SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MIROGAB TABLETS 10 MG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Mirogabalin (as besylate)..... 10 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Light Pink color, oval biconvex film coated tablet. Plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is indicated for the treatment of Peripheral Neuropathic Pain, Diabetic Peripheral Neuropathic Pain (DPNP) and Postherpetic Neuralgia (PHN).

4.2 Posology and method of administration

Posology

For adults, administer mirogabalin at an initial oral dose of 5 mg twice daily, and then increase the dose by 5 mg per dosing with an interval of at least 1 week up to 15 mg twice daily. The dose may be increased or decreased appropriately in the range between 10 mg and 15 mg twice daily, based on individual patient age or symptoms.

Since mirogabalin concentrations in plasma may increase in patients with reduced renal function, possibly increasing the risk of adverse reactions, careful administration with close monitoring is necessary for these patients. For patients with renal impairment, the dose and dosing intervals should be adjusted, referring to creatinine clearance levels listed in Table 1. show confirmed tolerability but insufficient effect.

	Severity grade of renal impairment (creatinine clearance [CLcr]: mL/min)mL/min)		
	Mild (90> CLcr ≥60)	Moderate 60>CLcr ≥ CLcr > 3	Severe (Including patients Including

				patients on hemodialysis) (30> CLcr)
Daily Dose		10 mg to 30 mg	55 mg to 15 mgmg to 15 mg	2. mg to 7.5 mg
Initial Dose		55 mg twice daily	2.5.mg twice daily	2.5 mg once daily
Effective Dose	Minimum dose	10 mg twice daily	55 mg twice daily	55 mg once daily
	Recommended dose	15mg twice daily	7.5 mg twice daily	7.5 mg once daily

Pediatric population

Clinical studies in children have not been conducted.

Elderly population:

Mirogabalin should be administered with care, and dose and dosing interval adjustment based on creatinine clearance levels is required. Elderly patients often have reduced renal function.

Elderly patients tend to experience falls resulting in fractures, etc. led by events (e.g., dizziness, somnolence, loss of consciousness).

Hepatic Impatient

No dose adjustment is required for patients with hepatic impairment

Method of administration

For oral use.

Mirogabalin can be taken with or without food

4.3 Contraindications

Patients with a history of hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings and precautions for use

Dizziness, somnolence, loss of consciousness

Dizziness, somnolence, and loss of consciousness, which may cause falls and subsequent fractures, etc., may occur. Patients being treated with Mirogabalin should be monitored closely; if any abnormalities are noted,

appropriate measures, such as discontinuation of treatment or dose reduction should be taken.

Hepatic function disorder

Hepatic function disorder (e.g., AST increased, ALT increased) may occur. Patients being treated with Mirogabalin should be monitored closely; if any abnormalities including early symptoms (e.g., general malaise, anorexia) are noted, treatment should be discontinued and appropriate measures should be taken.

Weight gain

Treatment with Mirogabalin may cause weight gain. Caution should therefore be exercised for potential occurrence of obesity. If signs of obesity are noted, appropriate measures, such as diet and/or exercise therapy, should be taken. In particular, since weight gain may be associated with dose increase or long-term use, body weight should be measured regularly.

Withdrawal symptoms

Abrupt discontinuation of treatment with Mirogabalin may cause drug withdrawal symptoms (e.g. insomnia, nausea, decreased appetite.)

Treatmrnt with Mirogabalin should be discontinued in a careful manner, such as gradual dose reduction.

Ophthalmic disorders

Treatment with Mirogabalin may cause ophthalmic disorders (e.g., amblyopia, abnormal vision, vision blurred, and diplopia). Caution should therefore be exercised for potential occurrence of ophthalmic disorders in medical examinations including careful history taking.

Other Precautions

- It should be noted that Mirogabalin for neuropathic pain is not a causal therapy but a supportive therapy. Therefore, the underlying disease of the pain should be diagnosed and treated concurrently, and the drug should not be used without intention.
- In multinational, placebo-controlled studies conducted in Asian countries, suicide related adverse events were reported in 5 of 1378 subjects (0.26%; completed suicide, 1 subject; suicidal ideation, 4 subjects) in the mirogabalin groups and in 4 of 869 subjects.
- In multinational, placebo-controlled studies conducted in Asian countries, death cases were reported in 3 of 1378 subjects (0.22%) in the mirogabalin groups and in none of 869 subjects in the placebo group.

4.5 Interaction with other medicinal products and other forms of interaction

Mirogabalin is predominantly excreted by renal glomerular filtration and tubular secretion. The Transporters involved in the secretion of mirogabalin are organic anion transporter (OAT) 1, OAT3, organic cation transporter (OCT) 2, H+/organic cation antiporter (MATE) 1, and MATE2-K. Mirogabalin is also metabolized by UDP-glucuronosyltransferases (UGTs).

Table 2: Precautions for Co-administration (Mirogabalin should be administered with caution when

Drugs	Clinical symptoms and measures	Mechanisms and risk factors
Probenecid	Coadministration may potentiate the effect of Mirogabalin	This is possibly due to the blood Mirogabalin. increased by the inhibitory effect of probenecid on OAT1, OAT3, and UGT
Climetidine	Co-administration may potentiate the effect of Mirogabalin	This is possibly due to blood mirogabalin concentration that increased by the inhibitory effect of cimentidine on MATE1 and MATE2-K
Lorazepam Alcohol (drinking)	Co-administration may facilitate the decrease in attention and balance function	This is possibly due to the interactively potentiated inhibitory effect on the central nervous system.

<u>In vitro study data</u>

- Mirogabalin was not metabolized by CYP but was metabolized by UGT1A3, UGT1A4, UGT1A9, UGT2B4, UGT2B7 and UGT2B17.
- Mirogabalin was secreted from the kidney and was suggested to be a substrate for OAT1, OAT3, OCT2, MATE1, and MATE2-K.
- Mirogabalin did not inhibit or induce major human CYP molecular species, and did not inhibit activities of drug transporters (OAT1,

OAT3, OCT1, OCT2, OATP1B1, OATP1B3, MATE1, and MATE2-K). Mirogabalin also did not inhibit activities of P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP).

In clinical study data

- Co-administration of probenecid (500 mg) with Mirogabalin (15 mg) increased the Cmax and AUClast of Mirogabalin by 29% and 76%, respectively.
- Co-administration of cimetidine (400 mg) with Mirogabalin (15 mg) increased the Cmax and AUClast of Mirogabalin by 17% and 44%, respectively.
- Co-administration of Mirogabalin with ethanol or lorazepam had no notable effect on the pharmacokinetics of Mirogabalin or these drugs. Co-administration of Mirogabalin with these drugs decreased attention and balance-function more profoundly than monotherapy with Mirogabalin.
- Co-administration of Mirogabalin with tramadol had no notable effect on the pharmacokinetics of Mirogabalin or tramadol.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

As the potential risk for humans is unknown, effective contraception must be used in women of child bearing potential.

Pregnancy

For pregnant women and women who may be pregnant, Mirogabalin should be administered only if the expected therapeutic benefits outweigh the possible risks associated with treatment. An animal study (in rats) has shown that mirogabalin crossed the placenta.

Breast-feeding

The continuation or discontinuation of breastfeeding should be considered while taking account of the expected therapeutic benefits and the benefits of maternal feeding. An animal study (in rats) has shown that mirogabalin transferred to breast milk.

Fertility

There are no clinical data on the effects of Mirogabalin on female fertility. There was no adverse effect on fertility in an animal study (in rats).

4.7 Effects on ability to drive and use machines

Mirogabalin may cause event(s) (e.g., dizziness, somnolence, loss of consciousness). Patients being treated with Mirogabalin must be warned not to operate potentially dangerous machinery, such as

driving a car.

4.8Undesirable effects

Summary of the safety profile

The safety profile of Mirogabalin is based on three Phase 3 and one Phase 2 studies (854 patients with diabetic peripheral neuropathic pain, 553 patients with postherpetic neuralgia and 306 patients with central neuropathic pain), and from post-authorisation experience.

The most commonly reported adverse reactions associated with Mirogabalin treatment in clinical trials are somnolence (16.8%), dizziness (9.7%) and oedema (7.5%).

Tabulated list of adverse reactions

Adverse reactions from Mirogabalin in clinical trials, post-authorisation safety studies and spontaneous reporting are summarized in Table 3.

The following terminologies have been used in order to classify the occurrence of adverse reactions: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Table 3: Mirogabalin Adverse Reactions

MedDRA	Adverse Reactions	Frequency
Metabolism and nutrition disorders	Increased appetite	Uncommon
	Decreased appetite	Uncommon
	Diabetes mellitus	Uncommon
Psychiatric disorders	Insomnia	Uncommon
	Hallucination	Not known
	Delirium	Not known

MedDRA	Adverse Reactions	Frequency
Nervous system disorders	Somnolence	Very common
	Dizziness	Common
	Dizziness postural	Uncommon
	Loss of consciousness	Uncommon
	Headache	Uncommon
	Tremor	Uncommon
	Memory impairment	Not known
	Amnesia	Not known
	Dysarthria	Not known
	Hypoaesthesia	Uncommon
	Taste disorder	Not known
	Dysgeusia	Not known
	Head discomfort	Not known
	Dyskinesia	Not known
	Myoclonus	Not known
Eye disorders	Vision blurred	Uncommon
	Diplopia	Not known
	Visual impairment	Not known
	Visual acuity reduced	Not known
Ear and labyrinth disorders	Vertigo	Uncommon
Vascular disorders	Orthostatic hypotension	Uncommon

MedDRA	Adverse Reactions	Frequency
	Hypertension	Uncommon
	Palpitations	Not known
	Hot flush	Not known
	Blood pressure decreased	Not known
Gastrointestinal disorders	Constipation	Common
	Abdominal distension	Uncommon
	Dry mouth	Uncommon
	Gastritis	Uncommon
	Vomiting	Uncommon
	Abdominal pain upper	Uncommon
	Gastrooesophageal reflux disease	Uncommon
	Diarrhoea	Not known
	Abdominal discomfort	Not known
Skin and subcutaneous tissue disorders	Rash	Uncommon
	Urticaria	Not known
	Erythema	Not known
	Pruritus	Not known
Musculoskeletal and connective tissue disorders	Muscular weakness	Uncommon
Renal and urinary disorders	Urinary incontinence	Not known
	Pollakiuria	Not known
	Dysuria	Not known

MedDRA	Adverse Reactions	Frequency
	Urinary retention	Not known
General disorders and administration site conditions	Oedema	Common
	Gait disturbance	Common
	Feeling abnormal	Uncommon
	Thirst	Uncommon
	Face oedema	Uncommon
	Malaise	Not known
	Asthenia	Not known
	Eyelid oedema	Uncommon
Investigations	Weight increased	Common
	Hepatic enzyme increased	Common
	Eosinophil count increased	Uncommon
	Blood CK increased	Uncommon
	Withdrawal syndrome	Uncommon
Injury, poisoning and procedural complications	Fall	Uncommon

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via the pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms: There have been reports on overdoses of up to 60 mg/day in an overseas clinical study in patients with fibromyalgia). Symptoms observed during a mirogabalin overdose included euphoric mood, dysarthria, headache, dysphagia, arthritis, joint swelling, and asthenia.

Treatment: Hemodialysis is reported to remove 15.3% of mirogabalin. The indication of MIROGABALIN is neuropathic pain.

5.1 Pharmacodynamic properties

Therapeutic group: Gabapentinoids, Adjunct anti-epileptic drugs, Primary antiepileptic Drugs

ATC Code: N02BF03

Mechanism of action

Mirogabalin is considered to exhibit its analgesic effect by reducing calcium current via binding to the α2δ subunit, which plays an auxiliary role in functions of voltage-gated calcium channels in the nervous system. The analgesic effect of mirogabalin is also suggested to involve activation of the noradrenergic pathway in the descending pain inhibitory system.

Pharmacodynamic effects

- Mirogabalin increased the pain threshold to mechanical stimulation in partial sciatic nerve ligation model rats.
- Mirogabalin increased the pain threshold to mechanical stimulation in streptozotocin-induced diabetic model rats.
- Mirogabalin increased the pain threshold to mechanical stimulation in spinal cord injury model rats.

5.2 Pharmacokinetic properties

Absorption

Mirogabalin was rapidly absorbed in healthy adults. Following the administration of mirogabalin at a single oral dose of 3, 5, 10, and 30 mg (6 subjects per dose level) in healthy adults, plasma mirogabalin concentrations reached the maximum concentration (Cmax) at 1 h post-dose. Following the administration of mirogabalin at a single oral dose of 15 mg in the fasted and fed states in 30 healthy adults, administration in the fed state resulted in a decrease of Cmax by approximately 18% and a delay of Tmax by 0.5 h,

whereas the AUCinf was only reduced by approximately 6%. The effect of food on the absorption rate of mirogabalin was limited, therefore mirogabalin can be given under both fasted and fed condition. Following the administration of mirogabalin at multiple oral doses of 10 mg and 15 mg (6 subjects per dose level) twice daily in Japanese healthy adult subjects for 7 days, steady state was reached by Day 3.

Distribution

Following the administration of mirogabalin at a single oral dose of 3, 5, 10, and 30 mg in 6 healthy adults, the apparent volume of distribution based on the terminal phase (Vz/F) was 78.01 to 87.97 L. In an in vitro study, mirogabalin labeled with 14C (abbreviated as 14C-mirogabalin) was distributed into red blood cells, with a ratio of whole blood concentration to plasma concentration of 0.85 to 0.87 in human. The 14C-mirogabalin human plasma protein binding ratios, determined by ultra-centrifugation, were 23.4% to 25.5% at plasma concentrations of 0.1 to 10 μg/mL.

Biotransformation

Following the administration of 14C-mirogabalin at a single oral dose of 30 mg (150 μCi) in healthy male adults (6 subjects), approximately 97% of the radioactivity was recovered in the urine, and approximately 76% of the radioactivity in the urine was recovered as unchanged mirogabalin. The metabolite of mirogabalin found in urine, other than the unchanged mirogabalin, was the lactam form of mirogabalin, and accounted for 0.6% of the dose. The N-glucuronide conjugate metabolized by UGT was also found.

Elimination

Following the administration of mirogabalin at a single oral dose of 3, 5, 10, and 30 mg in 6 healthy adults, the apparent total body clearance (CL/F) ranged between 16.50 and 18.24 L/h with a half-life (t½) of 2.96 to 3.37 h. In these subjects, 63.2% to 71.5% of the dose was excreted, unchanged, in the urine, and renal clearance was 10.4 to 12.4 L/h. Following the administration of 14C-mirogabalin at a single oral dose of 30 mg (150 μCi) in healthy male adults (6 subjects), a cumulative excretion rate of radioactivity up to 168 h post-dose was ≥98%; radioactivity recovered in urine and feces was approximately 97% and 1%, respectively.

Linearity/non-linearity

The Cmax and AUCinf of mirogabalin increased in a dose-proportional manner following the administration of mirogabalin at a single oral dose of 3,

5, 10, and 30 mg and multiple oral doses of 10 mg and 15 mg in healthy adults.

5.3 Preclinical safety data

- In safety pharmacology studies in rats and monkeys, mirogabalin besilate was well-tolerated at clinically relevant doses.
- In repeated dose toxicity studies in rats and monkeys, the dose-limiting toxicity of mirogabalin besilate was abnormal clinical signs (i.e. prone position, hypoactivity, staggering gait, ataxia) associated with depression of the central nervous system resulting from exaggerated pharmacological action. The mean AUC0-24h value at the NOAEL (10 mg/kg/day) in rats, the most sensitive species, was 4.7 times higher than that at the maximum recommended clinical dose of 15 mg twice daily.
- Mirogabalin besilate was not teratogenic in rats or rabbits, and did not show reproductive toxicity in males or disturbance in fertility and early embryonic development. But, prolonged proestrus and estrus were observed in the female at the dose of 100 mg/kg/day. In pre- and postnatal development studies including maternal function in rats, prolongation of the pregnancy period was noted at 100 mg/kg/day. In the F1 animals, a low live birth index was noted at 30 mg/kg/day or more. The mean AUC0-24h value at the NOAEL (10 mg/kg/day) for the next generation was 5.2 times higher than that at the maximum recommended clinical dose of 15 mg twice daily.
- Mirogabalin besilate did not show genotoxic potential in the bacterial reverse mutation study, chromosomal aberration study, or single dose rat bone marrow micronucleus study up to at 2000 mg/kg.
- Two-year carcinogenicity studies with mirogabalin besilate were conducted in mice and rats. No tumors were observed in mice at exposures up to 13.5 times the mean human exposure at the maximum recommended clinical dose (15 mg twice daily). In rats, an increased incidence of transitional cell papilloma in the urinary bladder was observed only in males at 100 mg/kg/day. However, the incidence of hyperplasia in the urinary bladder did not increase significantly in any group and mirogabalin besilate did not increase the labeling index of Ki-67-positive cells in the urinary bladder up to at 100 mg/kg/day in the 4-, 13-, 26- or 104-week repeated dose studies. At the dose (30 mg/kg/day) which the AUC0-24h value was 22.1 times higher than the maximum recommended clinical dose (15 mg twice daily), statistically significant increase of incidence of transitional cell papilloma was not observed. Taken together, the tumorigenic potential of mirogabalin besilate was considered to be very low. There is no evidence to suggest an associated risk to humans.

Environmental Risk Assessment (ERA)

The environmental risk assessment of mirogabalin besilate has been conducted in accordance to European guidelines on ERA. No environmental impact is anticipated from the clinical use of mirogabalin.

6. Pharmaceutical Particulars

6.1 Incompatibilities

Not applicable.

6.2 Shelf life

2 years.

6.3 Special precautions for storage

Protect from light, heat & moisture.

Store below 30°C.

Keep out of reach of children.

6.4 Nature and content of container

14's packed in Alu/Alu Blister.

7. Marketing Authorisation Holder

Helix Pharma (Pvt) Limited

Hakimsons House

A/56, S.I.T.E., Manghopir Road

Karachi, Pakistan.

8. MARKETING AUTHORISATION NUMBER(S)

H2026/CTD12989/27013

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 June 2026

10. DATE OF REVISION OF THE TEXT

20-08-2026