

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cidomycin Adult 80 mg/2 ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule (2ml) contains Gentamicin Sulphate equivalent to 80 mg Gentamicin base (40mg/ml).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

Clear colourless solution in easy open ampoules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Gentamicin injection is indicated for the treatment of serious systemic infections including those of the central nervous system due to organisms sensitive to this anti-infective.

4.2 Posology and method of administration

ADULTS:

Serious infections: If renal function is not impaired, 5mg/kg/daily in divided doses at six or eight hourly intervals. The total daily dose may be subsequently increased or decreased as clinically indicated.

Systemic infections: If renal function is not impaired, 3-5mg/kg/day in divided doses according to severity of infection, adjusting according to clinical response and body weight.

Urinary tract infections: As "Systemic infections". Or, if renal function is not impaired, 160mg once daily may be used.

Renal Impairment: Gentamicin is excreted by simple glomerular filtration and therefore reduced dosage is necessary where renal function is impaired. Nomograms are available for the calculation of dose, which depends on the patient's age, weight and renal function. The following table may be useful when treating adults.

The recommended dose and precautions for intramuscular and intravenous administration are identical. Gentamicin when given intravenously should be injected directly into a vein or into the drip set tubing over no less than three minutes. If administered by infusion, this should be over no longer than 20 minutes and in no greater volume of fluid than 100ml.

Blood urea mg/100ml (mmol/l)	Creatinine clearance (GRF) (ml/min)	Dose and frequency of administration
<40 (6-7)	>70	80mg* 8 hourly
40-100 (6-17)	30-70	80mg* 12 hourly
100-200 (17-34)	10-30	80mg* daily
>200 (>34)	5-10	80mg* every 48 hours
Twice weekly intermittent haemodialysis	<5	80mg after dialysis

* 60mg if body weight >60kg. Frequency of dosage in hours may also be approximated as serum creatinine (mg%) x eight or in SI units, as serum creatinine (micromol/l) divided by 11. If these dosage guides are used, peak serum levels must be measured. Peak levels of gentamicin occur approximately one hour after intramuscular and intravenous injection. Trough levels are measured just prior to the next injection. Assaying peak serum levels give confirmation of adequacy of dosage and also serves to detect levels above 10mg/l, at which the possibility of ototoxicity should be considered. One hour concentrations of gentamicin should not exceed 10mg/l (but should reach 4mg/l), while the pre-dose trough concentration should be less than 2mg/l.

ELDERLY:

Dosage is dependant on renal function status.

CHILDREN:

2 weeks to 12 years: The usual total daily dose is 6mg/kg in three divided doses.

Under two weeks of age: The usual daily dose is 6mg/kg in two divided doses.

4.3 Contraindications

Use in patients hypersensitive to gentamicin or to other aminoglycosides.

Use in early pregnancy unless the physician considers the infection life-threatening.

Use concurrently with other nephrotoxic or ototoxic drug substances.

Gentamicin should not be mixed with any other drug prior to administration.

4.4 Special warnings and precautions for use

In the presence of impaired renal function, frequency and the total dosage of gentamicin must be reduced to ensure the toxicity does not derive from peak serum levels over 10mg/l and troughs above 2ml.

Renal, auditory and vestibular function should be monitored in these patients. Regular monitoring of drug levels and renal function are necessary.

Gentamicin should be used with caution in the elderly, those with a history of, or existent ear disease, or those previously on aminoglycosides.

Gentamicin should only be used during pregnancy if considered essential by the physician.

4.5 Interaction with other medicinal products and other forms of interaction

Use of gentamicin concurrently with cephalosporins or loop diuretics may potentiate nephrotoxicity or ototoxicity respectively. Kidney function should be carefully monitored.

Aminoglycosides, including gentamicin may induce neuromuscular blockage and respiratory paralysis and should therefore only be used with great caution in patients receiving curare muscle relaxants or general anaesthetics.

Cross-sensitivity with neomycin and kanamycin may occur. Synergistic action has been demonstrated with penicillins. Concurrent use with amphotericin or cyclosporine may increase the risk of nephrotoxicity and ototoxicity. Concurrent use with oral anti coagulants may increase the hypoprothrombinaemic effect.

4.6 Pregnancy and lactation

Gentamicin should only be used during pregnancy if considered essential by the physician. There are no proven cases of intrauterine damage caused by gentamicin. However, in common with most drugs known to cross the placenta, usage in pregnancy should only be considered in life threatening situations where expected benefits outweigh possible risks. In the absence of gastro-intestinal inflammation, the amount of gentamicin ingested from the milk is unlikely to result in significant blood levels in breast-fed infants.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

Side effects include vestibular damage or hearing loss, particularly after exposure to ototoxic drugs or in the presence of renal dysfunction. Nephrotoxicity (usually reversible) and occasionally acute renal failure, hypersensitivity, anaemia, purpura, convulsions and effects on liver function occur occasionally.

4.9 Overdose

Haemodialysis and peritoneal dialysis will aid the removal from blood but the former is probably more efficient. Calcium salts given intravenously have been used to counter the neuromuscular blockade caused by gentamicin.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Gentamicin is a mixture of antibiotic substances produced by the growth of *micromonospora purpurea*. It is bactericidal with greater antibacterial activity than streptomycin, neomycin or kanamycin.

Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of rna, but its most important effects is inhibition of protein synthesis at the level of the 30s ribosomal subunit.

5.2 Pharmacokinetic properties

Gentamicin is not readily absorbed from the gastro-intestinal tract. Gentamicin is 70-85% bound to plasma albumin following administration and is excreted 90% unchanged in urine.

The half-life for its elimination in normal patients is 2 to 3 hours.

Effective plasma concentration is 4-8 micrograms/ml.

The volume of distribution (vd) is 0.3 l/kg.

The elimination rate constant is:

0.02 hr⁻¹ for anuric patients *

0.30 hr⁻¹ normal.

* Therefore in those with anuria care must be exercised following the usual initial dose, any subsequent administration being reduced in-line with plasma concentrations of gentamicin.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate

Water for injections

6.2 Incompatibilities

In general, gentamicin injection should not be mixed. In particular the following are incompatible in mixed solution with gentamicin injection: penicillins, cephalosporins, erythromycin, heparins, sodium bicarbonate. *Dilution in the body will obviate the danger of physical and chemical incompatibility and enable gentamicin to be given concurrently with the drugs listed above either as a bolus injection into the drip tubing, with adequate flushing, or at separate sites. In the case of carbenicillin, administration should only be at a separate site.

*Carbon dioxide may be liberated on addition of the two solutions. Normally this will dissolve in the solution, but under some circumstances small bubbles may form.

6.3 Shelf Life

Unopened: 3 years.

Opened: use immediately after opening.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Cidomycin Adult Injectable is supplied in ampoules. The ampoules comprise of Type I Ph. Eur. clear glass.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use only.

Discard any remaining solution after use.

7 MARKETING AUTHORISATION HOLDER

Sanofi-aventis Ireland Ltd.
Citywest Business Campus
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 540/36/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 March 1977

Date of last renewal: 09 March 2002

10 DATE OF REVISION OF THE TEXT

October 2006