BIOTECH GABAPENTIN 100; 300 & 400 capsules
(43/2.5/0332; 43/2.5/0329; 43/2.5/0333)
Each capsule contains gabapentin 100 mg, 300 mg or 400 mg respectively

0003
Date of approval: 08 March 2023

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

BIOTECH GABAPENTIN 100 (capsules)

BIOTECH GABAPENTIN 300 (capsules)

BIOTECH GABAPENTIN 400 (capsules)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

BIOTECH GABAPENTIN 100: Each capsule contains 100 mg gabapentin.

BIOTECH GABAPENTIN 300: Each capsule contains 300 mg gabapentin.

BIOTECH GABAPENTIN 400: Each capsule contains 400 mg gabapentin.

Excipient with known effect:

Contains sugar (lactose monohydrate): BIOTECH GABAPENTIN 100 contains 16,833 mg; BIOTECH GABAPENTIN 300 contains 50,50 mg and BIOTECH GABAPENTIN 400 contains 67,33 mg per each capsule.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsules

BIOTECH GABAPENTIN 100: Size 3 hard gelatine capsule with white body and white cap, containing white crystalline powder.

BIOTECH GABAPENTIN 300: Size 1 hard gelatine capsule with yellow body and yellow cap, containing white crystalline powder.

BIOTECH GABAPENTIN 400: Size 0 hard gelatine capsule with orange body and orange cap, containing white crystalline powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BIOTECH GABAPENTIN is indicated as adjunctive therapy to other standard anticonvulsant medications in patients who have not achieved adequate seizure control with these agents used alone or in combination.

BIOTECH GABAPENTIN is also used in controlling both simple and complex partial seizures with or without secondary generalised tonic clonic seizures.

4.2 Posology and method of administration

Posology

Adults and children over 12 years:

Initially 300 mg three times a day. The dosage may be gradually increased based on the clinical response.

Usual effective dose: 900 – 1800 mg/day in three divided doses with not more than 12 hours between doses.

Dosages of up to 3 600 mg/day in divided doses three times a day for short periods have been well tolerated.

Since titration to an effective dose can progress rapidly, this may be accomplished in as few as three days using one of the following approaches:

	Day 1	**Day 2**	**Day 3**
900 mg/day or	1 x 100 mg, three times daily	2 x 100 mg, three times daily	1 x 300 mg, three times daily

	1 x 300 mg, once daily	1 x 300 mg, twice daily	1 x 300 mg, three times daily
1 200 mg /day or	2 x 100 mg, three times daily	3 x 100 mg, three times daily	1 x 400 mg, three times daily
	1 x 400 mg, once daily	1 x 400 mg, twice daily	1 x 400 mg, three times daily

Paediatric use:

Safety and efficacy in children under 12 years of age has not been established (see section 4.3).

Elderly:

Elderly patients should be carefully monitored for adverse events. Elderly patients may require dosage adjustment because of declining renal function with age (see creatinine clearance under Impaired renal function heading).

Impaired renal function:

The elimination of BIOTECH GABAPENTIN is decreased in patients with impaired renal function. For patients with impaired renal function or those undergoing haemodialysis the following maintenance dosage regimen are recommended.

Renal Function **Creatinine Clearance** **(mL per minute)**	**Total daily Dose** **(mg/day)**	**Dose regimen (mg)**

> 60	1200	400 three times a day
30 - 60	600	300 two times a day
15 - 30	300	300 once a day
< 15	150	300 once every other day
Haemodialysis[a]	-	200 - 300[b]
[a] *Loading dose of 300 to 400 mg* [b] *Maintenance dose of 200 to 300 mg gabapentin* *Following each 4 hours of haemodialysis.*		

Gabapentin plasma concentration need not be monitored to optimise BIOTECH GABAPENTIN therapy.

BIOTECH GABAPENTIN may be used as adjunct with phenobarbital, phenytoin, valproic acid and carbamazepine without any alteration of the plasma concentrations or serum concentrations of gabapentin or the other antiepileptic medicines.

Withdrawal of BIOTECH GABAPENTIN therapy or the addition of another medication to the treatment should be done gradually over a minimum of one week.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to gabapentin or to any of the excipients of BIOTECH GABAPENTIN listed in section 6.1.
- Children under the age of 12.

- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Patients being treated with BIOTECH GABAPENTIN should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviour, or any unusual changes in mood or behaviour.

Misuse, abuse potential or dependence

Cases of misuse, abuse and dependence have been reported. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of BIOTECH GABAPENTIN misuse, abuse or dependence (development of tolerance, dose escalation, intentional overdose, drug-seeking behaviour have been reported).

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with Gabapentinoids in several indications. A meta-analysis of randomized placebo-controlled trials of AEOs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for Gabapentinoids. Therefore, patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients and caregivers should be advised to seek medical advice should sign of suicidal ideation or behaviour emerge.

Porphyria: Safety has not been established.

BIOTECH GABAPENTIN should also be used with caution in renal impairment. See table for dosage guidelines in renal impairment and haemodialysis (see section 4.2).

Abrupt withdrawal of BIOTECH GABAPENTIN in epileptic patients may precipitate status epilepticus. Should it be required to reduce the dosage, discontinue the treatment or substitute with another anticonvulsant medicine, it should be done gradually over a minimum of one week.

Respiratory depression

Furthermore, data from literature showed that when gabapentinoids were given concomitantly with opioids, they potentiate the respiratory effect of opioids especially in patients with risk factors such as, advanced age, renal dysfunction, respiratory conditions such as chronic obstructive pulmonary disease as well as co-use with other central nervous system (CNS) depressants.

Lactose intolerance:

BIOTECH GABAPENTIN contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take BIOTECH GABAPENTIN.

4.5 Interaction with other medicines and other forms of interaction

The absorption of BIOTECH GABAPENTIN from the gastrointestinal tract is reduced by antacids containing aluminium with magnesium. It is recommended that BIOTECH GABAPENTIN be taken at least two hours after the administration of an antacid.

Co-administration of BIOTECH GABAPENTIN with oral contraceptives, containing norethindrone and/or ethinyl estradiol, does not influence the steady-state plasma concentrations of either component.

The co-administration of BIOTECH GABAPENTIN with central nervous system depression-producing medication or alcohol, may lead to increase CNS depression.

There is no interaction between gabapentin, phenobarbitone, phenytoin, valproic acid, carbamazepine or carbamazepine 10,11-epoxide.

False positive tests for proteinuria may occur with Ames Multistix-SG.

4.6 Fertility, pregnancy and lactation

Safety during pregnancy and lactation has not been established (see section 4.3).

4.7 Effects on ability to drive and use machines

BIOTECH GABAPENTIN frequently causes dizziness and somnolence. Head and body injuries and road traffic incidents have also been reported with BIOTECH GABAPENTIN. Therefore, patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether this medication affects their ability to perform these activities.

The concomitant use of alcohol will intensify these effects.

4.8 Undesirable effects

Nervous system disorders	
Frequent:	Ataxia.
Less frequent:	Amnesia.
Frequency unknown:	Somnolence; paraesthesia; vertigo.
Eye disorders	
Frequent:	Nystagmus; vision abnormalities including blurred vision and diplopia.
Frequency unknown:	Amblyopia; conjunctivitis.
Psychiatric disorders	

Less frequent:	Depression; mood or mental changes, suicidal ideation and behaviour.
General disorders and administration site conditions	
Less frequent:	Irritability; dizziness; drowsiness; fatigue; tremor; dryness of mouth and throat; dysarthria; headache; insomnia; trouble in thinking.
Frequency unknown:	Viral infections.
Blood and lymphatic system disorders	
Less frequent:	Leucopoenia.
Musculoskeletal and connective tissue disorders	
Frequent:	Myalgia.
Less frequent:	Asthenia.
Frequency unknown:	Fractures.
Vascular disorders	
Frequent:	Peripheral oedema.
Renal and urinary disorders	
Less frequent:	Frequent urination.
Frequency unknown:	Urinary incontinence.
Gastrointestinal disorders	
Less frequent:	Gastrointestinal effects including diarrhoea and dyspepsia; nausea and vomiting.
Frequency unknown:	Abdominal pain; constipation; dental abnormalities.
Cardiac disorders	
Less frequent:	Hypotension; vasodilatation; chest pain; palpitations.
Respiratory, thoracic and mediastinal disorders	

Less frequent:	Rhinitis.
Frequency unknown:	Pharyngitis; coughing; respiratory tract infection, respiratory depression, dyspnoea.
Ear and labyrinth disorders	
Less frequent:	Tinnitus.
Frequency unknown:	Otitis media.
Metabolism and nutrition disorders	
Less frequent:	Weight gain.
Frequency unknown:	Increased appetite.
Skin and subcutaneous tissue disorder	
Frequency unknown:	Rash; pruritus; abrasion; acne; maculopapular rash; purpura; erythema multiforme; Stevens-Johnson syndrome.
Reproductive system and breast disorders	
Frequency unknown:	Impotence.
Endocrine disorders	
Frequency unknown:	Pancreatitis; blood glucose fluctuations in patients with diabetes.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms of overdose include dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhoea. See section 4.8. Treatment is symptomatic and supportive. Haemodialysis has been shown to be effective in eliminating gabapentin and may be indicated in patients with renal impairment.

Reduced absorption of BIOTECH GABAPENTIN at higher doses may limit drug absorption and hence minimize toxicity at the time of overdosing.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.5 Anticonvulsants, including anti-epileptics

Gabapentin is an analogue of the neurotransmitter GABA (gamma-aminobutyric acid) and is neither a GABA agonist nor antagonist. The precise mechanism of action is unknown.

5.2 Pharmacokinetic properties

Absorption:

Gabapentin is absorbed from the gastrointestinal tract by means of a saturable mechanism. Bioavailability decreases as the dose increase.

Distribution:

Peak plasma concentrations are achieved within 2 to 3 hours, after administration. The steady state is achieved within 1 to 2 days. Absolute bioavailability of 300 mg and 400 mg gabapentin capsules is approximately 55 %.

Gabapentin has an apparent volume of distribution of approximately 50 to 60 L [~~£~~]. Gabapentin penetrates the blood-brain barrier, yielding cerebrospinal fluid (CSF) concentrations in the range of 7 to 35 % of corresponding steady-state plasma trough concentrations in patients with epilepsy.

Biotransformation:

Gabapentin is not metabolised and most of a dose is excreted unchanged in the urine with the remainder appearing in the faeces. Gabapentin does not induce hepatic mixed-function oxidase enzymes responsible for metabolism. Gabapentin elimination parameters are independent of dose.

Elimination:

In elderly patients with a decrease in renal function, the plasma clearance is decreased and elimination half-life is increased. Gabapentin elimination-rate constant, plasma clearance, and renal clearance are directly proportional to creatinine clearance.

Gabapentin is removed from plasma by haemodialysis.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Lactose monohydrate

Maize starch

Purified talc

Hard capsule shell (cap and body):

BIOTECH GABAPENTIN 100:

Titanium dioxide

Gelatine

BIOTECH GABAPENTIN 300:

Titanium dioxide

Yellow iron oxide

Gelatine

BIOTECH GABAPENTIN 400:

Titanium dioxide

Yellow iron oxide

Red iron oxide

Gelatine

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 ºC in a dry place.

6.5 Nature and contents of container

BIOTECH GABAPENTIN 100: Transparent PVC and printed aluminium foil blister strips containing 10 capsules packed in an outer carton containing 100 capsules.

BIOTECH GABAPENTIN 300: Transparent PVC and printed aluminium foil blister strips containing 10 capsules packed in an outer carton containing 100 capsules.

BIOTECH GABAPENTIN 400: Transparent PVC and printed aluminium foil blister strips containing 10 capsules packed in an outer carton containing 100 capsules.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park

400 16th Road, Randjespark,

Midrand, 1685

South Africa

8 REGISTRATION NUMBER(S)

BIOTECH GABAPENTIN 100: 43/2.5/0332

BIOTECH GABAPENTIN 300: 43/2.5/0329

BIOTECH GABAPENTIN 400: 43/2.5/0333

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of registration: 27 November 2014

NAMIBIA:

Biotech Gabapentin 100 Reg No. 16/2.5/0187	 NS2
Biotech Gabapentin 300 Reg No. 16/2.5/0188	 NS2
Biotech Gabapentin 400 Reg No. 16/2.5/0189	 NS2

10 DATE OF REVISION OF THE TEXT

08 March 2023