Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ampicillin Syrup BP 125 mg/5 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml spoonful of reconstituted suspension contains ampicillin trihydrate BP equivalent to 125 mg of ampicillin.

3 PHARMACEUTICAL FORM

Powder for syrup 125 mg/5 ml.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of infections due to organisms sensitive to ampicillin.

4.2 Posology and method of adminstration

Route of administration: Oral

Adults and Children over 20 kg b.w.

ENT infections	1000 mg daily in divided doses
Bronchitis	1000 mg - 4000 mg daily in divided doses
Pneumonia	2000 mg daily in divided doses
Urinary tract infection	1500 mg daily in divided doses
Gastrointestinal infections	1500 mg - 3000 mg daily in divided doses

Children under 20 kg b.w.

Moderately severe infections	50 - 100 mg/kg/day in divided doses every 6-8 hours
Severe infections	200 mg/kg/day in divided doses every 6 hours

4.3 Contraindications

Use in patients with hypersensitivity to ampicillin, penicillins or cephalosporins.

4.4 Special warnings and special precautions for use

This drug should be used with caution in patients with a history of allergy.

Care must be taken when giving this drug especially in high dosage to patients with impaired renal function.

Patients with infectious mononucleosis are particularly prone to develop rashes with ampicillin.

4.5 Interaction with other medicinal products and other forms of interaction

1. Ampicillin should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates).

2. Ampicillin may reduce the efficacy of oral contraceptives.

3. Food can interfere with absorption of ampicillin, therefore doses should be taken 30 minutes to one hour before meals.

4.6 Pregnancy and lactation

Anti-infectives should not be used during pregnancy or lactation unless considered essential by the physician.

The drug has been shown to cross the placenta and is excreted in breast milk. Studies in animals and experience of human use to date have shown no evidence of teratogenic effects.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Side effects include maculopapular rashes, urticaria and other evidence of hypersensitivity, gastrointestinal disturbances and diarrhoea. Transiently raised liver enzymes occur occasionally and pseudomembranous colitis has been reported in a few cases.

Prolonged use of an anti-infective may result in the development of superinfection due to organisms resistant to that anti-infective.

4.9 Overdose

Cutaneous reactions when they occur may subside spontaneously within a few hours or days and can be controlled with the administration of an antihistamine. For allergic reactions, 0.3-1.0ml of adrenaline injection should be given intramuscularly followed by a further dose if no improvement occurs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ampicillin is a broad spectrum penicillin for the treatment of a wide range of infections caused by ampicillin-sensitive organisms.

Ampicillin is bactericidal, this action depends on the ability to reach and bind penicillin-binding proteins located in bacterial cytoplasmic membranes. It inhibits bacterial septum and cell wall synthesis, probably by acylation of the transpeptidase enzyme. Transpeptidase is a membrane bound bacterial enzyme responsible for cross-linking of peptidoglycan during the final stage of synthesis of bacterial cell walls. Hence, cross-linkage of peptidoglycan chains is prevented which is necessary for bacterial cell wall strength and rigidity. Therefore, bacterial cell division and growth are inhibited and lysis and elongation of susceptible bacteria frequently occur.

Rapidly dividing bacteria are those most susceptible to the action of penicillins. Certain micro-organisms, during their growth, produce an enzyme penicillinase which inhibits the action of ampicillin.

Minimum inhibitory concentrations for gram-positive organisms have been reported to range from 0.2 to 5 microgram per ml and for gram-negative organisms from 0.2 to 8 microgram per ml. It is inactive against most strains of Pseudomonas aeruginosa.

Ampicillin is acid stable and may be administered orally; an oral dose of 500 mg produces a peak blood level in one to three hours of about 4 mcg/ml and detectable amounts persist for about six hours. It is widely distributed in the tissues. Within six hours of administration, about 30% of the dose is excreted for the most part unchanged in the urine, while a concentration at least ten times in excess of plasma levels may be obtained in bile.

Ampicillin crosses the intact meninges in only minute amounts; in bacterial meningitis higher concentrations are found in the cerebrospinal fluid. Pregnant women given ampicillin may have therapeutic levels of the drug in the amniotic fluid in the later stages of pregnancy.

5.2 Pharmacokinetic properties

Ampicillin is incompletely absorbed from the gastrointestinal tract after oral administration. About 32-53 percent is absorbed. It is stable in acid gastric secretion. Whereas absorption efficiency appears to be independent of dose up to 1,000 mg, food appears to delay the onset and reduce the total amount absorbed. Ampicillin should therefore be administered ½ - 1 hour before meals. Peak serum concentration is attained in about two hours and following an oral dose of 500 mg it may range between 2 - 6 mcg/ml.

Protein binding of ampicillin is low, about 20 percent is bound to plasma proteins in circulation and plasma half-life is 1 - 2 hours.

It is widely distributed in most body fluids and bone; penetration into cells, the eyes and across normal meninges is poor. Inflammation increases the amount which crosses the blood brain barrier. Ampicillin crosses the placenta and appears in cord blood and amniotic fluid. It does not penetrate and is not bound to human erythrocyte.

Ampicillin serum levels in pregnant women are approximately one-half those in non-pregnant women after a comparable dose but urinary recoveries appear similar. Therefore, renal clearance rate is doubled during pregnancy. Ampicillin levels in the placenta and umbilical blood are the same as those in maternal serum. Serum clearance in the newborn is about one-half to two-thirds that of an adult with normal kidney function. Serum half-life is about 2.2 h in infants 2-5 days old, 3.4 h in those under one day and 1.1 h in those older than four months.

About 12-50 percent is metabolised by the liver. Ampicillin is excreted by the kidneys both as a result of tubular secretion and glomerular filtration. The amount excreted by glomerular filtration depends on the extent of protein binding.

Renal concentration range between one-half and twice those in serum and appear to be uniformly distributed among the cortex, medulla and papilla. Within six hours of administration, about thirty percent of the dose is excreted for most part unchanged in the urine. About twenty percent of the oral dose is excreted in the urine as penicilloic acid. Small amounts of ampicillin are excreted in bile and breast milk. Concomitant probenecid administration effectively reduces the renal clearance of ampicillin to that of the glomerular filtration rate. The net effect is to increase mean serum concentrations by a factor of two and to decrease urinary recovery by 18 percent. Concomitant administration of oxacillin or cimetidine had no effect on ampicillin absorption, biotransformation or excretion.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium carboxymethylcellulose (E466)
Propyl hydroxybenzoate (E216)
Methyl hydroxybenzoate (E218)
Sodium citrate (E331)

Sodium benzoate (E211)
Sucrose (refined sugar)
Aerosil 200
Amaranth 1508 (E123)
Sunset yellow (E110)
Vanilla flavour IFF 17.41. 0067
Apricot flavour IFF 17.41. 0070

6.2 Incompatibilities

None.

6.3 Shelf Life

The shelf life expiry date for this product shall not exceed three years from the date of its manufacture.

6.4 Special precautions for storage

Before reconstitution: Store below 25°C.
After reconstitution: Store in a refrigerator (2-8°C) and use within 7 days.

6.5 Nature and contents of container

1. Amber glass bottles with screw caps packed in individual carton OR packed in units of tens in cardboard boxes.

2. Translucent high density polyethylene, round bottles with plastic screw caps.

Pack sizes: 86 and 100 ml.

6.6 Instructions for use and handling

To reconstitute the granules, add 50 ml of water and shake well until all the powder is dissolved.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 493/3/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 29th January 2001

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