

## **Summary of Product Characteristics (SmPC)**

### **1. NAME OF THE MEDICINAL PRODUCT**

GENTABETA

(Gentamicin Sulfate Injection 80mg/2ml)

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

Each 2 ml contains:

Gentamicin (as Sulphate) ....80mg

For a full list of excipients, see section 6.1

### **3. PHARMACEUTICAL FORM**

Solution for injection.

Ampoules containing a clear colourless solution.

### **4. CLINICAL PARTICULARS**

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

Gentamicin is bactericidal and is active against many strains of Gram-positive and Gram-negative pathogens including species of Escherichia, Enterobacter, Klebsiella, Salmonella, Serratia, Shigella, Staphylococcus aureus, some Proteus and against Pseudomonas aeruginosa.

Gentamicin is often effective against strains of these organisms which are resistant to other antibiotics such as streptomycin, kanamycin and neomycin. Gentamicin is effective against penicillin-resistant Staphylococci, but rarely effective against Streptococci.

Gentamicin is indicated in the treatment of the following infections when caused by susceptible organisms. Consideration should be given to official local guidance on the appropriate use of antibacterial agents

#### ***Severe Gram-Negative Infections:***

Upper and lower urinary tract infections

Burn and wound Infections

Septicaemia, Bacteraemia

Abscesses

Subacute Bacterial Endocarditis

Respiratory Tract infections (Bronchopneumonia)

Neonatal infections, Gynecological infections

#### ***Gram-Positive Infections:***

Bacteremia

Abscesses

Accidental and operative trauma

Burns and serious skin lesions.

## 4.2. Posology and Method of Administration

### Posology

The same dosage schedule is recommended for intramuscular and intravenous dosing. Dosage is related to the severity of infection, the age of the patient and the patient's renal function.

The daily dose recommended in children, adolescents and adults with normal renal function, is 3-6 mg/kg bodyweight per day as 1 (preferred) up to 2 single doses.

The daily dose in infants after the first month of life is 4.5-7.5 mg/kg body weight per day as 1 (preferred) up to 2 single doses.

The daily dose in newborns is 4-7 mg/kg body weight per day. Due to the longer half-life, newborns are given the required daily dose in 1 single dose.

In impaired renal function, the recommended daily dose has to be decreased and adjusted to the renal function.

Doses in Patients with Impaired Renal Function:

Dosage is adjusted for patients with renal impairment to minimize the risk of toxicity. The first dose should be as normal - after this, doses should be given less frequently, the interval being determined by results of renal function tests as below:

Renal Function Tests:

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

\*60 mg if body weight <60 kg. Frequency of dosage in hours may also be approximated as serum creatinine (mg%) x eight or in SI units, as serum creatinine ( $\mu\text{mol/l}$ ) 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 injection and intravenous injection. Trough levels are measured just prior to the next injection. Assay of peak serum levels gives confirmation of adequacy of dosage and also serves to detect levels above 10 mg/l, at which the possibility of ototoxicity should be considered. One hour concentrations of gentamicin should not exceed 10 mg/l (but should reach 4 mg/l), while the pre-dose trough concentration should be less than 2 mg/l.

The recommended dose and precautions for intramuscular and intravenous administration are identical. GENTABETA 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 100 ml.

**Monitoring advice:**

Serum concentration monitoring of gentamicin is recommended, especially in elderly, in newborns and in patients with impaired renal function. Samples are taken at the end of a dosing interval (trough level). Trough levels should not exceed 2 µg/ml administering gentamicin twice daily and 1 µg/ml for a once daily dose. Please refer to section 4.4.

**Method of Administration**

GENTABETA is normally given by the intramuscular route, but can be given intravenously when intramuscular administration is not feasible, e.g. in shocked or severely burned patients. When given intravenously, the prescribed dose should be administered slowly over no less than 3 minutes directly into a vein or into the rubber tubing of a giving set. Rapid, direct intravenous administration may give rise, initially to potentially neurotoxic concentrations and it is

essential that the prescribed dose is administered over the recommended period of time. Alternatively, the prescribed dose should be dissolved in up to 100 ml of normal saline or 5% glucose in water, but not solutions containing bicarbonate (see Incompatibilities 6.1.), and the solution infused over no longer than 20 minutes.

**4.3. Contraindications**

Patients being treated with gentamicin should be under close clinical observation because of its potential toxicity. Hypersensitivity to gentamicin, any other ingredient or other aminoglycosides. Myasthenia gravis. Gentamicin should be used with caution in premature infants because of their renal immaturity, in elderly people and generally in patients with impaired renal function. Diabetes, auditory vestibular dysfunctions, otitis media, a history of otitis media, previous use of ototoxic drugs and a genetically determined high sensitivity to aminoglycoside induced ototoxicity, are other main factors which may pre-dispose the patient to toxicity.

**4.4. Special Warnings and Precautions for Use**

Patients being treated with gentamicin should be under close clinical observation because of its potential toxicity. As with other aminoglycosides toxicity is related to serum concentration. At serum levels more than 10 micrograms/ml the vestibular mechanism may be affected.

Toxicity can be minimized by monitoring serum concentrations and it is advisable to check serum levels to confirm that peak levels (one hour) do not exceed 10 micrograms/ml and that trough levels (one hour before next injection) do not exceed 2micrograms/ml when administering Gentamicin twice daily and 1µg/ml for a once daily dose.

Evidence of toxicity requires adjustment of dosage or withdrawal of the drug.

As there is some evidence that the risk of both ototoxicity and nephrotoxicity is related to the level of total exposure, duration of therapy should be the shortest possible compatible with clinical recovery.

In some patients with impaired renal function, there has been a transient rise in blood- urea-nitrogen, which has usually reverted to normal during or following cessation of therapy. It is important to adjust the frequency of dosage according to the degree of renal function.

Gentamicin should be used with care in conditions characterized by muscular weakness.

In cases of significant obesity gentamicin serum concentrations should be closely monitored and a reduction in dose should be considered.

Concurrent use of other neurotoxic and/or nephrotoxic drugs can increase the possibility of gentamicin toxicity.

Co-administration with the following agents should be avoided:

Neuromuscular blocking agents such as succinylcholine and tubocurarine.

Other potentially nephrotoxic or ototoxic drugs such as cephalosporins and methicillin.

Potent diuretics such as ethacrynic acid and furosemide.

Other aminoglycosides.

To avoid adverse events, continuous monitoring (before, during and after) of renal function (serum creatinin, creatinin clearance), control of function of vestibule and cochlea as well as hepatic and laboratory parameters is recommended.

Sulphites can cause allergic-type reactions including anaphylactic symptoms and bronchospasm in susceptible people, especially those with a history of asthma or allergy.

The ampoule stopper contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

#### **4.5. Interaction with Other Medicinal Products and Other Forms of Interaction**

I. Antibacterials: increased risk of nephrotoxicity with cephalosporins notably cephalothin.

II. Gentamicin has been known to potentiate anticoagulants such as warfarin and phenindione.

III. Antifungals: increased risk of nephrotoxicity with amphotericin B.

IV. Cholinergics: antagonism of effect of neostigmine and pyridostigmine.

V. Cyclosporin, cisplatin: increased risk of nephrotoxicity.

VI. Cytotoxics: increased risk of nephrotoxicity and possible risk of ototoxicity with cisplatin.

VII. Diuretics: increased risk of ototoxicity with loop diuretics.

VIII. Muscle relaxants: effect of non-depolarising muscle relaxants such as tubocurarine enhanced. Neuromuscular blockade and respiratory paralysis have been reported from administration of aminoglycosides to patients who have received curare-type muscle relaxants during anesthesia.

IX. Indomethacin possibly increases plasma concentrations of gentamicin in neonates.

X. Concurrent use of bisphosphonates may increase the risk of hypocalcaemia.

XI. Concurrent use of the Botulinum Toxin and gentamicin may increase the risk of toxicity due to enhanced neuromuscular block.

#### **4.6. Fertility, Pregnancy and Lactation**

##### **Use in Pregnancy:**

Although no teratogenic effects have been observed, gentamicin is known to cross the placenta. Ototoxicity in the fetus is also a potential hazard. The benefits should, therefore, be weighed against such hazards to the fetus before using gentamicin during pregnancy.

##### **Use in Lactation:**

Small amounts of gentamicin have been reported in breast milk. Because of the potential for serious adverse reactions to an aminoglycoside in nursing infants, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the woman.

In the absence of gastro-intestinal inflammation, the amount of gentamicin ingested from the milk is unlikely to result insignificant blood levels in breast-fed infants.

#### **4.7. Effects on Ability to Drive and Use Machines**

Not applicable.

#### **4.8. Undesirable Effects**

Ototoxicity and nephrotoxicity are the most common side effects associated with Gentamicin therapy. Both effects are related to renal impairment and hence the dosage in such patients should be altered as suggested.

In addition, there have been rare reports of changes in electrolyte balance including hypocalcaemia and hypokalaemia caused by renal tubular dysfunction.

##### ***Ear and labyrinth disorders:***

Vestibular damage and ototoxicity may occur. This is usually reversible if observed promptly and the dose adjusted. Frequency Unknown (cannot be estimated from the available data): Irreversible hearing loss, deafness

##### ***Renal and urinary disorders:***

Nephrotoxicity. Frequency Very rare (< 1/10,000).: Acute renal failure, Fanconi-like syndrome in patients treated with a prolonged course of high-dose

##### ***Immune system disorders:***

Hypersensitivity, anaphylactic reactions associated with gentamicin containing therapy.

##### ***Blood and lymphatic system disorder:***

Anemia, blood dyscrasias, granulocytopenia (reversible)

***Nervous system disorders:***

Convulsions, central nervous system toxicity (including encephalopathy, confusion, lethargy, mental depression and hallucinations), neuromuscular blockade

***Hepatobiliary disorders:***

Hepatic function abnormal

***Metabolism and nutrition disorders:***

Hypomagnesaemia (on prolonged therapy)

***Infections and infestations:***

Combinations of antibiotics containing gentamicin have been associated with rare reports of *Clostridium difficile* diarrhoea.

***Gastrointestinal disorders:***

Stomatitis, nausea, vomiting

***Skin and subcutaneous tissue disorders:***

Urticaria, allergic contact dermatitis, purpura

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

**4.9. Overdose**

As in the case of other aminoglycosides, toxicity is associated with serum levels above a critical value.

In patients with normal renal function it is unlikely that toxic serum levels (in excess of 10 micrograms/ml) will be reached after administration of recommended doses. Where higher levels occur because of renal impairment, dosage should be reduced. In the event of an overdose or toxic reaction, peritoneal dialysis or hemodialysis will lower serum gentamicin levels. Calcium salts given intravenously have been used to counter the neuromuscular blockade caused by gentamicin.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamics Properties

Gentamicin is usually bactericidal in action. Although the exact mechanism of action has not been fully elucidated, the drug appears to inhibit protein synthesis in susceptible bacteria by irreversibly binding to 30S ribosomal subunits.

In general, gentamicin is active against many aerobic gram-negative bacteria and some aerobic gram-positive bacteria. Gentamicin is inactive against fungi, viruses, and most anaerobic bacteria. In vitro, gentamicin concentrations of 1-8 µg/ml inhibit most susceptible strains of *Escherichia coli*, *Haemophilus influenzae*, *Moraxella lacunata*, *Neisseria*, indole positive and indole negative *Proteus*, *Pseudomonas* (including most strains of *Ps. aeruginosa*), *Staphylococcus aureus*, *S. epidermidis*, and *Serratia*. However, different species and different strains of the same species may exhibit wide variations in susceptibility in vitro. In addition, in vitro susceptibility does not always correlate with in vivo activity. Gentamicin is only minimally active against *Streptococci*.

Natural and acquired resistance to gentamicin has been demonstrated in both gram-negative and gram-positive bacteria. Gentamicin resistance may be due to decreased permeability of the bacterial cell wall, alteration in the ribosomal binding site, or the presence of a plasmid-mediated resistance factor which is acquired by conjugation. Plasmid-mediated resistance enables the resistant bacteria to enzymatically modify the drug by acetylation, phosphorylation, or adenylation and can be transferred between organisms of the same or different species. Resistance to other aminoglycosides and several other anti-infectives (e.g. chloramphenicol, sulphonamides, tetracycline) may be transferred on the same plasmid.

There is partial cross-resistance between gentamicin and other aminoglycosides.

### 5.2. Pharmacokinetic Properties

#### Distribution

The distribution volume of gentamicin is about equivalent to the volume of extracellular water. In the newborn, water makes up 70 to 75% of bodyweight, compared with 50 to 55% in adults. The extracellular water compartment is larger (40% of body weight compared with 25% of body weight in adults). Therefore, the volume of distribution of gentamicin per kg bodyweight is affected and decreases with increasing age from 0.5 to 0.7L/kg for a premature newborn to 0.25 L/kg for an adolescent. The larger volume of distribution per kg bodyweight means that for adequate peak blood concentration a higher dose per kg bodyweight needs to be administered.

#### Elimination

Gentamicin is not metabolized in the body but is excreted unchanged in microbiologically active form predominantly via the kidneys. In patients with normal renal function the elimination half life is about 2 to 3 hours.

In neonates elimination rate is reduced due to immature renal function.

Elimination half-life averages approximately 8 hours in neonates at a gestational age of 26 to 34 weeks compared with about 6.7 hours in neonates at a gestational age of 35 to 37 weeks.

Correspondingly, clearance values increase from about 0.05 L/h in neonates at a gestational age of 27 to 0.2L/h in neonates at a gestational age of 40 weeks.

### **5.3. Preclinical Safety Data**

There is no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1. List of Excipients**

Sodium metabisulfite

EDTA-2Na

Anhydrous sodium carbonate

Water for injection.

### **6.2. Incompatibilities**

Gentamicin Injection should not be mixed with other drugs before injection and where co-administration of penicillins, cephalosporins, erythromycin, sulphadiazine, furosemide and betalactam antibiotics and heparin is necessary, the drugs should be administered separately, either as bolus injections into the tubing of the giving set or at separate sites. Addition of gentamicin to solutions containing bicarbonate may lead to the release of carbon dioxide.

### **6.3. Shelf Life**

36 months.

### **6.4. Special Precautions for Storage**

Do not store above 30°C.

### **6.5. Nature and Contents of Container**

2ml packed in one ampoule, such 10 ampoules packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

### **6.6. Special Precautions for Disposal and other Handling**

No special requirements



**7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION**

LABETA DRUGS LIMITED

125C, Olaitan street, Surulere, Lagos.

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+238174828411

**8. DRUG PRODUCT MANUFACTURER**

ANHUI CHENGSHI PHARMACEUTICAL CO. LIMITED.

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Telephone: 13151968065

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**9. NAFDAC REGISTRATION NUMBER**

B4-4094

Manufactured by:  
Anhui chengshi Pharmaceutical Co.,Ltd  
No.5068,Huaishang Road,Bengbu,Anhui Province,China.

Marketed by:  
LABETA DRUGS LIMITED

10 Ampoules

**GENTABETA<sup>®</sup>**

**GENTAMYCIN INJECTION 80MG/2ML**

**I.M./I.V.**

Each ml contains: Gentamycin 40mg Bp.  
Store in a dry place below 25°C  
Protect from heat and light  
Keep medicines out of reach of Children



**GENTABETA<sup>®</sup>**  
GENTAMYCIN INJECTION 80MG/2ML

NAFDAC REG NO.:B4-4094  
BATCH NO.: 101230906  
MFG DATE: 09/2023  
EXP.DATE: 09/2026



10 Ampoules

**GENTABETA<sup>®</sup>**

**GENTAMYCIN INJECTION 80MG/2ML**

**I.M./I.V.**

Chaque ml contient: Gentamicine 40 mg Bp.  
Conserver dans un endroit sec en dessous de 25 °C  
Protéger de la chaleur et de la lumière  
Gardez les médicaments hors de portée des enfants



**GENTABETA<sup>®</sup>**  
GENTAMYCIN INJECTION 80MG/2ML

CS

-  C60M40
-  C15M10
-  MY100
-  Y100

庆大小盒101230906

成品尺寸: 144x74x13mm

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