Storage: Store in a cool and dry place below 30°C, protected from light.
KEEP OUT OF REACH OF CHILDREN.

NAFDAC REG. NO.: **B4-7577**

2ml x 10amps

FRUSEMIDE INJECTION 20MG/2ML BP

FECCOX FRUSEMIDE

Each ampoule contains: Frusemide 20mg. **I.M./I.V.**

SOLE AGENT :
FECCOX PHARM.GEN.ENT.LTD
No 2 JABBA LAYOUT PANISAU, KANO, NIGERIA,

Manufactured by:
Guizhou Tiandi Pharmaceutical Company Ltd
No 6 Baokang Road, Yilong Hongxing Pharmaceutical Park,
Qianxi'nan Buyi and Miao Autonomous Prefecture,
Guizhou Province China

Frusemide Injection

Batch No.: **Mfg. Date:** **Exp. Date:**

Frusemide Injection

NAFDAC REG. NO.: **B4-7577**

2ml x 10amps

FRUSEMIDE INJECTION 20MG/2ML BP

FECCOX FRUSEMIDE

Each ampoule contains: Frusemide 20mg. **I.M./I.V.**

INDICATION: For detail see enclosed insert.

DOSAGE & ADMINISTRATION: As directed by the physician. Pis refer to insert.

CAREFULLY READ ENCLOSED PACKAGE INSERT BEFORE USE.

200526呋塞米小盒14.5x7.5x1.4cm

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed.

Summary Product Characteristics

1. **Name of the proprietary product:** -----

   Name of the nonproprietary International Product: Furosemide Injection BP 20 mg/2 ml

   Route of Administration: Intramuscular or slow intravenous injection.

2. **Qualitative and Quantitative composition:**

Batch Size: 100 Liter

Sr. No.	Ingredients	Specification	Qty/Ampoule (mg)	Overages	Qty/batch (kg)	Reason for inclusion
Active						
1.	Furosemide	BP	20.00	Nil	1.000	Active
Excipients						
2.	Sodium Chloride	BP	16.00	Nil	0.800	Buffering agent
3.	Anhydrous Sodium Sulfite	BP	2.00	Nil	0.100	Preservative
4.	Sodium Hydroxide	BP	2.00	Nil	0.100	Buffering agent
5.	Water for Injection	BP	q.s to 2 ml	Nil	q.s. to 100 Ltr.	Solvent
Total			**2 ml**	---	**100 Ltr.**	---

Where, BP: British Pharmacopoeia, q.s.: quantity sufficient

* Quantity of Furosemide will vary with potency and water content.

3. Pharmaceutical Form: Liquid Injection

4. Clinical Particulars:

4.1 Therapeutic Indications:
Furosemide Injection BP is indicated for the treatment of oedema associated with congestive heart failure and renal and hepatic disorders and for the control of hypertension. Furosemide Injection BP may be effective in patients unresponsive to thiazine diuretics. It may also be used to treat moderate renal insufficiency. Furosemide Injection BP may be indicated in conditions where diuresis is considered necessary.

4.2 Posology and method of administration:
Oedema: Initially 40mg once daily reducing to 20mg daily or 40mg on alternate days. Some patients may require 80mg daily while severe cases may require gradual titration up to 600mg daily. In severe cases 20mg to 40mg may be given by intramuscular or slow intravenous injection. The next dose should be given not less than 2 hours later.
Pulmonary oedema: 40mg to 50mg by slow intravenous injection followed by a second dose one to one and a half hours later.
Hypertension: Oral, initially 40mg two times a day, the dose then being adjusted according to patient response.
Renal failure: Furosemide Injection BP clearance is influenced by age, underlying disease state and drug interactions. Clearance reduces with increasing age probably due to decreasing renal function. Impaired renal function in renal or cardiac disease reduces renal clearance, although this may be compensated by increases in non-renal clearance. Hepatic failure has little impact on clearance.
Children - diuretic: Oral, initially 2mg per kg of body weight as a single dose, the dosage then being increased by an additional 1 to 2mg per kg of body weight at six to eight hour intervals until the desired response is obtained.
Doses as large as 5mg per kg may be required in some children with nephrotic syndrome. Suggested doses by injection are 0.5 to 1.5mg per kg daily to a maximum of 20mg daily.
Doses larger than 6mg per kg of body weight are not recommended. Dosing interval should be extended in neonates because of prolonged half-life.

4.3 Contraindications
Hypokalaemia, anuria and history of hypersensitivity to Furosemide Injection BP.

4.4 Special warnings and precautions for use
Hepatic cirrhosis and **ascites**, Furosemide Injection BP therapy is best initiated in hospital. Therapy should not be initiated in hepatic coma or electrolyte depletion until the basic condition is improved. Sudden alterations of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma, therefore, strict observation is required during diuretic treatment. Supplemental potassium chloride and, if required, an aldosterone antagonist are helpful in preventing hypokalaemia and metabolic alkalosis. Increasing azotemia and oliguria occurring during therapy of severe progressive renal disease requires discontinuation of Furosemide Injection BP.
Furosemide Injection BP should be used with caution in patients with prostatic hypertrophy or impairment of micturition since it can precipitate acute urinary retention.

At high doses and especially if serum concentrations are over 50µg/ml cases of tinnitus, and reversible or irreversible hearing loss, have been reported with Furosemide Injection BP therapy.
These effects have also been associated with rapid injection, severe renal impairment, doses exceeding by several times the usual recommended dose or concomitant therapy with other medicines associated with ototoxic side effects. Consideration should be given to using an alternative non-ototoxic diuretic. Excessive diuresis may lead to decreases in glomerular filtration rate and increased BUN. This can cause dehydration and blood volume reduction with circulatory collapse and possible vascular thrombosis and embolism particularly in elderly patients. The vasodilatory action of Furosemide Injection BP can also cause postural hypotension

4.5 Interaction with other medicinal products and other forms of interaction:
General- The dosage of concurrently administered cardiac glycosides, diuretics, anti-hypertensive agents, or other drugs with blood-pressure-lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given concomitantly with furosemide.
The toxic effects of nephrotoxic drugs may be increased by concomitant administration of potent diuretics such as furosemide.
Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).
Antihypertensives – enhanced hypotensive effect possible with all types. Concurrent use with ACE inhibitors or Angiotensin II receptor antagonists can result in marked falls in blood pressure, furosemide should be stopped or the dose reduced before starting an ACE-inhibitor or Angiotensin II receptor antagonists.
Antipsychotics – furosemide-induced hypokalaemia increases the risk of cardiac toxicity. Avoid concurrent use with pimozide. Increased risk of ventricular arrhythmias with amisulpride or sertindole.Enhanced hypotensive effect with phenothiazines.
When administering risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use.
Anti-arrhythmics (including amiodarone, disopyramide, flecanaide and sotalol) - risk of cardiac toxicity (because of furosemide-induced hypokalaemia). The effects of lidocaine, tocainide or mexiletine may be antagonised by furosemide.
Cardiac glycosides – hypokalaemia and electrolyte disturbances (including hypomagnesia) increase the risk of cardiac toxicity.
Drugs that prolong Q-T interval – increased risk of toxicity with furosemide-induced electrolyte disturbances
Vasodilators – enhanced hypotensive effect with moxisylyte (thymoxamine) or hydralazine
Other diuretics – profound diures is possible when furosemide given with metolazone.
Increased risk of hypokalaemia with thiazides.
Renin inhibitors – aliskiren reduces plasma concentrations of furosemide
Nitrates – enhanced hypotensive effect
Lithium - In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with furosemide, resulting in increased lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. Therefore, it is recommended

that lithium levels are carefully monitored and where necessary the lithium dosage is adjusted in patients receiving this combination.

Chelating agents – sucralfate may decrease the gastro-intestinal absorption of furosemide – the 2 drugs should be taken at least 2 hours apart

NSAIDs – increased risk of nephrotoxicity. Indometacin and ketorolac may antagonise the effects of furosemide. NSAIDs may attenuate the action of furosemide and may cause acute renal failure in cases of pre-existing hypovolaemia or dehydration.

Salicylates – effects may be potentiated by furosemide. Salycylic toxicity may be increased by furosemide

Antibiotics – increased risk of ototoxicity with aminoglycosides, polymixins or vancomycin - only use concurrently if compelling reasons. Increased risk of nephrotoxicity with aminoglycosides or cefaloridine. Furosemide can decrease vancomycin serum levels after cardiac surgery. Increased risk of hyponatraemia with trimethoprim. Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.

Antidepressants – enhanced hypotensive effect with MAOIs. Increased risk of postural hypotension with TCAs (tricyclic antidepressants). Increased risk of hypokalaemia with reboxetine

Antidiabetics – hypoglycaemic effects antagonised by furosemide

Antiepileptics – increased risk of hyponatraemia with carbamazepine. Diuretic effect reduced by phenytoin.

Antihistamines – hypokalaemia with increased risk of cardiac toxicity

Antifungals – increased risk of hypokalaemia and nephrotoxicity with amphotericin

Anxiolytics and hypnotics – enhanced hypotensive effect. Chloral or triclorfos may displace thyroid hormone from binding site.

CNS stimulants (drugs used for ADHD) – hypokalaemia increases the risk of ventricular arrhythmias

Corticosteroids – diuretic effect anatgonised (sodium retention) and increased risk of hypokalaemia

Glychyrrizin -(contained in liquorice) may and increase the risk of developing hypokalaemia.

Cytotoxics – increased risk of nephrotoxicity and ototoxicity with platinum compounds/cisplatin. Nephrotoxicity of cisplatin may be enhanced if furosemide is not given in low doses (e.g. 40 mg in patients with normal renal function) and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.

Anti-metabolites – effects of furosemide may be reduced by methotrexate and furosemide may reduce renal clearance of methotrexate

Dopaminergics – enhanced hypotensive effect with levodopa.

Immunomodulators – enhanced hypotensive effect with aldesleukin. Increased risk of hyperkalaemia with ciclosprin and tacrolimus. Increased risk of gouty arthritis with ciclosporin

Muscle relaxants – enhanced hypotensive effect with baclofen or tizanidine. Increased effect of curare-like muscle relaxants

Oestrogens – diuretic effect antagonised

Progestogens (drosperidone) – increased risk of hyperkalaemia

Prostaglandins – enhanced hypotensive effect with alprostadil

Sympathomimetics – increased risk of hypokalaemia with high doses of beta^2 sympathomimetics

Theophylline – enhanced hypotensive effect

Probenecid – effects of furosemide may be reduced by probenecid and furosemide may reduce renal clearance of probenecid.
Anaesthetic agents – general anaesthetic agents may enhance the hypotensive effects of furosemide. The effects of curare may be enhanced by furosemide.
Alcohol – enhanced hypotensive effect
Laxative abuse - increases the risk of potassium loss
Others: Concomitant administration of aminoglutethimide may increase the risk of hyponatraemia.

4.6 Pregnancy and Lactation:
There are no adequate controlled clinical studies of the use of Furosemide Injection BP in pregnant women so that it should only be used in pregnancy if its potential benefit outweighs the potential risk. Similarly since Furosemide Injection BP appears in breast milk caution is advised when Furosemide Injection BP is required for a nursing mother.

4.7 Effects on the ability to drive and use machines
Reduced mental alertness may impair ability to drive or operate dangerous machinery.

4.8 Undesirable effects:
Hypersensitivity: Photosensitivity reactions, necrotisingangiitis, skin rash, exfoliative dermatitis, erythema multiforme, purpura, urticaria, and pruritus.
Gastrointestinal disturbances: Nausea, diarrhoea, anorexia, vomiting, pancreatitis, jaundice, oral and gastric irritation, cramping and constipation. These are uncommon and account for less than 1% of all adverse reactions, with normal doses.
CNS effects: Blurred vision, dizziness, headache, tinnitus and deafness, paresthesias, vertigo, xanthopsia.
Cardiovascular: Orthostatic hypotension which may be aggravated by alcohol, barbiturates and narcotics.
Haematological: Agranulocytosis, aplastic anaemia, thrombocytopenia, leucopenia and anaemia.
Biochemical: Furosemide Injection BP may provoke hyperglycaemia, glycosuria, and hyperuricaemia leading to gout, however, such effects are rare in comparison to thiazides.
Other effects: Pancreatitis, liver damage, weakness, muscle spasm, restlessness, urinary bladder spasm and thrombophlebitis.

4.9 Overdose
The most frequently encountered problem of overdosage is excessive depletion of blood volume that may lead to profound shock, frequently complicated by hypokalaemia. Treatment is symptomatic and directed at fluid and electrolyte replacement.

5. Pharmacological Particulars:
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Diuretics
ATC code: C03CA01

Furosemide, an anthranilic acid derivative, is a loop diuretic having a rapid effect. its mode of action have utilisedmicropuncture studies in both human and experimental animals and stop flow experiments in dogs. It is reported to exert inhibiting effects on electrolyte reabsorption in

the proximal and distal renal tubules and especially in the ascending loop of Henle. The net effect is to enhance excretion of sodium, potassium and chloride ions and water. Furosemide Injection BP has no effect on carbonic anhydrase. Furosemide Injection BP has a steep dose-response curve and wide therapeutic range. In addition to its diuretic actions, Furosemide Injection BP has been shown to increase peripheral venous capacitance and reduce forearm blood flow. It also reduces renal vascular resistance with a resultant increase in renal blood flow the degree of which is proportional to the initial resistance. Furosemide Injection BP may be effective in patients with moderate renal insufficiency. Onset of diuresis following oral administration is within one hour, with peak effect occurring between 1-2 hours. Duration of effect is 6-8 hours. After intravenous administration the onset of diuresis is within 5 minutes and somewhat later after intramuscular injection. Duration of effect is approximately 2 hours.

5.2 Pharmacokinetic properties
Approximately 60 to 70% of an oral dose of Furosemide Injection BP is absorbed. Peak plasma concentrations occur 60 minutes after oral administration and 30 minutes after intramuscular injection. They increase with increasing dose. Administration after food apparently delays absorption producing lower but more persistent blood concentrations. Plasma protein binding of Furosemide Injection BP to albumin is between 95-99%, however, the response to Furosemide Injection BP is determined more by the medicine concentration in the tissue compartment than that in the plasma. Furosemide Injection BP is excreted in the urine mainly as unchanged Furosemide Injection BP but glucuronide and free amine metabolites also appear. The site of metabolism of the glucuronide metabolite is unknown. Approximately 80% of a dose appears in the urine within 24 hours. The terminal half-life is approximately 2 hours. Non-renal elimination also occurs especially in renal failure. Furosemide Injection BP crosses the placental barrier and is excreted in milk. Absorption is reduced to 43 – 46% in patients with end-stage renal disease, and is probably reduced also in patients with edematous bowel caused by congestive heart failure or nephrotic syndrome; parenteral administration may be preferable in these patients.

5.3 Pre-clinical Safety:
Toxicity studies in animals have not demonstrated toxic effects relevant to clinical use. There is no evidence of mutagenic or carcinogenic potential.

6. Pharmaceutical Particulars:

List of Excipients:

Sodium Chloride	BP
Anhydrous Sodium Sulfite	BP
Sodium Hydroxide	BP
Water for Injection	BP

6.2 Incompatibilities:
Nil.

6.3 Shelf Life: 36 months.

6.4 Special Precautions for storage:

Store below 30°C in a dry place. Protect from light.
The ampoules should be stored at room temperature in their original containers and protected from light.

6.5 Nature and contents of container:
An amber colored glass Ampoule of 2 ml, such 10 ampoules packed in a plastic tray and one such tray is packed in a carton along with pack insert.

6.6 Special precautions for disposal and other handling:
None.

7. Marketing Authorization Holder: FECCOX PHARMACY AND GENERAL ENTERPRISE LTD

8. Marketing Authorization Number: ---

9. Date of first Authorization /renewal of the authorization: ---

10. Date of revision of text: Jan. 2022