Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Claritek (Clarithromycin) Granules 250mg/5mL

2. Qualitative and quantitative composition

Each reconstituted 5mL contains:
Clarithromycin USP...250mg

For the full list of excipients, see section 6.1

3. Pharmaceutical form

White to off-white granular powder filled in HDPE plastic bottle.

4. Clinical particulars

4.1 Therapeutic indications

CLARITEK (Clarithromycin) is indicated for treatment of infections due to susceptible organisms.
Such infections include:
- Lower respiratory tract infections (e.g., bronchitis, pneumonia).
- Upper respiratory tract infections (e.g. pharyngitis, sinusitis, tonsillitis).
- Acute otitis media in children.
- Skin and soft tissue infections (e.g., folliculitis, cellulitis and erysipelas).

4.2 Posology and method of administration

Paediatric patients under 12 years of age

Clinical trials have been conducted using clarithromycin paediatric suspension in children 6 months to 12 years of age. Therefore, children under 12 years of age should use clarithromycin paediatric suspension

Recommended doses and dosage schedules:

The usual duration of treatment is for 5 to 10 days depending on the pathogen involved and the severity of the condition. The recommended daily dosage of Clarithromycin 250 mg/ 5 ml granules for oral suspension in children is given in the following table and is based on a 7.5mg/ kg twice a day (b.i.d) dosing regime, up to a maximum dose of 500 mg b.i.d.

DOSAGE IN CHILDREN

Dosage based on body weight (kg)		
Weight* (kg)	***Approx Age (years)***	***Dosage (ml) b.i.d.***
8 – 11	1 – 2	1.25
12 - 19	3 – 6	2.50
20 - 29	7 - 9	3.75

30 - 40	10 - 12	5.00

*Children < 8 kg should be dosed on a per kg basis: 0.15 ml/kg twice a day (approx. 7.5 mg/kg twice a day)

***Renal Impaired Patients**:*
The maximum recommended dosages should be reduced proportionately to renal impairment. At creatinine clearance rate of < 30 mL/min, the dosage should be halved to 250mg daily or in the most severe infections to 250mg twice daily for adults and 7.5 mg/kg once a day for children. The duration of treatment should not exceed 14 days in these patients.

Direction for reconstituition
Fill previously boiled and cooled water up to the mark on the bottle and shake gently. After mixing, do not refrigerate. Keep tightly closed after use.

4.3 Contraindications

- Clarithromycin is contraindicated in patients with known hypersensitivity to the active substance, other macrolide antibiotics or to any of the excipients.
- Concomitant administration of clarithromycin with any of the following medicines is contraindicated: astemizole, cisapride, pimozide and terfenadine.
- Concomitant administration of Clarithromycin with ergot derivatives is contraindicated.

4.4 Special warnings and precautions for use

- Caution should be taken in administering Clarithromycin to patients with impaired hepatic function.
- Caution should also be paid to the possibility of cross-resistances between Clarithromycin and other macrolide drugs, as well as lincomycin and clindamycin.
- Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Therefore, it is important to consider its diagnosis in patients who develop severe diarrhea during or after therapy with Clarithromycin.
- Prolonged or repeated use of Clarithromycin may result in superinfections with insusceptible organisms. In case of superinfection, Clarithromycin therapy should be stopped.
- Clarithromycin should be used with caution whenever indicated for use in patients receiving treatment with an inducer of CYP3A4.
- Clarithromycin in combination with ranitidine bismuth citrate therapy should not be used in patients with a history of acute porphyria.
- Clarithromycin is an inhibitor of the metabolising enzyme CYP3A4 should not be used concomitantly with different CYP3A4 substrates unless plasma levels, therapeutic effect or adverse events of the CYP3A4 substrate are closely monitored.

4.5 Interaction with other medicinal products and other forms of interaction

Digoxin: Elevated digoxin serum concentrations have been reported in patients receiving clarithromycin and digoxin concomitantly. Monitoring of serum digoxin levels should be considered.

Quinidine/Disopyramide: Concurrent use of clarithromycin and quinidine or disopyramide may cause Torsades de Pointes. Electrocardiogram and serum levels of these medications should be monitored during clarithromycin therapy.

HMG-CoA Reductase Inhibitors: As with other macrolides, clarithromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g. statins). Rare reports of rhabdomyolysis have been reported in patients taking these drugs concomitantly.

Zidovudine: Simultaneous oral administration of clarithromycin tablets and zidovudine to HIV-infected adult patients may result in decreased steady-state zidovudine concentrations. This interaction does not appear to occur in pediatric HIV-infected patients taking clarithromycin suspension with zidovudine or dideoxyinosine.

Ritonavir: Concomitant administration of clarithromycin and ritonavir resulted in a 77% increase in clarithromycin AUC and a 100% decrease in the AUC of 14OH clarithromycin. Clarithromycin may be administered without dosage adjustment to patients with normal renal function taking ritonavir. However, for patients with renal impairment, dosage adjustments should be considered.

4.6 Pregnancy and Lactation

Pregnancy

There are no adequate or well-controlled studies in pregnant women. Clarithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Clarithromycin and its active metabolite are excreted in breast milk. Therefore, diarrhea and fungus infection of the mucous membranes could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitisation should be born in mind. The benefit of treatment of the mother should be weighed against the potential risk for the infant.

4.7 Effects on ability to drive and use machines

There are no data available on the effect of clarithromycin on the ability to drive or use machines. The potential for dizziness, vertigo, confusion and disorientation should be taken into account before patients drive or use machines.

4.8 Undesirable effects

The following side effects were reported with the use of Clarithromycin:

Common:
Oral monilia, headache, smell alteration, nausea, diarrhea, vomiting, abdominal pain, dyspepsia, stomatitis, glossitis, reversible tooth and tongue discoloration, and taste perversion, i.e. metallic or bitter taste.

Uncommon:
Decreased leucocyte levels, allergic reactions ranging from urticaria and mild skin eruptions to anaphylaxis, hepatic dysfunction which is usually transient and reversible, hepatitis and cholestasis with or without jaundice, arthralgia and myalgia.

Very Rare:
Thrombocytopenia, anxiety, insomnia, hallucinations, psychosis, disorientation, depersonalisation, bad dreams and confusion, dizziness, vertigo, paraesthesia, convulsions, Reversible hearing loss, QT prolongation, ventricular tachycardia and Torsades de Pointes, pancreatitis, pseudomembranous colitis in range of severity from mild to life threatening, fatal hepatic failure in patients with pre-existing liver disease or taking other hepatotoxic medicinal products, Stevens-Johnson syndrome, toxic epidermal necrolysis, interstitial nephritis and renal failure.

Reporting of suspected adverse reactions Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board pharmacovigilance Electronic Reporting system (PvERS) https://pv.phamacyboardkenya.org

4.9 Overdose

Overdose of clarithromycin can cause gastrointestinal symptoms such as abdominal pain, vomiting, nausea, and diarrhea. Adverse reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug and supportive measures. As with other macrolides, clarithromycin serum concentrations are not expected to be appreciably affected by hemodialysis or peritoneal dialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Macrolides, ATC code: J01FA09

Mechanism of Action

Clarithromycin exerts its anti-bacterial action by binding to the 50s ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis. It is highly potent against a wide variety of aerobic and anaerobic gram-positive and gramnegative organisms

5.2 Pharmacokinetic properties

Clarithromycin is rapidly and well absorbed from the gastro-intestinal tract after oral administration. The microbiologically active metabolite 14(R)-hydroxyclarithromycin is formed by first pass metabolism. Clarithromycin may be given without regard to meals as food does not affect the extent of bioavailability. Food does slightly delay the onset of absorption of clarithromycin and formation of the 14-hydroxy metabolite.

Distribution

Clarithromycin provides tissue concentrations that are several times higher than the circulating active substance levels. Increased levels of clarithromycin have been found in both tonsillar and lung tissue. Clarithromycin penetrates into the middle ear fluid at concentrations greater than in the serum. Clarithromycin is 80% bound to plasma proteins at therapeutic levels.

Biotransformation

14-hydroxyclarithromycin is the major urinary metabolite and accounts for 10-15% of the dose.

Elimination

Most of the remainder of the dose is eliminated in the faeces, primarily via the bile. 5-10% of the parent active substance is recovered from the faeces.

Linearity

Although the pharmacokinetics of clarithromycin are non linear, steady state is attained within 2 days of dosing.

5.3 Preclinical safety data

In 4-week-studies in animals, toxicity of clarithromycin was found to be related to the dose and to the duration of the treatment. In all species, the first signs of toxicity were observed in the liver, in which lesions were seen within 14 days in dogs and monkeys. The systemic levels of exposure, related to this toxicity, are not known in detail, but toxic doses (300 mg/kg/day) were clearly higher than the therapeutic doses recommended for humans. Other tissues affected included the stomach, thymus and other lymphoid tissues as well as the kidneys. At near therapeutic doses conjunctival injection and lacrimation occurred only in dogs. At a dose of 400mg/kg/day some dogs and monkeys developed corneal opacities and/or oedema.

In vitro and in vivo studies showed that clarithromycin did not have genotoxic potential.

Studies on reproduction toxicity showed that administration of clarithromycin at doses 2x the clinical dose in rabbit (IV) and 10x the clinical dose in monkey (po) resulted in an increased incidence of spontaneous abortions. These doses were related to maternal toxicity. No embryotoxicity or teratogenicity was generally noted in rat studies. However, cardiovascular malformations were observed in two studies in rats treated with doses of 150 mg/kg/d.

In mice at doses 70x the clinical dose, cleft palate occurred at varying incidence (3-30%).

Clarithromycin has been found in the milk of lactating animals.

In 3-day old mice and rats, the LD50 values were approximately half those in adult animals. Juvenile animals presented similar toxicity profiles to mature animals although enhanced nephrotoxicity in neonatal rats has been reported in some studies. Slight reductions in erythrocytes, platelets and leukocytes have also been found in juvenile animals.

Clarithromycin has not been tested for carcinogenicity.

6. Pharmaceutical Particulars

6.1 List of Excipients

- Sucrose (Extra Fine)
- Titanium Dioxide
- Colliodal Anhydrous Silica (Aerosil 200)
- Xanthan Gum
- Methyl Paraben
- Trusil Powder Orange Flavour (B/B)
- Sodium Saccharine

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

2 years

The reconstituted suspension can be used for up to 14 days, when stored at room temperature.

The expiration date refers to the product correctly stored at the required conditions.

6.4 Special Precautions for storage

Store below 30° C. Do not refrigerate or freeze the reconstituted suspension.

6.5 Nature and Content of container

Clarithromycin is packed in clear translucent HDPE bottles with continuous ring mark for specific fill volume, having an inner translucent PP-induction 'lift and peel' seal liner and a child-resistant white opaque PP-cap closure.

6.6 Special precautions for disposal and other handling

Instructions for Reconstitution

Step-A The bottle should be removed from the box.

Step-B The bottle should be inverted and shaken to loosen the powder until no powder is adhered to the bottom. This should be checked by holding the bottle upside down against light. The cap should be opened as instructed below and the seal should be opened by lifting the tab and then peeling off.

Step-C The water should be added slowly up to the ring mark. If necessary, the bottle should be held against light in order to be able to recognize the correct filling level better. The bottle should be closed, inverted and shaken well for about 1 minute until no powder is adhered to the bottom. This should be checked by holding the bottle upside down against light.

The suspension should be left to settle and if it would be necessary to add more water as to make it up to the ring mark, step D should be followed.

Step-D If necessary, water should be added again up to the ring mark. If necessary, the bottle should be held against light in order to be able to recognize the correct filling level better. The bottle should be closed, inverted and shaken well until no powder is adhered to the bottom (See Figure 4). This should be checked by holding the bottle upside down against light.

Instructions on Use

1. To open the bottle, the child-proof cap should be removed from the bottle by pushing down on the cap while turning it anticlockwise.

2. The plastic circular adaptor should be taken from the carton and pushed into the neck of the bottle. This should fit tightly and once it is in place it should not be removed.

3. The oral syringe should be taken out of the carton and it should be ensured that the plunger is pressed down inside the barrel as far as it will go. This gets rid of any air that may be inside the barrel.

4. The nozzle of the oral syringe should be inserted into the hole in the adaptor.

5. The bottle should be turned upside down and held in one hand and the oral syringe in the other.

6. The barrel of the oral syringe should be held steady and slowly while pulling the plunger down, until you see the medicine fill the barrel to the mark, which matches the number of ml that you need to give to the patient.

7. The bottle should be turned the correct way up. The whole oral syringe should be removed from the adaptor, keeping hold of the barrel.

8. The oral syringe tip should be placed into the patient's mouth and the medicinal product should be dripped in by pushing down the plunger gently while still holding the barrel. The patient shouldn't be hurried, he or she should be allowed to swallow the medicine slowly. Alternatively, the measured dose from the oral syringe should be emptied onto a spoon for the patient to take the medicinal product from.

9. After administration, the bottle should be closed with the cap.

10. The oral syringe should be washed out in warm soapy water and rinsed well. The oral syringe should be held under water and the plunger should be moved up and down several times to make sure the inside of the barrel is clean. The oral syringe should be stored in a hygienic place with the medicinal product.

Administration of the suspension dose

Clarithromycin can cause a bitter after-taste. This can be avoided by eating some food or drinking juice or water soon after intake of the suspension.

Close the bottle and shake vigorously.

7. Marketing Authorization Holder

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8. Marketing Authorization Number

061347

9. Date of first authorization/renewal of the authorization

April 28, 2010

10. Date of revision of the text

5/5/2025