APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS: S3

PROPRIETARY NAME (and dosage form):

AURO-GABAPENTIN CAPSULES 100 mg (Capsule)

AURO-GABAPENTIN CAPSULES 300 mg (Capsule)

AURO-GABAPENTIN CAPSULES 400 mg (Capsule)

COMPOSITION:

AURO-GABAPENTIN CAPSULES 100 mg: Each capsule contains 100 mg gabapentin.

AURO-GABAPENTIN CAPSULES 300 mg: Each capsule contains 300 mg gabapentin.

AURO-GABAPENTIN CAPSULES 400 mg: Each capsule contains 400 mg gabapentin.

The inactive excipients are maize starch and talc. The empty hard gelatin capsule shell contains gelatin, sodium lauryl sulphate and titanium dioxide (C.I. No.: 77891), yellow iron oxide (C.I. No.: 77492) in **AURO-GABAPENTIN CAPSULES 300 mg** and **AURO-GABAPENTIN CAPSULES 400 mg**, and red iron oxide (C.I. No.: 77491) in **AURO-GABAPENTIN CAPSULES 400 mg**. The printing ink contains black iron oxide (C.I. No: 77499), butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac and strong ammonia solution.

PHARMACOLOGICAL CLASSIFICATION:

A 2.5 Central nervous system depressant. Anticonvulsants, including anti-epileptics.

PHARMACOLOGICAL ACTION:

Pharmacodynamics

Gabapentin is an analogue of the neurotransmitter GABA (gamma-aminobutyric acid). It is neither a GABA agonist nor antagonist and its mechanism of action as an anti-epileptic medicine remains unclear.

Pharmacokinetics

Gabapentin is absorbed after oral administration in part by the L-amino acid transport system, which is a carrier-mediated, saturable transport system. As the dose increases, bioavailability decreases.

Peak plasma concentrations are reached within 2 to 3 hours after administration. Absorption is unaffected by food and plasma protein binding is very low.

Absolute bioavailability of 300 mg and 400 mg gabapentin capsules is approximately 55 %. Gabapentin elimination parameters are independent of dose.

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 – 35 % of corresponding steady-state plasma trough concentrations in patients with epilepsy.

Gabapentin is not metabolised and is eliminated solely by renal excretion. Gabapentin does not induce hepatic mixed-function oxidase enzymes responsible for drug metabolism.

In elderly patients with decrease in renal function, 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.

INDICATIONS:

AURO-GABAPENTIN is indicated:

- As an adjunct to other standard anticonvulsant medications in patients who have not achieved adequate seizure control with these agents used alone or in combination.
- In controlling both simple and complex partial seizures with or without secondarily generalised tonic clonic seizures.

CONTRA-INDICATIONS:

Hypersensitivity to gabapentin or the product's excipients.

Children under 12 years

Pregnancy and lactation (See **"Pregnancy and lactation"**).

WARNINGS:

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

Porphyria: Safety has not been established.

INTERACTIONS:

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

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

Concomitant use of **AURO-GABAPENTIN** with a magnesium- and aluminium-containing antacid reduces gabapentin bioavailability by approximately 20 %. It is recommended that gabapentin be taken about two hours following antacid administration.

Concurrent use of **AURO-GABAPENTIN** with alcohol and other CNS depressants may increase the CNS depressant effects.

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

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Adults and children over 12 years:

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

response. Dosages of 900 to 1800 mg per day taken in three divided doses with not more than 12 hours between doses are effective for most patients. Dosages of up to 3600 mg 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:

900 mg/day:

Day 1 – 1 x 100 mg, three times a day

or 1 x 300 mg, once a day.

Day 2 – 2 x 100 mg, three times a day

or 1 x 300 mg twice a day.

Day 3 – 1 x 300 mg, three times a day

1200 mg/day:

Day 1 – 2 x 100 mg, three times a day

or 1 x 400 mg, once a day.

Day 2 – 3 x 100 mg, three times a day

or 1 x 400 mg, twice daily.

Day 3 – 1 x 400 mg, three times a day

Children under 12 years:

Safety and efficacy in children under 12 years have not been established.

Elderly patients and patients with impaired renal function:

Elderly patients may require dosage adjustment because of decrease in renal function with age. Dosage adjustments may be made on clinical response.

For patients with impaired renal function or those undergoing haemodialysis the following maintenance dosage regimen is recommended.

Renal Function Creatinine Clearance (ml per minute)	**Total daily Dose (mg/day)**	**Dosage 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	-	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 concentrations need not be monitored to optimise **AURO-GABAPENTIN** therapy.

AURO-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 agents.

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

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side Effects:

Adverse events are usually mild to moderate in severity and tend to diminish with continued use**.**

The most frequent side effects are somnolence, dizziness, ataxia, headache, nystagmus, tremor, fatigue, diplopia, nausea and/or vomiting and rhinitis.

Side effects are categorised by organ class system.

Blood and the lymphatic system disorders:

Less frequent: Leucopenia.

The following side effects have been reported and frequencies are unknown: Purpura.

Psychiatric disorders:

Frequent: Thinking abnormal, emotional lability.

Less frequent: Nervousness, depression.

Nervous system disorders:

Frequent: Somnolence, dizziness, ataxia, nystagmus, tremor.

Less frequent: Amnesia, dysarthria, insomnia, twitching, abnormal co-ordination.

The following side effects have been reported and frequencies are unknown: Confusion, paraesthesia, vertigo.

Eye disorders:

Frequent: Diplopia.

Less frequent: Amblyopia, conjunctivitis.

Vascular disorders:

Less frequent: Vasodilation.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Rhinitis, pharyngitis, coughing, respiratory tract infection.

Gastrointestinal disorders:

Less frequent: Nausea and vomiting, dyspepsia, abdominal pain, mouth or throat dry, constipation, dental abnormalities, diarrhoea, increased appetite.

Skin and subcutaneous tissue disorders:

Less frequent: Pruritus, abrasion

The following side effects have been reported and frequencies are unknown: Rash, acne, maculopapular rash.

Musculoskeletal, connective tissue and bone disorders

Frequent: Myalgia.

Less frequent: Fracture.

Reproductive system and breast disorders:

Less frequent: Impotence.

General disorders and administrative site conditions:

Frequent: Fatigue, peripheral oedema, viral infection, fever.

Less frequent: Headache, weight increase, back pain.

Investigations:

The following side effects have been reported and frequencies are unknown: White blood cells decreased.

Special Precautions:

AURO-GABAPENTIN should be used with caution in patients with a history of psychotic illness.

AURO-GABAPENTIN should also be used with caution in renal impairment. See table for dosage guidelines in renal impairment and haemodialysis.

Abrupt withdrawal of **AURO-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.

Ability to drive or use machinery:

Patients should be warned that **AURO-GABAPENTIN** may affect their alertness and that caution should be exercised when driving a vehicle, operating machinery or performing hazardous tasks. The concomitant use of alcohol will intensify these effects.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of overdose include dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhoea (see **"Side-Effects and Special Precautions"**). Treatment is symptomatic and supportive. Haemodialysis has been shown to be effective in eliminating **AURO-GABAPENTIN** and may be indicated in patients with renal impairment.

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

IDENTIFICATION:

AURO-GABAPENTIN CAPSULES 100 mg: White / White size '3' hard gelatin capsules imprinted with 'D' on white cap and '02' on white body with black edible ink filled with white to off-white crystalline powder.

AURO-GABAPENTIN CAPSULES 300 mg: Yellow / Yellow size '1' hard gelatin capsules imprinted with 'D' on yellow cap and '03' on yellow body with black edible ink filled with white to off-white crystalline powder.

AURO-GABAPENTIN CAPSULES 400 mg: Orange / Orange size '0' hard gelatin capsules imprinted with 'D' on orange cap and '04' on orange body with black edible ink filled with white to off-white crystalline powder.

PRESENTATION:

AURO-GABAPENTIN CAPSULES 100 mg:

1) **Blister:**

Capsules are packed in polyamide / aluminium foil / PVC film and printed aluminium foil with heat seal lacquer. Each blister contains 10 capsules.

Pack size: 100's – Each carton contains 10 blisters of 10 capsules.

2) **HDPE Container:**

Capsules are packed in a 100 ml white opaque HDPE container with a white opaque polypropylene child resistant closure with induction seal wad.

A desiccant (silica gel sachet) is included in the container. Each container contains 100 capsules.

Pack size: 100's – One white opaque HDPE container with 100 capsules.

AURO-GABAPENTIN CAPSULES 300 mg:

1) **Blister:**

Capsules are packed in polyamide / aluminium foil / PVC film and printed aluminium foil with heat seal lacquer. Each blister contains 10 capsules.

Pack size: 100's – Each carton contains 10 blisters of 10 capsules.

2) **HDPE Container:**

Capsules are packed in a 120 ml white opaque HDPE container with a white opaque polypropylene child resistant closure with induction seal wad.

A desiccant (silica gel sachet) is included in the container. Each container contains 100 capsules.

Pack size: 100's – One white opaque HDPE container with 100 capsules.

AURO-GABAPENTIN CAPSULES 400 mg:

1) **Blister:**

Capsules are packed in polyamide / aluminium foil / PVC film and printed aluminium foil with heat seal lacquer. Each blister contains 10 capsules.

Pack size: 100's – Each carton contains 10 blisters of 10 capsules.

2) HDPE Container:

Capsules are packed in a 200 ml white opaque HDPE container with a white opaque polypropylene child resistant closure with induction seal wad.

A desiccant (silica gel sachet) is included in the container. Each container contains 100 capsules.

Pack size: 100's – One white opaque HDPE container with 100 capsules.

STORAGE INSTRUCTIONS:

1) Blister:

Store at or below 25 °C. Keep blisters in the original carton until required for use. KEEP OUT OF REACH OF CHILDREN.

2) HDPE Container:

Store at or below 25 °C. Keep the containers tightly closed. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

AURO-GABAPENTIN CAPSULES 100 mg (Capsule): 43/2.5/0284

AURO-GABAPENTIN CAPSULES 300 mg (Capsule): 43/2.5/0285

AURO-GABAPENTIN CAPSULES 400 mg (Capsule): 43/2.5/0286

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Aurogen South Africa (Pty) Ltd

Woodhill Office Park, Building 1

53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12

1448, Johannesburg

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

Date of registration:

6 March 2014

Date of revision:

09 February 2022