PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ACTIMENTIN ES 600 (600 mg/42,9 mg per 5 ml) powder for oral suspension.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted, every 1 ml of ACTIMENTIN ES 600 oral suspension contains amoxicillin trihydrate equivalent to 120 mg amoxicillin and potassium clavulanate equivalent to 8,58 mg of clavulanic acid (i.e. each 5 ml contains amoxicillin trihydrate equivalent to 600 mg amoxicillin and potassium clavulanate equivalent to 42,9 mg clavulanic acid).

The amoxicillin is present as amoxicillin trihydrate and the clavulanic acid is present as potassium clavulanate in a ratio of 14:1.

Excipients with known effect:

ACTIMENTIN ES 600 contains maltodextrin (glucose) as an ingredient of the flavourant. It also contains 1,92 mg acesulfame potassium (E950) and 0,96 mg saccharin sodium (E954) per 1 ml, as sweeteners.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension.

ACTIMENTIN ES 600 is a white to yellowish powder with strawberry flavour packed in a glass bottle.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ACTIMENTIN ES 600 is indicated for short term treatment of acute bacterial otitis media infections when caused by the following sensitive organisms: *Haemophilus influenzae, Streptococcus pneumoniae* (penicillin MIC < 4 microgram/ml) and *Moraxella catarrhalis.*

4.2 Posology and method of administration

Posology

Duration of therapy should be appropriate to the indication and should not exceed 14 days without review.

ACTIMENTIN ES 600 is recommended for dosing at 90/6,4 mg/kg/day in two divided doses at 12 hourly intervals for 10 days, in children aged 3 months and older. There is no experience in paediatric patients weighing > 40 kg or in adults. There are no clinical data in children under 3 months of age.

Body Weight (kg)	**Volume of ACTIMENTIN ES 600 providing 90/6,4 mg/kg/day**
8	3,0 ml twice daily
12	4,5 ml twice daily
16	6,0 ml twice daily
20	7,5 ml twice daily
24	9,0 ml twice daily
28	10,5 ml twice daily
32	12,0 ml twice daily
36	13,5 ml twice daily

ACTIMENTIN ES 600 does not contain the same amount of clavulanic acid (as the potassium salt) as any of the other suspensions containing a combination of amoxicillin and potassium clavulanate. Therefore, these suspensions should not be substituted for ACTIMENTIN ES 600, as they are not interchangeable.

Special populations

Hepatic impairment

There are insufficient data on which to base a dosage recommendation.

Renal impairment:

There are no dosing recommendations for ACTIMENTIN ES 600 in patients with renal impairment.

Method of administration

ACTIMENTIN ES 600 should be taken immediately before a meal.

For instructions on reconstitution of ACTIMENTIN ES 600 before administration, see section 6.6.

4.3 Contraindications

ACTIMENTIN ES 600 is contraindicated in:

- patients with hypersensitivity to the active substances (amoxicillin or clavulanate), to any of the penicillins or to any of the excipients of ACTIMENTIN ES 600 listed in section 6.1.
- patients with a history of hypersensitivity, including severe immediate hypersensitivity reaction (e.g. anaphylaxis), to another β-lactams (e.g. cephalosporins, carbapenem or monobactam).
- patients with a previous history of jaundice or hepatic dysfunction associated with amoxicillin/clavulanic acid treatment (see section 4.8).
- children under 3 months of age, as there are no clinical data available for this age group. Safety in children under 2 months of age has not been established.

4.4 Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship.

Serious allergic reactions, including anaphylaxis

Before initiating therapy with ACTIMENTIN ES 600, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, beta-lactam medicines or other allergens (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) angioneurotic oedema have been reported in patients on penicillin therapy, including amoxicillin/clavulanic acid. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity, who have experienced severe reactions when treated with cephalosporins.

If an allergic reaction occurs, ACTIMENTIN ES 600 must be discontinued, and appropriate alternative therapy instituted. Serious anaphylactic reactions require emergency treatment with epinephrine (adrenaline).

Hepatic dysfunction

Use ACTIMENTIN ES 600 with caution in patients with evidence of hepatic dysfunction (see sections 4.3 and 4.8).

Changes in liver function tests have been observed in some patients receiving amoxicillin/clavulanic acid. It should be used with care in patients with evidence of severe hepatic dysfunction and hepatic function should be monitored at regular intervals (see section 4.2). Transient hepatitis and cholestatic jaundice have been reported.

Hepatic events may be severe and fatal. It has been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events

have been reported less frequently 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. It has been reported that such hepatic events most frequently occurred in patients with serious underlying disease or taking concomitant medication known to have the potential for hepatic effects (see section 4.8).

Antibiotic-associated diarrhoea

Prolonged use may 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 (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. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, ACTIMENTIN ES 600 treatment should be discontinued immediately and the patient investigated further. Anti-peristaltic medicines are contraindicated in this situation.

Mononucleosis

Since ACTIMENTIN ES 600 contains amoxicillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of which there is a high incidence of rash if amoxicillin is used. ACTIMENTIN ES 600 should be avoided if infectious mononucleosis is suspected.

Prothrombin time

Abnormal prolongation of prothrombin time (increased international normalised ratio (INR)) has been reported in patients receiving an amoxicillin/clavulanic acid combination with oral anticoagulants (see sections 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria has been observed less frequently, predominantly with parenteral therapy. During the administration of high doses or overdosage of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output to reduce the possibility of amoxicillin crystalluria (see section 4.9). In patients with bladder catheters, a regular check of patency should be maintained.

Potential for microbial overgrowth

Prolonged use may also result in overgrowth of non-susceptible organisms. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving *Aerobacter, Pseudomonas* or *Candida*), ACTIMENTIN ES 600 should be discontinued and / or appropriate therapy instituted.

Sensitivity testing / susceptibility data

ACTIMENTIN ES 600 use may lead to resistant strains of organisms and, therefore, sensitivity testing should be carried out whenever possible to demonstrate the appropriateness of therapy. In the case that an infection is proven to be due to amoxicillin-susceptible organisms(s), consideration should be given to switching from ACTIMENTIN ES 600 acid to an amoxicillin only medicine in accordance with official guidance.

ACTIMENTIN ES 600 should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data. Susceptibility to ACTIMENTIN ES 600 will vary with geography and time. Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Convulsions

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

Concomitant allopurinol use

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions (see section 4.5).

Acute generalised exanthemous pustulosis (AGEP)

The occurrence of a feverish generalised erythema associated with pustula at treatment initiation may be a symptom of AGEP (see section 4.8). This reaction requires treatment discontinuation and contraindicates any subsequent administration of amoxicillin.

Organ system functions

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

Leukaemia

ACTIMENTIN ES 600 should be given with caution to patients with lymphatic leukaemia since such patients are especially susceptible to amoxicillin-induced skin rashes.

Interference with laboratory test

Urine glucose

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

Coombs test

The presence of clavulanic acid in ACTIMENTIN ES 600 may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

Bio-Rad Laboratories Platelia Aspergillus EIA

There have been reports of positive test results using the Bio-Rad Laboratories Platelia *Aspergillus* EIA test in patients receiving amoxicillin/clavulanic acid who were subsequently found to be free of *Aspergillus* infection. Cross-reactions with non-*Aspergillus* polysaccharides and polyfuranoses with Bio-Rad Laboratories Platelia *Aspergillus* EIA test have been reported. Therefore, positive test results in patients taking ACTIMENTIN ES 600 should be interpreted cautiously and confirmed by other diagnostic methods.

Maltodextrin

ACTIMENTIN ES 600 contains maltodextrin (glucose) as an ingredient of the flavourant. Patients with rare glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

Concurrent use of probenecid with ACTIMENTIN ES 600 is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin but does not affect clavulanic acid excretion. Concomitant use of probenecid with ACTIMENTIN ES 600 may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

Allopurinol

The concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. It is reported that the concurrent administration of allopurinol and ampicillin could substantially increase the incidence of skin rashes in patients receiving both medicines, as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricaemia present in these patients. There are no data on the combination of amoxicillin and potassium clavulanate used concurrently with allopurinol.

Oral anticoagulants

Abnormal prolongation of prothrombin time (increased INR) has been reported in patients receiving amoxicillin-clavulanate with oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently with ACTIMENTIN ES 600 (or during addition or treatment withdrawal). Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.4 and 4.8).

Oral contraceptives

ACTIMENTIN ES 600 may affect the gut flora, leading to lower estrogen re-absorption and, subsequently, reduced efficacy of combined oral contraceptives. Patients should be warned accordingly.

Methotrexate

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

Mycophenolate mofetil

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) of approximately 50 % has been reported following commencement of oral amoxicillin plus clavulanic acid treatment. The change in pre-dose level may not accurately represent changes in overall MPA exposure. [2, 4] Therefore, a change in the dose of mycophenolate mofetil should normally not be required in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed with concurrent use and shortly after antibiotic treatment.

Alcohol

No information is available about the concurrent use of the amoxicillin/clavulanic acid combination, as contained in ACTIMENTIN ES 600, and alcohol. However, the ingestion of

alcohol whilst being treated with some other β-lactam antibiotics has precipitated a disulfiram-like reaction in some patients. Therefore, the ingestion of alcohol should be avoided during and for several days after treatment with ACTIMENTIN ES 600.

4.6 Pregnancy and lactation

Pregnancy

Use should be avoided during pregnancy, as safety in pregnancy has not been established. Results from a single study in women with preterm, premature rupture of the foetal membrane (pPROM) reported that prophylactic treatment with amoxicillin/clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates.

Breastfeeding

Both amoxicillin and clavulanic acid are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breastfed infant). Consequently, candidiasis and skin rash are possible in breastfed infants. Mothers on treatment with ACTIMENTIN ES 600 should not breastfeed their infants.

4.7 Effects on ability to drive and use machines

There are no data available from studies on the effects on the ability to drive and use machines. 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

Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.

Tabulated list of adverse reactions

Infections and infestations:

Frequent: Mucocutaneous candidiasis (including vaginitis, stomatitis and glossitis).

*Frequency unknown:** Overgrowth of non-susceptible organisms.

Blood and lymphatic system disorders:

Less frequent: Reversible leucopenia (including neutropenia) and thrombocytopenia.

*Frequency unknown:** Reversible agranulocytosis, haemolytic anaemia, prolongation of bleeding time and prothrombin time (see section 4.4).

Immune system disorders:

*Frequency unknown:** Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome and hypersensitivity vasculitis (see sections 4.3 and 4.4).

Nervous system disorders:

Less frequent: Dizziness and headache.

*Frequency unknown:** Reversible hyperactivity, aseptic meningitis [(2)] and convulsions (see section 4.4).

Gastrointestinal disorders:

Frequent: Diarrhoea, nausea [A] and vomiting.

Less frequent: Indigestion and gastritis.

*Frequency unknown:** Antibiotic-associated colitis (including pseudo-membranous colitis and haemorrhagic colitis – see section 4.4), tooth discolouration[B] and black hairy tongue.

Hepato-biliary disorders:

Less frequent: Moderate rise in aspartate aminotransferase (AST) and / or elevated alanine aminotransferase (ALT). [C]

*Frequency Unknown:** Hepatitis and cholestatic jaundice. [D]

Skin and subcutaneous tissue disorders: [E]

Less frequent: Skin rash, pruritis, urticaria and erythema multiforme.

*Frequency Unknown:** Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (see section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS). [E]

Renal and urinary disorders:

*Frequency Unknown:** Interstitial nephritis and crystalluria (see section 4.9).

[A] Nausea is more often associated with higher oral doses. If gastrointestinal reactions are evident, it may be reduced by taking ACTIMENTIN ES 600 at the start of a meal.

[B] Superficial tooth discolouration has been reported less frequently in children. Good oral hygiene may help to prevent tooth discolouration and can usually be removed by brushing.

[C] 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.

[D] These events have been noted with other penicillins and cephalosporins (see section 4.4).

[E] If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued (see section 4.4).

*Reported post marketing and therefore, the frequency of occurrence is unknown as it cannot be estimated from available data.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms and signs of overdose

Gastrointestinal symptoms (nausea, vomiting and diarrhoea) as well as disturbance of the fluid and electrolyte balances may be evident with overdosage.

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.

Treatment of overdose

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

ACTIMENTIN ES 600 can be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification: A 20.1.2 Penicillins.

Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors; ATC code: J01CR02.

Mechanism of action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes, that is 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. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

Bactericidal action: the amoxicillin component of ACTIMENTIN ES 600 exerts a bactericidal action against many strains of Gram-positive and Gram-negative organisms. The clavulanic acid component has little bactericidal action. It does however, by inactivation of susceptible β-lactamases, protect amoxicillin from degradation by a large number of β-lactamase enzymes produced by penicillin-resistant strains of organisms.

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

Mechanisms of resistance

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

- inactivation by those bacterial beta-lactamases that are not inhibited by clavulanic acid, including class B, C and D.
- alteration of PBPs, which reduce the affinity of amoxicillin for the target.

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

Spectrum

ACTIMENTIN ES 600 should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data. Susceptibility to ACTIMENTIN ES 600 will vary with geography and time. Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

Inherently resistant organisms:

Aerobic Gram-negative micro-organisms

Acinetobacter spp.

Citrobacter freundii

Enterobacter spp.

Hafnia alvei

Legionella pneumophila

Morganella morganii

Providencia spp.

Pseudomonas spp.

Serratia spp.

Stenotrophomas maltophilia

Yersinia enterolitica

Other micro-organisms

Chlamydophila pneumoniae

Chlamydophila psittaci

Chlamydia spp.

Coxiella burnetti

Mycoplasma pneumoniae

5.2 Pharmacokinetic 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 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 (T_{max}) in each case is approximately one hour.

Amoxicillin serum concentrations achieved with the amoxicillin/clavulanic acid combination are similar to those produced by the oral administration of equivalent doses of amoxicillin alone. The same applies for clavulanic acid.

Distribution

Neither amoxicillin nor clavulanic acid is highly protein bound, with approximately 25 % of total plasma clavulanic acid and 18 % of total plasma amoxicillin 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.

Amoxicillin and clavulanic acid diffuse readily into most body tissues and fluids with the exception of spinal fluid and the brain. 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.

Results from animal studies report that there is no evidence for significant tissue retention of drug-derived material for either component.

Amoxicillin, like most penicillin antibiotics, 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 metabolite (inactive penicilloic acid) in quantities equivalent to 10 to 25 % of the initial dose. Clavulanic acid is extensively metabolised in man and eliminated in urine and faeces. It is also eliminated as carbon dioxide in expired air.

Elimination

The major route of elimination for amoxicillin is via the kidneys, 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 hours after administration. Results from various studies indicate 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 is excreted during the first 2 hours after administration.

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

Paediatric population

Results from pharmacokinetic studies performed in children, comparing three times a day and twice daily formulations, indicate that the elimination pharmacokinetics seen in adults apply to children with mature kidney function.

Dosing schedule

The mean AUC values for amoxicillin are essentially the same following twice-a-day (b.i.d) dosing or three-times-a-day (t.i.d) dosing, in adults. No differences between the twice daily (bd) and three times a day (tid) dosing regimens are seen when comparing the amoxicillin $T_{1/2}$, or C_{max} after normalisation for the different doses of amoxicillin administered. Similarly, no differences are seen for the clavulanate $T_{1/2}$, C_{rnax} or AUC values after appropriate dose normalisation.

Gender

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 clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route.

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acesulfame Potassium (E950)

Carmellose Sodium

Colloidal anhydrous silica

Crospovidone, Type A

Silicon dioxide

Xanthan gum

Saccharin Sodium (E954)

Strawberry flavour, containing maize maltodextrin, triethyl citrate (E1505) and propylene glycol (E1520).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Dry powder: 2 years.

Reconstituted suspensions: 7 days stored at 2 ˚C – 8 ˚C. Discard unused suspension after 7 days.

6.4 Special precautions for storage

Dry powder: store at or below 25 ˚C. Store in the original container in order to protect from moisture.

Reconstituted suspensions: store at 2 ˚C – 8 ˚C, in original container. Do not freeze.

6.5 Nature and contents of container

ACTIMENTIN ES 600 is available as 30 ml, 50 ml, 70 ml or 100 ml oral suspension. It is filled in amber type III glass bottles, with a nominal volume of 60 ml (for 30 ml oral suspension), 100 ml (for 50 ml or 70 ml oral suspension) or 150 ml (for 100 ml oral suspension). Bottles are closed with HDPE or PP white screw caps containing a liner (or sealing disk). The bottles are packed together with a dosing device; either:

- a 6 ml PE/PS syringe (with CE marking 0373) or
- a 5 ml PS spoon (with CE marking 0373) or
- a 5 ml PP cup (with CE marking 0546).

The glass bottles and dosing device are packed into outer cartons.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling of the product

For reconstitution, tap the bottle until all the powder flows freely. Add approximately 2/3 of the total amount of water for reconstitution (see table below) and shake vigorously to suspend powder. Add remainder of the water and again shake vigorously.

After reconstitution, invert and shake bottle well before each use.

Table 2: Reconstitution instructions

Strength	Volume of water to be added at reconstitution (ml)	Final volume of reconstituted oral suspension (ml)
600 mg / 42,9 mg per 5 ml	26	30
	43	50
	60	70
	85	100

The reconstituted solution is off-white to yellowish coloured homogeneous suspension with strawberry odour.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Activo Health (Pty) Ltd

Block B, Arena Office Park

272 West Avenue

Centurion

0157

8. REGISTRATION NUMBER(S)

54/20.1.2/0009

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 May 2023

10. DATE OF REVISION OF THE TEXT

To be allocated.