

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. Name of the medicinal product**

SYNERCEF 250 (Cefuroxime Axetil Tablets USP 250mg)

#### ***International Non-Proprietary Name (INN)***

Cefuroxime Axetil Tablets USP 250mg

#### **Strength**

250mg

#### **Pharmaceutical form**

Solid Dosage form

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each film coated tablet

contains: Cefuroxime Axetil

Eq. to Cefuroxime.....250 mg

For the full list of excipients, see section 6.1.

### **3. Pharmaceutical form**

Solid Dosage form

**Visual/ Physical description of FPP:** A White to off white, elongated, biconvex, film coated tablet having breakline on one side and plain on other side.

### **4. Clinical particulars**

#### ***4.1 Therapeutic indications***

Cefuroxime is indicated for the treatment of the infections listed below in adults and children from the age of 3 months.

- Acute streptococcal tonsillitis and pharyngitis.
- Acute bacterial sinusitis.
- Acute otitis media.
- Acute exacerbations of chronic bronchitis.
- Cystitis.
- Pyelonephritis.

- Uncomplicated skin and soft tissue infections.
- Treatment of early Lyme disease.

#### 4.2 Posology and method of administration

The usual course of therapy is seven days (may range from five to ten days).

| Indication                                                   | Dosage                                                  |
|--------------------------------------------------------------|---------------------------------------------------------|
| Acute tonsillitis and pharyngitis, acute bacterial sinusitis | 250 mg twice daily                                      |
| Acute otitis media                                           | 500 mg twice daily                                      |
| Acute exacerbations of chronic bronchitis                    | 500 mg twice daily                                      |
| Cystitis                                                     | 250 mg twice daily                                      |
| Pyelonephritis                                               | 250 mg twice daily                                      |
| Uncomplicated skin and soft tissue infections                | 250 mg twice daily                                      |
| Lyme disease                                                 | 500 mg twice daily for 14 days (range of 10 to 21 days) |

*Table 1. Adults and children*

( $\geq 40$  kg) *Table 2. Children (<40*

| Indication                                                                                            | Dosage                                                                              |
|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Acute tonsillitis and pharyngitis, acute bacterial sinusitis                                          | 10 mg/kg twice daily to a maximum of 125 mg twice daily                             |
| Children aged two years or older with otitis media or, where appropriate, with more severe infections | 15 mg/kg twice daily to a maximum of 250 mg twice daily                             |
| Cystitis                                                                                              | 15 mg/kg twice daily to a maximum of 250 mg twice daily                             |
| Pyelonephritis                                                                                        | 15 mg/kg twice daily to a maximum of 250 mg twice daily for 10 to 14 days           |
| Uncomplicated skin and soft tissue infections                                                         | 15 mg/kg twice daily to a maximum of 250 mg twice daily                             |
| Lyme disease                                                                                          | 15 mg/kg twice daily to a maximum of 250 mg twice daily for 14 days (10 to 21 days) |

There is no experience of using Cefuroxime axetil in children under the age of 3 months.

#### *Renal impairment*

The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established.

Cefuroxime is primarily excreted by the kidneys. In patients with markedly impaired renal function it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.

*Table 3. Recommended doses for Cefuroxime axetil in renal impairment*

| Creatinine clearance             | T <sub>1/2</sub><br>(hrs) | Recommended dosage                                                                 |
|----------------------------------|---------------------------|------------------------------------------------------------------------------------|
| ≥ 30 mL/min/1.73 m <sup>2</sup>  | 1.4– 2.4                  | no dose adjustment necessary (standard dose of 125 mg to 500 mg given twice daily) |
| 10-29 mL/min/1.73 m <sup>2</sup> | 4.6                       | standard individual dose given every 24 hours                                      |
| <10 mL/min/1.73 m <sup>2</sup>   | 16.8                      | standard individual dose given every 48 hours                                      |
| Patients on haemodialysis        | 2– 4                      | a further standard individual dose should be given at the end of each dialysis     |

#### *Hepatic impairment*

There are no data available for patients with hepatic impairment. Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

#### **Method of administration**

Oral use

Cefuroxime axetil tablets should be taken after food for optimum absorption.

Cefuroxime axetil tablets should not be crushed and are therefore unsuitable for treatment of patients who cannot swallow tablets. In children Cefuroxime axetil oral suspension may be used.

#### **4.3 Contraindications**

Hypersensitivity to cefuroxime or to any of the excipients used in formulation. Patients with known hypersensitivity to cephalosporin antibiotics.

History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of betalactam antibacterial agent (penicillins, monobactams and carbapenems).

#### **4.4 Special warnings and precautions for use**

##### **Hypersensitivity reactions**

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactam antibiotics because there is a risk of cross-sensitivity. As with all betalactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction). In case of severe hypersensitivity reactions, treatment with cefuroxime must be discontinued immediately and adequate emergency measures must be initiated.

Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefuroxime, to other cephalosporins or to any other type of betalactam agent. Caution should be used if cefuroxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.

##### **Severe cutaneous adverse reactions (SCARS)**

Severe cutaneous adverse reactions including: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms

(DRESS), which can be life-threatening or fatal, have been reported in association with cefuroxime treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefuroxime should be withdrawn immediately and an alternative treatment considered. If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of cefuroxime, treatment with cefuroxime must not be restarted in this patient at any time.

#### **Jarisch-Herxheimer reaction**

The Jarisch-Herxheimer reaction has been seen following cefuroxime axetil treatment of Lyme disease. It results directly from the bactericidal activity of cefuroxime axetil on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

#### **Overgrowth of non-susceptible microorganisms**

As with other antibiotics, use of cefuroxime axetil may result in the overgrowth of *Candida*. Prolonged use may also result in the overgrowth of other non-susceptible microorganisms (e.g. enterococci and *Clostridium difficile*), which may require interruption of treatment.

Antibacterial agent-associated pseudomembranous colitis have been reported with nearly all antibacterial agents, including cefuroxime and may range in severity from mild to life threatening. This diagnosis should be considered in patients with diarrhoea during or subsequent to the administration of cefuroxime. Discontinuation of therapy with cefuroxime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

#### **Interference with diagnostic tests**

The development of a positive Coombs' Test associated with the use of cefuroxime may interfere with cross matching of blood.

As a false negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving cefuroxime axetil.

#### **Cefuroxime 250 mg tablets contain sodium.**

This medicinal product contains less than 1 mmol sodium (23 mg) per

coated tablet, that is to say essentially 'sodium-free'.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

Drugs which reduce gastric acidity may result in a lower bioavailability of cefuroxime axetil compared with that of the fasting state and tend to cancel the effect of enhanced absorption after food.

Cefuroxime is excreted by glomerular filtration and tubular secretion. Concomitant use of probenecid is not recommended. Concurrent administration of probenecid significantly increases the peak concentration, area under the serum concentration time curve and elimination half-life of cefuroxime.

Concomitant use with oral anticoagulants may give rise to increased INR.

#### **4.6 Fertility, pregnancy**

##### **and lactation Pregnancy**

There are limited data from the use of cefuroxime in pregnant women. Studies in animals have shown no harmful effects on pregnancy, embryonal or foetal development, parturition or postnatal development. Cefuroxime axetil should be prescribed to pregnant women only if the benefit outweighs the risk.

##### **Breastfeeding**

Cefuroxime is excreted in human milk in small quantities. Adverse effects at therapeutic doses are not expected, although a risk of diarrhoea and fungus infection of the mucous membranes cannot be excluded. Breastfeeding might have to be discontinued due to these effects. The possibility of sensitisation should be taken into account. Cefuroxime should only be used during breastfeeding after benefit/risk assessment by the physician in charge.

##### **Fertility**

There are no data on the effects of cefuroxime axetil on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

#### **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, as this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

## 4.8 Undesirable effects

The most common adverse reactions are *Candida* overgrowth, eosinophilia, headache, dizziness, gastrointestinal disturbances and transient rise in liver enzymes.

The frequency categories assigned to the adverse reactions below are estimates, as for most reactions suitable data (for example from placebo-controlled studies) for calculating incidence were not available. In addition the incidence of adverse reactions associated with cefuroxime axetil may vary according to the indication.

Data from large clinical studies were used to determine the frequency of very common to rare 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 true frequency. Placebo-controlled trial data were not available. Where incidences have been calculated from clinical trial data, these were based on drug-related (investigator assessed) data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Treatment related adverse reactions, all grades, are listed below by MedDRA body system organ class, frequency and grade of severity. The following convention has been utilised for the classification of frequency: very common  $\geq 1/10$ ; common  $\geq 1/100$  to  $< 1/10$ , uncommon  $\geq 1/1,000$  to  $< 1/100$ ; rare  $\geq 1/10,000$  to  $< 1/1,000$ ; very rare  $< 1/10,000$  and not known (cannot be estimated from the available data).

| System organ class                   | Common                    | Uncommon                                                                 | Not known                               |
|--------------------------------------|---------------------------|--------------------------------------------------------------------------|-----------------------------------------|
| Infections and infestations          | <i>Candida</i> overgrowth |                                                                          | <i>Clostridium difficile</i> overgrowth |
| Blood and lymphatic system disorders | eosinophilia              | positive Coombs' test, thrombocytopenia, leukopenia (sometimes profound) | haemolytic anaemia                      |

|                                        |                                              |             |                                                                                                                                                                                                                                                                     |
|----------------------------------------|----------------------------------------------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Immune system disorders                |                                              |             | drug fever, serum sickness, anaphylaxis, Jarisch-Herxheimer reaction                                                                                                                                                                                                |
| Cardiac disorders                      |                                              |             | Kounis syndrome                                                                                                                                                                                                                                                     |
| Nervous system disorders               | headache, dizziness                          |             |                                                                                                                                                                                                                                                                     |
| Gastrointestinal disorders             | diarrhoea, nausea, abdominal pain            | vomiting    | pseudomembranous colitis                                                                                                                                                                                                                                            |
| Hepatobiliary disorders                | transient increases of hepatic enzyme levels |             | jaundice (predominantly cholestatic), hepatitis                                                                                                                                                                                                                     |
| Skin and subcutaneous tissue disorders |                                              | skin rashes | urticaria, pruritus, severe cutaneous adverse reactions (SCARs), including erythema multiforme (EM), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (exanthematic necrolysis) (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and |

|  |  |  |                      |
|--|--|--|----------------------|
|  |  |  | angioneurotic oedema |
|--|--|--|----------------------|

#### *Description of selected adverse reactions*

Cephalosporins as a class tend to be absorbed onto the surface of red cells membranes and react with antibodies directed against the drug to produce a positive Coombs' test (which can interfere with cross-matching of blood) and very rarely haemolytic anaemia. Transient rises in serum liver enzymes have been observed which are usually reversible.

#### *Paediatric population*

The safety profile for cefuroxime axetil in children is consistent with the profile in adults.

**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.pharmacyboardkenya.org>

## **4.9 Overdose**

Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma. Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment.

Serum levels of cefuroxime can be reduced by haemodialysis and peritoneal dialysis.

## **5. Pharmacological properties**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antibacterials for systemic use, second-generation cephalosporins, ATC-Code: J01DC02

#### **Mechanism of action**

Cefuroxime axetil undergoes hydrolysis by esterase enzymes to the active antibiotic, cefuroxime.

Cefuroxime inhibits bacterial cell wall synthesis following attachment to

penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

### **Mechanism of resistance**

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases; including (but not limited to) by extended-spectrum beta-lactamases (ESBLs), and AmpC enzymes that may be induced or stably derepressed in certain aerobic Gram-negative bacteria species;
- reduced affinity of penicillin-binding proteins for cefuroxime;
- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative bacteria;
- bacterial efflux pumps.

Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime.

Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime.

### **Cefuroxime axetil breakpoints**

Minimum inhibitory concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are as follows:

| Microorganism                                | Breakpoints (mg/L) |                   |
|----------------------------------------------|--------------------|-------------------|
|                                              | <b>S</b>           | <b>R</b>          |
| <i>Enterobacteriaceae</i> <sup>1, 2</sup>    | ≤ 8                | >8                |
| <i>Staphylococcus</i> spp.                   | Note <sup>3</sup>  | Note <sup>3</sup> |
| <i>Streptococcus</i> A, B, C and G           | Note <sup>4</sup>  | Note <sup>4</sup> |
| <i>Streptococcus pneumoniae</i>              | ≤ 0.25             | >0.5              |
| <i>Moraxella catarrhalis</i>                 | ≤ 0.125            | >4                |
| <i>Haemophilus influenzae</i>                | ≤ 0.125            | >1                |
| Non-species related breakpoints <sup>1</sup> | IE <sup>5</sup>    | IE <sup>5</sup>   |

<sup>1</sup> The cephalosporin breakpoints for *Enterobacteriaceae* will detect all clinically important resistance mechanisms (including ESBL and plasmid mediated AmpC). Some strains that produce beta-lactamases are susceptible or intermediate to 3rd or 4th generation cephalosporins with these breakpoints and should be reported as found, i.e. the presence or absence of an ESBL does not in itself influence the categorization of susceptibility. In many areas, ESBL detection and characterization is recommended or mandatory for infection control purposes.

<sup>2</sup> Uncomplicated UTI (cystitis) only.

<sup>3</sup> Susceptibility of staphylococci to cephalosporins is inferred from the methicillin susceptibility except for ceftazidime and cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections.

<sup>4</sup> The beta-lactam susceptibility of beta-haemolytic streptococci groups A, B, C and G is inferred from the penicillin susceptibility.

<sup>5</sup> insufficient evidence that the species in question is a good target for therapy with the drug.

An MIC with a comment but without an accompanying S or R-categorization may be reported.

S=susceptible, R=resistant

### **Microbiological susceptibility**

The prevalence of acquired 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 cefuroxime axetil in at least some types of infections is questionable.

Cefuroxime is usually active against the following microorganisms *in vitro*.

| Commonly susceptible species                                                                                                                                                                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Gram-positive aerobes:</b><br><i>Staphylococcus aureus</i> (methicillin-susceptible)* <i>Coagulase negative staphylococcus</i> (methicillin susceptible)<br><i>Streptococcus pyogenes</i> |
| <i>Streptococcus agalactiae</i>                                                                                                                                                              |

|                                                                                                                                                                                                                                                                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Gram-negative aerobes:</b><br><i>Haemophilus influenzae</i><br><i>Haemophilus parainfluenzae</i><br><i>Moraxella catarrhalis</i>                                                                                                                                                                    |
| <b>Spirochaetes:</b><br><i>Borrelia burgdorferi</i>                                                                                                                                                                                                                                                    |
| Microorganisms for which acquired resistance may be a problem                                                                                                                                                                                                                                          |
| <b>Gram-positive aerobes:</b><br><i>Streptococcus pneumoniae</i>                                                                                                                                                                                                                                       |
| <b>Gram-negative aerobes:</b><br><i>Citrobacter freundii</i><br><i>Enterobacter aerogenes</i><br><i>Enterobacter cloacae</i><br><i>Escherichia coli</i><br><i>Klebsiella pneumoniae</i><br><i>Proteus mirabilis</i><br><i>Proteus</i> spp. (other than <i>P. vulgaris</i> )<br><i>Providencia</i> spp. |
| <b>Gram-positive anaerobes:</b><br><i>Peptostreptococcus</i> spp.<br><i>Propionibacterium</i> spp.                                                                                                                                                                                                     |
| <b>Gram-negative anaerobes:</b><br><i>Fusobacterium</i> spp.<br><i>Bacteroides</i> spp.                                                                                                                                                                                                                |
| Inherently resistant microorganisms                                                                                                                                                                                                                                                                    |
| <b>Gram-positive aerobes:</b><br><i>Enterococcus faecalis</i><br><i>Enterococcus faecium</i>                                                                                                                                                                                                           |

**Gram-negative aerobes:**

*Acinetobacter* spp.  
*Campylobacter* spp.  
*Morganella*  
*morganii* *Proteus*  
*vulgaris*  
*Pseudomonas*  
*aeruginosa* *Serratia*  
*marcescens*

**Gram-negative anaerobes:**

*Bacteroides fragilis*

**Others:**

*Chlamydia* spp.  
*Mycoplasma* spp.  
*Legionella* spp.

\* All methicillin-resistant *S. aureus* are resistant to cefuroxime.

## 5.2 Pharmacokinetic properties

After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation. Optimum absorption occurs when it is administered shortly after a meal.

Following administration of cefuroxime axetil tablets peak serum levels (2.9 µg/mL for a 125 mg dose, 4.4 µg/mL for a 250 mg dose, 7.7 µg/mL for a 500 mg dose and 13.6 µg/mL for a 1000 mg dose) occur approximately 2.4 hours after dosing when taken with food. The pharmacokinetics of cefuroxime is linear over the oral dosage range of 125 to 1000 mg. No accumulation of cefuroxime occurred following repeat oral doses of 250 to 500 mg.

### Distribution

Protein binding has been stated as 33 to 50% depending on the methodology used. Following a single dose of cefuroxime axetil 500 mg tablet to 12 healthy volunteers, the apparent volume of distribution was 50 L (CV%=28%). Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

**Biotransformation**

Cefuroxime is not metabolised.

**Elimination**

The serum half-life is between 1 and 1.5 hours. Cefuroxime is excreted by glomerular filtration and tubular secretion. The renal clearance is in the region of 125 to 148 mL/min/1.73 m<sup>2</sup>.

***Special patient populations*****Gender**

No differences in the pharmacokinetics of cefuroxime were observed between males and females.

**Elderly**

No special precaution is necessary in the elderly patients with normal renal function at dosages up to the normal maximum of 1 g per day. Elderly patients are more likely to have decreased renal function; therefore, the dose should be adjusted in accordance with the renal function in the elderly.

**Paediatric population**

In older infants (aged >3 months) and in children, the pharmacokinetics of cefuroxime are similar to that observed in adults.

There is no clinical trial data available on the use of cefuroxime axetil in children under the age of 3 months.

**Renal impairment**

The safety and efficacy of cefuroxime axetil in patients with renal failure have not been established.

Cefuroxime is primarily excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function (i.e.  $Cl_{cr} < 30$  mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.

**Hepatic impairment**

There are no data available for patients with hepatic impairment. Since cefuroxime is primarily eliminated by the kidney, the presence of hepatic dysfunction is expected to have no effect on the pharmacokinetics of cefuroxime.

**PK/PD relationship**

For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with *in vivo* efficacy has been shown

to be the percentage of the dosing interval (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

### **5.3 Preclinical Safety Data**

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential.

Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

## **6. Pharmaceutical particulars**

### **6.1 List of excipients**

- Microcrystalline Cellulose pH 802
- Colloidal Silicon Dioxide
- Citric Acid
- Sodium Bicarbonate
- Polacrillin Potassium
- Sodium Lauryl Sulphate
- Crospovidone
- Croscarmellose Sodium
- Magnesium stearate
- Sodium Starch Glycolate
- Polyethylene Glycol
- Titanium Dioxide
- Hydroxy Propyl Methyl Cellulose E-15
- Talc
- Methylene Dichloride
- Isopropyl Alcohol

### **6.2 Incompatibilities**

Not applicable

**6.3 Shelf life**

36 Months

**6.4 Special precautions for storage**

Store protected from moisture at a temperature not exceeding 30°C.

**6.5 Nature and contents of container**

10 x 1 x 10 Tablets of Alu Alu blister packed in a carton along with package insert.

**6.6 Special precautions for disposal and other handling**

None.

**7. Manufacturing Authorization Holder and****Manufacturing Site Addresses Manufacturing****Authorisation Holder****Syner-Med Pharmaceutical (Kenya) Limited**

Gayatri House,  
P.O. Box No. 52096 - 00200,  
ICD Road, Off. Mombasa  
Road, Nairobi, Kenya

**Manufacturing Site****Addresses Scott-Edil****Pharmacia Ltd.**

56, EPIP, Phase-I, Jharmajri,  
Baddi, Distt. Solan (H.P.), 173205, INDIA.

**8. MARKETING AUTHORISATION NUMBER**

18766

**9. Date OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION**

16<sup>TH</sup> August 2026

**10.      Date of revision of the text**

16<sup>TH</sup> August 2026