APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S5

PROPRIETARY NAME (AND DOSAGE FORM):

LENIO 20 mg (Tablet)

LENIO 30 mg (Tablet)

COMPOSITION:

LENIO 20 mg:

Each film-coated tablet contains Paroxetine hydrochloride hemihydrate equivalent to 20 mg Paroxetine.

LENIO 30 mg:

Each film-coated tablet contains Paroxetine hydrochloride hemihydrate equivalent to 30 mg Paroxetine.

PHARMACOLOGICAL CLASSIFICATION:

A 1.2 Psychoanaleptics (Antidepressants)

PHARMACOLOGICAL ACTION:

Paroxetine is a selective serotonin re-uptake inhibitor (SSRI). The antidepressant effect of paroxetine is thought to be related to its effect on serotonergic neurotransmission.

Pharmacokinetics:

After oral administration, paroxetine is readily absorbed from the gastrointestinal tract. Absorption is not influenced by the presence of food, milk or antacids. Paroxetine is highly protein bound (95%) and undergoes extensive first-pass metabolism in the liver where it is metabolised in part by cytochrome P450 2D6 (CYP2D6). The metabolites appear to be clinically inactive. The elimination half-life is about 24 hours, but there is wide intersubject variability. Steady-state is achieved in 7 to 14 days in most patients. Paroxetine is excreted renally (approximately 64%) and in the faeces (approximately 36%) mainly as inactive metabolites.

INDICATIONS:

- Depression
- Obsessive Compulsive Disorder (OCD)
- Social phobia
- Panic disorder

CONTRA-INDICATIONS:

- Hypersensitivity to paroxetine or any of the ingredients of **LENIO**.
- MAO Inhibitors: **LENIO** should not be used in combination with MAO inhibitors or within 2 weeks of terminating treatment with MAO inhibitors. MAO inhibitors should not be introduced within 2 weeks of cessation of therapy with **LENIO**.
- Children under the age of 18 years (see **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"SIDE-EFFECTS"**).
- Co-administration with thioridazine.

WARNINGS AND SPECIAL PRECAUTIONS:

Safety and efficacy in children under 18 years have not been established (see **"CONTRA-INDICATIONS"** and **"SIDE-EFFECTS"**).

Patients with major depressive disorder, both adults and children, may experience worsening of their depression and or the emergence of suicidal ideation and behaviour, whether or not they are taking antidepressant medicines. This risk may persist until significant remission occurs. A causal role, however, for antidepressant medicines in inducing such behaviour has not been established. Patients being treated with **LENIO** should, nevertheless, be observed closely for clinical worsening and suicidality, especially at the beginning of a course of therapy, or at any time of dose changes, either increases or decreases.

Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric and non-psychiatric disorders.

The following symptoms have been reported in patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric: anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, and mania. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing **LENIO**, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If the decision is made to discontinue treatment, the dose of **LENIO** should be tapered (see **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"DOSAGE AND DIRECTIONS FOR USE"**).

LENIO should be used with caution in:

- patients with a history of mania.
- patients already receiving neuroleptics, since symptoms suggestive of Neuroleptic Malignant Syndrome may occur with this combination.
- patients concomitantly treated with medicines that give an increased risk for bleeding, and in patients with a known tendency for bleeding or those with predisposing conditions. Treatment with **LENIO** may cause skin and mucous membrane bleedings.

Co-administration with risperidone may lead to increased toxicity thereof (see **"INTERACTIONS"**).
Patients should be cautioned about their ability to drive a car and operate machinery.
The concomitant use of **LENIO** and alcohol is not advised.

Special Precautions:

Cardiac Condition:

Administration of **LENIO** to patients with a serious cardiovascular disorder such as (unstable) angina pectoris, poorly monitored cardiac decompensation, ventricular rhythm disorder and acute myocardial infarction, has not been studied and must therefore be avoided. If antidepressant medication is nevertheless indicated for such patients, **LENIO** should be administered with caution.

Epilepsy:

LENIO should be used with caution in patients with epilepsy.

Seizures:

Seizures may occur in patients treated with **LENIO**.

LENIO should be discontinued in any patient who develops seizures.

Electroconvulsive Therapy (ECT):

Clinical experience of the concurrent administration of **LENIO** and electroconvulsive therapy is lacking.

Hyponatraemia:

Hyponatraemia, which is generally reversible on discontinuation of **LENIO**, may occur predominantly in the elderly.

Glaucoma:

LENIO may cause mydriasis and should be used with caution in patients with narrow angle glaucoma.

INTERACTIONS:

Cimetidine, a medicine metabolising inhibitor, can increase the bioavailability of **LENIO**, whereas the medicine metabolising inducer phenytoin can decrease it.

When **LENIO** is to be co-administered with a known medicine metabolising enzyme inhibitor, consideration should be given to using doses at the lower end of the range. No initial dosage adjustment of **LENIO** is considered necessary when the medicine is to be co-administered with known medicine metabolising enzyme inducers. Any subsequent dosage adjustment should be guided by clinical effects (tolerability and efficacy).

LENIO inhibits the specific hepatic cytochrome P450 isozyme CYP2D6 responsible for the metabolism of debrisoquine and sparteine. This may lead to enhanced plasma levels of those co-administered medicines which are metabolised by this isozyme.

Medicines metabolised by this isozyme include certain tricyclic antidepressants (e.g. nortriptyline, amitriptyline, imipramine and desipramine), phenothiazine neuroleptics (e.g. perphenazine and thioridazine), risperidone, Type 1c antiarrhythmics (e.g. propafenone) and metoprolol.

Co-administration with risperidone may lead to increased toxicity thereof.

Interaction between **LENIO** and monoamine oxidase (MAO) inhibitors (see **"CONTRA-INDICATIONS"**), and also between **LENIO** and tryptophan medication may occur, resulting in a "serotonin syndrome".

Concurrent administration of **LENIO** and lithium should be undertaken with caution. Lithium levels should be monitored.

Co-administration of **LENIO** and phenytoin is associated with decreased plasma concentrations of paroxetine and increased adverse experiences (diarrhoea, indifference, imbalance, nervousness, ataxia and vertigo). No initial dosage adjustment of paroxetine is considered necessary when these agents are co-administered. Any subsequent adjustments should be guided by clinical effect.

Co-administration of **LENIO** with anti-convulsants may be associated with an increased incidence of adverse events.

Daily administration of **LENIO** may significantly increase the plasma levels of procyclidine; other anti-cholinergic medicines may be similarly affected. If anti-cholinergic effects are seen, the dose of procyclidine should be reduced.

LENIO should be administered with great caution to patients receiving oral anticoagulants (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Co-administration of **LENIO** with warfarin may result in increased bleeding in the presence of unaltered prothrombin times.

PREGNANCY AND LACTATION:

The safety of **LENIO** in pregnancy or lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

It is recommended that **LENIO** is administered in the morning with food.

LENIO should be swallowed rather than chewed.

Depression: 20 mg daily. This dose can be increased gradually if needed by 10 mg increments to a maximum of 50 mg daily according to the patient's response.

Panic Disorder: The recommended dose is 40 mg daily. The initial starting dose is 10 mg daily, which may be increased by 10 mg increments. The maximum dose is 60 mg daily.

The low initial starting dose is recommended to minimise the potential worsening of panic symptoms when initiating treatment with **LENIO**.

Obsessive Compulsive Disorder: The recommended dose is 40 mg daily. The initial starting dose is 20 mg daily, which may be increased by 10 mg increments to a maximum of 60 mg daily.

Social Phobia: The recommended daily dose is 20 mg. This dose may be increased gradually if needed by 10 mg increments to a maximum of 60 mg according to the patient's response.
Children: The safety and efficacy of **LENIO** in children under the age of 18 years have not been established. In children hostility, suicide ideation and self-harm may occur with **LENIO**.

Elderly: Elderly subjects may experience increased plasma concentrations with **LENIO**. Dosing should commence at the adult starting dose and may be increased gradually by 10 mg increments up to 40 mg daily.

Hepatic and renal impairment: Increased plasma concentrations of **LENIO** may occur in patients with severe renal impairment (creatinine clearance < 30 ml/min) or severe hepatic impairment. The dosage should therefore be restricted to the lower end of the dosage range.

Patients should be treated for a sufficient period to ensure that they remain free from symptoms. This may be several months or longer.

Abrupt discontinuation of **LENIO** should be avoided (see **"SIDE-EFFECTS"**).

SIDE-EFFECTS:

Definition of frequencies:

rare (≥ 1/10 000, < 1/1 000)

very rare (< 1/10 000), including isolated reports.

very common (≥ 1/10)

common (≥ 1/100, < 1/10)

uncommon (≥ 1/1 000, < 1/100)

Blood and lymphatic system disorders:

Uncommon: abnormal bleeding, predominantly of the skin and mucous membranes (mostly ecchymosis, but also in the gastrointestinal tract, central nervous system and eye).

Endocrine disorders

Very rare: syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Psychiatric disorders

Common: somnolence, insomnia.

Uncommon: confusion, hallucinations.

Rare: manic reactions.

Immune system disorders

Very rare: allergic reactions (including urticaria and angioedema).

Metabolism and nutrition disorders

Common: decreased appetite.

Rare: hyponatraemia.

Hyponatraemia, which may occur predominantly in elderly patients, is sometimes due to syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Nervous system disorders

Common: dizziness, tremor.

Uncommon: extrapyramidal disorders.

Rare: convulsions.

Very rare: serotonin syndrome (symptoms may include agitation, confusion, diaphoresis, hallucinations, hyperreflexia, myoclonus, shivering, tachycardia and tremor).

Extrapyramidal disorders may occur in patients using neuroleptic medication.

General disorders and administration site conditions

Common: asthenia.

Very rare: peripheral oedema.

Eye disorders

Common: blurred vision.

Very rare: acute glaucoma.

Respiratory, thoracic and mediastinal disorders

Common: yawning.

Renal and urinary disorders

Uncommon: urinary retention.

Reproductive system and breast disorders

Very common: sexual dysfunction.

Rare: hyperprolactinaemia / galactorrhoea.

Gastrointestinal disorders

Very common: nausea.

Common: constipation, diarrhoea, dry mouth.

Hepato-biliary disorders

Rare: elevation of hepatic enzymes.

Very rare: hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure). Elevation of hepatic enzymes may occur. Hepatic events, which may be fatal (such as hepatitis, sometimes associated with jaundice, and/or liver failure) may occur. Discontinuation of **LENIO** should be considered if there is prolonged elevation of liver function test results.

Skin and subcutaneous tissue disorders

Common: sweating.

Uncommon: skin rashes.

Very rare: photosensitivity reactions.

Symptoms seen on discontinuation of LENIO treatment

Common: Dizziness, sensory disturbances, sleep disturbances, anxiety, headache.

Uncommon: Agitation, nausea, tremor, confusion, sweating, diarrhoea.

Abrupt discontinuation of **LENIO** may lead to withdrawal symptoms such as dizziness, sensory disturbances, (including paraesthesia and electric shock sensations), sleep disturbances, insomnia, tremor, confusion, agitation or anxiety, headache, nervousness, vertigo, nausea and sweating. It is therefore advised that when **LENIO** treatment is no longer required, gradual discontinuation by dose tapering be carried out (see **"DOSAGE AND DIRECTIONS FOR USE"** and **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Children: The safety and efficacy of **LENIO** in children under the age of 18 years have not been established. In children hostility, suicide ideation and self-harm may occur with **LENIO**.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See **"SIDE-EFFECTS"**).

Symptoms of overdose:

Vomiting, dilated pupils, fever, blood pressure changes, headache, involuntary muscle contractions, agitation, anxiety, tachycardia, coma, and ECG changes.

Treatment of overdose:

Treatment is symptomatic and supportive.

There is no specific antidote. To decrease absorption, the stomach should be emptied by gastric lavage or induction of emesis or both. This should be followed by administration of 20 to 30 g of activated charcoal every four to six hours during the first 24 hours after ingestion. Frequent monitoring of vital signs and careful observation is recommended.

IDENTIFICATION:

LENIO 20 mg:

White to off-white coloured film-coated modified capsule shaped, biconvex tablets debossed with '56' on one side and 'C' with a deep breakline on the other side.

LENIO 30 mg:

Blue coloured film-coated modified capsule shaped, biconvex tablets debossed with 'F' on one side and '12' on the other side.

PRESENTATION:

LENIO 20 mg:

Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 90 gsm PVdC and 25 micron printed Aluminium foil. Each blister contains 10 tablets.

Pack size: 30's: 3 blisters of 10 tablets each.

LENIO 30 mg:

Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 90 gsm PVdC and 25 micron printed Aluminium foil. Each blister contains 10 tablets.

Pack size: 30's: 3 blisters of 10 tablets each.

STORAGE INSTRUCTIONS:

Store at or below 25 °C. Protect from light and moisture. Do not remove from the outer carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER:

LENIO 20 mg: 42/1.2/0208

LENIO 30 mg: 42/1.2/0209

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 PACKAGE INSERT:

Date of registration:

2 March 2012

Date of revision:

11 November 2022