SUMMARY OF PRODUCT CHARACTERISTICS
REGINOR (Pregabalin 75 mg / Nortriptyline Hydrochloride 10 mg Film-Coated Tablets)

1. NAME OF THE MEDICINAL PRODUCT

REGINOR (Pregabalin 75 mg / Nortriptyline Hydrochloride BP equivalent to Nortriptyline 10 mg Film-Coated Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains pregabalin BP 75 mg and nortriptyline hydrochloride BP equivalent to nortriptyline 10 mg.

Excipients with known effect:

Each tablet contains lactose monohydrate 45 mg, methylparaben sodium 0.30 mg and propylparaben sodium 0.08 mg. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White coloured, round shaped, standard concave, film-coated tablet, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

REGINOR is indicated for the treatment of neuropathic pain in adults.

4.2 Posology and method of administration

Adults

One tablet twice daily (b.d.) for oral use, or as recommended by a physician. The total daily dose of pregabalin is 150 mg and of nortriptyline is 20 mg. Dosage should be titrated based on clinical response and tolerability. The lowest effective dose should be used.

Discontinuation

Pregabalin should be withdrawn gradually over a minimum of 1 week. Nortriptyline should also be withdrawn gradually to avoid withdrawal symptoms.

Renal impairment

Pregabalin is eliminated predominantly by renal excretion; dose adjustment is required in patients with renal impairment. This fixed-dose combination may not be appropriate in patients with significant renal impairment. Nortriptyline should be used with caution in renal impairment.

Hepatic impairment

Nortriptyline requires careful dosing in patients with hepatic impairment. Pregabalin does not undergo significant hepatic metabolism and dose adjustment is not generally required for hepatic impairment alone. This combination is contraindicated in severe liver disease.

Elderly patients

Pregabalin clearance decreases with age, consistent with decreasing creatinine clearance; dose reduction may be required. Nortriptyline should be used with caution in the elderly, who are particularly susceptible to agitation, confusion and postural hypotension.

Paediatric population

Safety and efficacy in patients under 18 years have not been established.

Method of administration

Oral. May be taken with or without food.

4.3 Contraindications

- Hypersensitivity to pregabalin, nortriptyline or to any of the excipients listed in section 6.1.

- Concomitant use with monoamine oxidase inhibitors (MAOIs). A minimum 2-week interval is required between discontinuation of an MAOI and initiation of nortriptyline.
- Severe liver disease.
- Nursing mothers.

4.4 Special warnings and precautions for use

Pregabalin — suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents. A meta-analysis showed a small increased risk of suicidal ideation and behaviour with antiepileptic drugs. Patients should be monitored for signs of suicidal ideation. Patients and caregivers should be advised to seek medical advice if such signs emerge.

Pregabalin — vision-related effects

Visual adverse reactions including loss of vision, visual blurring or other changes of visual acuity have been reported; many were transient. Discontinuation of pregabalin may result in resolution or improvement of these visual symptoms.

Pregabalin — encephalopathy

Cases of encephalopathy have been reported, mostly in patients with underlying conditions that may precipitate encephalopathy.

Pregabalin — renal failure

Cases of renal failure have been reported; in some cases discontinuation showed reversibility.

Pregabalin — seizures

Pregabalin should not be abruptly discontinued in patients with epilepsy, to avoid precipitating status epilepticus. Convulsions, including status epilepticus and grand mal convulsions, may occur during medication. Concomitant withdrawal of antiepileptic medicinal products in treatment-refractory patients has a low success rate.

Pregabalin — diabetes

Diabetic patients who gain weight on pregabalin may need to adjust their hypoglycaemic medicinal products.

Nortriptyline — suicidal thoughts and worsening

Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide. Close supervision should accompany therapy, especially in early treatment and following dose changes. Patients and caregivers must be alerted to monitor for any clinical worsening, suicidal behaviour or unusual changes in behaviour and to seek medical advice immediately.

Nortriptyline — cardiac effects

Patients with cardiovascular disease should be given nortriptyline only under close supervision because of the tendency to produce sinus tachycardia and to prolong conduction time. Myocardial infarction, arrhythmia and strokes have occurred. Nortriptyline should be used with caution in hyperthyroid patients or those receiving thyroid medication. The use of nortriptyline should be avoided, if possible, in patients with a history of epilepsy, as nortriptyline lowers the convulsive threshold.

Nortriptyline — psychiatric cautions

In schizophrenic patients, nortriptyline may exacerbate psychosis or activate latent schizophrenic symptoms. In manic-depressive patients, nortriptyline may cause symptoms of the manic phase to emerge. Cross-sensitivity between nortriptyline and other tricyclic antidepressants is possible.

Alcohol

Alcohol should be avoided when taking REGINOR, as CNS effects may be potentiated.

Lactose and paraben content

This product contains lactose monohydrate 45 mg per tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This product contains methylparaben sodium and propylparaben sodium, which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

Pregabalin interactions

Pregabalin is predominantly excreted unchanged in the urine (<2% metabolised); it does not bind to plasma proteins. Pharmacokinetic interactions with other drugs are unlikely. No pharmacokinetic interactions have been observed with carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital or topiramate.

CNS depressants (benzodiazepines, opioids, alcohol, sedatives):

Concomitant use may enhance CNS depression. Opioids, particularly morphine, may increase gabapentinoid exposure.

Thiazolidinediones (pioglitazone, rosiglitazone):

Potential additive effects on oedema and weight gain when used with pregabalin.

Nortriptyline interactions
MAOIs (contraindicated):

Hyperpyretic crises, severe convulsions and fatalities have occurred.

Sympathomimetics (not recommended):

Nortriptyline should not be given with adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine or phenylpropanolamine.

CYP2D6 inhibitors (fluoxetine, quinidine, antidepressants, phenothiazines, carbamazepine):

May lead to increased nortriptyline plasma concentrations; supervision and dosage adjustment required.

Antihypertensives:

Nortriptyline may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and clonidine. All antihypertensive therapy should be reviewed during TCA treatment.

QT-prolonging drugs, barbiturates, alcohol, anticholinergic agents:

Require caution or monitoring as described in the amitriptyline/nortriptyline class labelling.

4.6 Fertility, pregnancy and lactation

Pregnancy

REGINOR is not recommended during pregnancy. Pregabalin has been shown to be foetotoxic in rats and rabbits at exposures above human exposure. Nortriptyline: safety in pregnancy has not been established and animal studies indicate a risk of hazard; do not administer unless the potential benefits clearly outweigh the risk.

Breast-feeding

REGINOR is not recommended during breast-feeding. Pregabalin is excreted into human breast milk. Nortriptyline is contraindicated in nursing mothers.

Fertility

No adverse effects on fertility were observed in rats at clinically relevant pregabalin doses.

4.7 Effects on ability to drive and use machines

Patients should not drive, use machinery or participate in dangerous activities while taking REGINOR due to the potential for somnolence, dizziness and impaired coordination from both components.

4.8 Undesirable effects

Summary of the safety profile

The adverse reaction profile reflects the combined profiles of pregabalin and nortriptyline. Pregabalin most commonly causes dizziness, somnolence and headache. Nortriptyline most commonly causes anticholinergic effects, QT prolongation and cardiac effects.

Pregabalin adverse reactions (selected, from pooled clinical trial data): Very common: dizziness, somnolence. Common: nasopharyngitis, neutropenia, increased appetite, euphoric mood, confusion, irritability, disorientation, insomnia, abnormal dreams, ataxia, coordination abnormal, tremor, dysarthria, amnesia, memory impairment, disturbance in attention, paraesthesia, hypoaesthesia, sedation, balance disorder, lethargy, visual blurring, diplopia, dry mouth, constipation, vomiting, flatulence, distension, peripheral oedema, fatigue, oedema, weight gain. Uncommon: syncope, myoclonus, dyskinesia, nystagmus, cognitive disorder. Rare: loss of consciousness, vision loss. Not known: angioedema, hallucinations, encephalopathy, renal failure, heart failure.

Nortriptyline adverse reactions (selected): Cardiovascular: hypotension, tachycardia, palpitations, MI, arrhythmias, heart block, stroke; QT prolongation, sinus tachycardia. Psychiatric: confusional states, hallucinations, disorientation, anxiety, agitation, insomnia, hypomania; suicidal ideation and behaviour. Neurological: paraesthesia, peripheral neuropathy, extrapyramidal symptoms, seizures. Anticholinergic: dry mouth, blurred vision, constipation, paralytic ileus, urinary retention. Haematological: bone marrow depression,

agranulocytosis, aplastic anaemia. Other: rash, urticaria, photosensitisation, jaundice, hepatitis, hepatic necrosis, weight changes, gynaecomastia, galactorrhoea, impotence.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose

Pregabalin

Signs of overdose include somnolence, confusional state, agitation and restlessness. Treatment includes general supportive measures and may include haemodialysis if necessary. Activated charcoal may reduce absorption.

Nortriptyline

Symptoms: blurred vision, confusion, restlessness, dizziness, hypothermia or hyperthermia, agitation, vomiting, hyperactive reflexes, dilated pupils, myoclonic jerks, seizures, respiratory depression, hypotension, cardiac arrhythmias, QRS widening, QT prolongation, AV block and ventricular tachyarrhythmias. QRS duration >100 ms is predictive of more severe toxicity. Treatment: symptomatic and supportive; activated charcoal; sodium bicarbonate for arrhythmias with widened QRS; monitoring until QRS normalises.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC codes: Pregabalin: N03AX16; Nortriptyline: N06AA10.

Pregabalin:

A gamma-aminobutyric acid (GABA) analogue [(S)-3-(aminomethyl)-5-methylhexanoic acid]. Pregabalin binds potently to the α2-δ (alpha-2-delta) subunit of voltage-gated calcium channels in the CNS, reducing the release of excitatory neurotransmitters including glutamate, noradrenaline, serotonin, dopamine and substance P. This modulation of calcium channel activity underlies its analgesic, anticonvulsant and anxiolytic activity.

Nortriptyline:

A tricyclic antidepressant and the principal active metabolite of amitriptyline. Nortriptyline inhibits the re-uptake of noradrenaline and (to a lesser extent) serotonin at nerve terminals. Its analgesic activity in neuropathic pain involves noradrenaline reuptake inhibition at the spinal level, modulating descending pain inhibitory pathways. Nortriptyline also has ion-channel blocking effects and anticholinergic and sedative properties.

5.2 Pharmacokinetic properties

Pregabalin

Absorption: Rapidly absorbed when administered fasted; peak plasma concentrations within 1 hour after single and multiple dosing. Oral bioavailability ≥90%, independent of dose. Steady state achieved within 24–48 hours. Food decreases Cmax by approximately 25–30% and delays Tmax to approximately 2.5 hours, but does not affect the total extent of absorption. Distribution: Apparent volume of distribution approximately 0.56 L/kg; not bound to plasma proteins. Biotransformation: Negligible (<2% of dose recovered as metabolites in urine). Elimination: Predominantly by renal excretion as unchanged drug; mean elimination half-life 6.3 hours. Pregabalin clearance is directly proportional to creatinine clearance.

Nortriptyline

Absorption: Tmax approximately 5.5 hours (range 4.0–8.8 hours); mean oral bioavailability approximately 51%. Distribution: Apparent volume of distribution approximately 1,633 L (21 L/kg); plasma protein binding approximately 93%. Nortriptyline crosses the placental barrier. Biotransformation: Demethylation and hydroxylation (CYP2D6) followed by conjugation with glucuronic acid; main active metabolite is 10-hydroxynortriptyline. Elimination: Half-life approximately 26 hours (range 16–38 hours); excreted predominantly in urine; renal elimination of unchanged drug insignificant (approximately 2%). Therapeutic plasma concentration in neuropathic pain: approximately 50–140 ng/ml (amitriptyline + nortriptyline). Levels above 170–200 ng/ml are associated with an increased risk of cardiac conduction disturbance.

5.3 Preclinical safety data

Pregabalin: No evidence of mutagenicity or genotoxicity. In carcinogenicity studies, an increased incidence of haemangiosarcoma was observed in mice at higher exposures; no tumours in rats at exposures up to 24 times

human exposure. In juvenile rats, CNS signs of hyperactivity and bruxism and some growth changes were observed at therapeutic exposures. Foetal toxicity in rats and rabbits only at exposures sufficiently above human exposure; no teratogenic effects in mice, rats or rabbits. Pregabalin crosses the blood-brain barrier, placenta and is present in milk of lactating rats.

Nortriptyline: Cranial malformations and encephalocele have been observed in animal reproduction studies. Nortriptyline inhibited hERG channels, suggesting a risk for cardiac arrhythmia at clinical plasma concentrations.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, microcrystalline cellulose (MCCP-101), lactose monohydrate (excipient with known effect — 45 mg/tablet), povidone K-30, methylparaben sodium (excipient with known effect — 0.30 mg/tablet), propylparaben sodium (excipient with known effect — 0.08 mg/tablet), sodium starch glycolate, aerosol-200 (colloidal silicon dioxide), croscarmellose sodium, magnesium stearate, Mediicoatt-Uni WT335 white universal (film coat).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30°C. Keep out of the reach and sight of children.

6.5 Nature and contents of container

ALU-ALU blister pack in carton box with package leaflet. Pack size: 30 tablets (3×10).

6.6 Special precautions for disposal and other handling

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SYMBIOTICA BIOCEUTICALS LTD.

P.O. Box 64001-00620, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

H2026/CTD11543/24492

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

12.03.2026

10. DATE OF REVISION OF THE TEXT

12.03.2026