented in amber colored Type III glass bottle well closed with HDPE cap, on which 100 ml level mark, with a 2.5-5 mL marked measuring spoon and leaflet in a carton box.

6.6 Special precautions for disposal and other handling:

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

Preparation of Suspension:

Klamoks is powder, so firstly reconstitution is necessary.

Please follow up the instructions below:

Please tap the bottle until the whole powder flows freely.

1. Add water until the half of marked line on the bottle and shake well to obtain suspension. (Boiled and cooled water should be used)

2. To obtain completely dispersion, rest for 5 minutes.
3. Add remaining water until the marked line and shake bottle again.
4. Suspension can be administered with 5 ml measuring spoon.

Shake well the bottle before each dose.

After using, close the bottle tightly and immediately.

7. Marketing Authorization Holder:

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9.- Marketing Authorization Number :

05288/07384/REN/2020

10.- Data of First Authorization / Renewal of Authorization:

Aug 27, 2020

11.- Date of Last/Partial Revision of the Text :