Summary of Product Characteristics
MIROGAB 5
(Mirogabalin Tablets 5 mg)

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1. Name of the medicinal product

MIROGAB 5

Mirogabalin Tablets 5 mg

2. Qualitative and quantitative composition

Each film-coated tablet contains mirogabalin (as besylate) 5 mg.

Excipient with known effect
This medicinal product contains mannitol.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Red, oval, biconvex film-coated tablets, plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology
In adults, the recommended starting dose is 5 mg twice daily, increased by 5 mg per dose at intervals of at least 1 week up to 15 mg twice daily. The dose may be increased or decreased within the range of 10 mg to 15 mg twice daily according to the individual patient's age, symptoms and tolerability.

Special populations

Renal impairment
Plasma mirogabalin concentrations may increase in patients with reduced renal function, with a possible increase in the risk of adverse reactions; careful administration with close monitoring is required. The dose and dosing interval should be adjusted according to creatinine clearance (CLcr) as shown in Table 1. Treatment should be started at a low dose and increased in patients who show adequate tolerability but insufficient effect.

Table 1. Dose adjustment based on renal function

Dose	Mild (90 > CLcr ≥ 60)	Moderate (60 > CLcr ≥ 30)	Severe, including patients on haemodialysis (30 > CLcr)
Daily dose range	10 mg to 30 mg	5 mg to 15 mg	2.5 mg to 7.5 mg
Initial dose	5 mg twice daily	2.5 mg twice daily	2.5 mg once daily
Effective dose (minimum)	10 mg twice daily	5 mg twice daily	5 mg once daily
Effective dose (recommended)	15 mg twice daily	7.5 mg twice daily	7.5 mg once daily

Paediatric population
The safety and efficacy of mirogabalin in children have not been established; no clinical studies have been conducted in children.

Elderly population
Mirogabalin should be administered with care, with dose and dosing-interval adjustment based on creatinine clearance, as elderly patients often have reduced renal function. Elderly patients are also prone to falls and consequent fractures following events such as dizziness, somnolence and loss of consciousness.

Hepatic impairment
No dose adjustment is required for patients with hepatic impairment.

Method of administration
For oral use. Mirogabalin may be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Dizziness, somnolence and loss of consciousness
Dizziness, somnolence and loss of consciousness, which may cause falls and consequent fractures, may occur. Patients should be monitored closely and, if abnormalities are noted, appropriate measures such as discontinuation of treatment or dose reduction should be taken.

Hepatic function disorder
Hepatic function disorder (e.g. increased AST and ALT) may occur. Patients should be monitored closely and, if abnormalities including early symptoms such as general malaise or anorexia are noted, treatment should be discontinued and appropriate measures taken.

Weight gain
Treatment may cause weight gain, and caution is required regarding the potential occurrence of obesity, particularly with dose increase or long-term use. Body weight should be measured regularly and appropriate measures (such as diet and/or exercise) taken if signs of obesity are noted.

Withdrawal symptoms

Abrupt discontinuation may cause withdrawal symptoms (e.g. insomnia, nausea, diarrhoea, decreased appetite). Treatment should be discontinued gradually, for example by tapering the dose.

Ophthalmic disorders

Ophthalmic disorders (e.g. amblyopia, abnormal vision, blurred vision and diplopia) may occur; caution is advised, including careful history taking during medical examinations.

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported with medicinal products acting on the central nervous system. In multinational placebo-controlled studies conducted in Asian countries, suicide-related adverse events were reported in 5 of 1,378 subjects (0.26%; one completed suicide and four with suicidal ideation) in the mirogabalin groups and in 4 of 869 subjects (0.46%; suicidal ideation) in the placebo group. Deaths were reported in 3 of 1,378 subjects (0.22%) in the mirogabalin groups and in none of 869 placebo subjects. Patients and caregivers should be advised to seek medical advice if signs of suicidal ideation or behaviour emerge.

Other precautions

Mirogabalin for neuropathic pain is a supportive rather than a causal therapy; the underlying disease should be diagnosed and treated concurrently, and the medicinal product should not be used without a defined therapeutic aim.

Excipients

This medicinal product contains mannitol, which may have a mild laxative effect.

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 are OAT1, OAT3, OCT2, MATE1 and MATE2-K. It is also metabolised by UDP-glucuronosyltransferases (UGTs). Mirogabalin is not metabolised by cytochrome P450 (CYP) enzymes and does not inhibit or induce major CYP isoforms or inhibit the drug transporters tested (including P-gp and BCRP).

Table 2. Precautions for co-administration

Medicinal product	Clinical symptoms and measures	Mechanism and risk factors
Probenecid	Co-administration may potentiate the effect of mirogabalin.	Increased mirogabalin plasma concentration due to inhibition of OAT1, OAT3 and UGT by probenecid.
Cimetidine	Co-administration may potentiate the effect of mirogabalin.	Increased mirogabalin plasma concentration due to inhibition of MATE1 and MATE2-K by cimetidine.

Medicinal product	Clinical symptoms and measures	Mechanism and risk factors
Lorazepam; alcohol (drinking)	Co-administration may increase the impairment of attention and balance function.	Interactively potentiated inhibitory effect on the central nervous system.

Clinical interaction data

- Probenecid (500 mg) increased mirogabalin (15 mg) Cmax and AUClast by 29% and 76%, respectively.
- Cimetidine (400 mg) increased mirogabalin (15 mg) Cmax and AUClast by 17% and 44%, respectively.
- Co-administration with ethanol or lorazepam did not notably affect the pharmacokinetics of mirogabalin or of these agents, but decreased attention and balance function more than mirogabalin alone.
- Co-administration with tramadol had no notable effect on the pharmacokinetics of mirogabalin or tramadol.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / contraception

As the potential risk to humans is unknown, women of childbearing potential must use effective contraception during treatment.

Pregnancy

Mirogabalin should be used in pregnant women, or women who may be pregnant, only if the expected therapeutic benefit outweighs the possible risk of treatment. An animal study (in rats) has shown that mirogabalin crosses the placenta.

Breast-feeding

A decision on whether to continue or discontinue breast-feeding should take into account the expected therapeutic benefit to the mother and the benefit of breast-feeding to the child. An animal study (in rats) has shown that mirogabalin is transferred into breast milk.

Fertility

There are no clinical data on the effect of mirogabalin on 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 dizziness, somnolence and loss of consciousness. Patients should be warned not to drive or operate potentially dangerous machinery until it is established that mirogabalin does not adversely affect their ability to perform such activities.

4.8 Undesirable effects

Summary of the safety profile

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

most commonly reported adverse reactions were somnolence (16.8%), dizziness (9.7%) and oedema (7.5%).

Tabulated list of adverse reactions

Adverse reactions are listed by system organ class and frequency, defined as: 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); and not known (cannot be estimated from the available data).

System Organ Class	**Adverse reaction**	**Frequency**
Metabolism and nutrition disorders	Increased appetite	Uncommon
	Decreased appetite	Uncommon
	Diabetes mellitus	Uncommon
Psychiatric disorders	Insomnia	Uncommon
	Hallucination	Not known
	Delirium	Not known
Nervous system disorders	Somnolence	Very common
	Dizziness	Common
	Postural dizziness	Uncommon
	Loss of consciousness	Uncommon
	Headache	Uncommon
	Tremor	Uncommon
	Hypoaesthesia	Uncommon
	Memory impairment	Not known
	Amnesia	Not known
	Dysarthria	Not known
	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
	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

System Organ Class	Adverse reaction	Frequency
	Upper abdominal pain	Uncommon
	Gastro-oesophageal 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
	Urinary retention	Not known
General disorders and administration site conditions	Oedema	Common
	Gait disturbance	Common
	Feeling abnormal	Uncommon
	Thirst	Uncommon
	Face oedema	Uncommon
	Eyelid oedema	Uncommon
	Malaise	Uncommon
	Asthenia	Not known
Investigations	Weight increased	Common
	Hepatic enzyme increased	Common
	Eosinophil count increased	Uncommon
	Blood creatine phosphokinase increased	Uncommon
	Withdrawal syndrome	Uncommon
Injury, poisoning and procedural complications	Fall	Uncommon

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 to the National Regulatory Authority.

4.9 Overdose

Symptoms

Experience of overdose is limited; doses of up to 60 mg/day were reported in an overseas clinical study in patients with fibromyalgia. Symptoms observed with mirogabalin overdose included euphoric mood, dysarthria, headache, dysphagia, arthritis, joint swelling and asthenia.

Management

There is no specific antidote; management should consist of general supportive measures. Haemodialysis has been reported to remove approximately 15.3% of mirogabalin and may be considered in severe cases.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other analgesics and antipyretics, gabapentinoids. ATC code: N02BF03.

Mechanism of action

Mirogabalin is a selective ligand for the α2δ subunit of voltage-gated calcium channels in the nervous system. It is considered to exert its analgesic effect by binding to the α2δ subunit and reducing calcium current; activation of the noradrenergic descending pain-inhibitory pathway is also thought to contribute.

Pharmacodynamic effects

In animal models, mirogabalin increased the pain threshold to mechanical stimulation in partial sciatic nerve ligation, streptozotocin-induced diabetic and spinal cord injury model rats.

Clinical efficacy and safety

Efficacy was established in randomised, double-blind, placebo-controlled Phase 3 studies in patients with peripheral and central neuropathic pain, supported by long-term open-label studies. In diabetic peripheral neuropathic pain, mirogabalin 30 mg/day produced a statistically significant reduction in average daily pain score at Week 14 versus placebo (difference −0.50; 95% CI −0.82 to −0.17; p = 0.0027), while 20 mg/day was not significant. In postherpetic neuralgia, both 20 mg/day (difference −0.47; 95% CI −0.81 to −0.14; p = 0.0058) and 30 mg/day (difference −0.77; p < 0.0001) were significant. In central neuropathic pain after spinal cord injury, mirogabalin was significantly superior to placebo (difference −0.71; 95% CI −1.08 to −0.34; p = 0.0001). In 52-week open-label studies the reduction in pain intensity was maintained over time.

5.2 Pharmacokinetic properties

Absorption

Mirogabalin is rapidly absorbed, reaching maximum plasma concentration approximately 1 hour after dosing. Food has a limited effect (Cmax reduced by about 18% and Tmax delayed by about 0.5 hours, with AUCinf reduced by only about 6%), so mirogabalin may be taken with or without food. Steady state is reached by Day 3 of twice-daily dosing.

Distribution

The apparent volume of distribution is approximately 78 to 88 L. Plasma protein binding is low (approximately 23% to 26%) and the whole-blood-to-plasma concentration ratio is about 0.85.

Biotransformation

Mirogabalin is not metabolised by CYP enzymes. Following a radiolabelled dose, about 76% of the urinary radioactivity was recovered as unchanged mirogabalin; minor metabolites were the lactam form and an N-glucuronide conjugate formed by UGT.

Elimination

Mirogabalin is eliminated principally by renal excretion of unchanged drug; approximately 63% to 72% of a dose is excreted unchanged in urine, with an apparent total clearance of about 16.5 to 18.2 L/h and a terminal half-life of approximately 3 hours. Cmax and AUC increase in a dose-proportional manner.

Special populations

Exposure (AUClast) increased with decreasing creatinine clearance, rising from about 321 ng·h/mL in subjects with normal renal function to about 1,990 ng·h/mL in patients with end-stage renal disease; approximately 15.3% of a dose was removed during a 4-hour haemodialysis session. Pharmacokinetics in elderly subjects did not differ significantly from those in younger adults, and mild to moderate hepatic impairment had no clinically relevant effect on exposure.

5.3 Preclinical safety data

In safety pharmacology studies in rats and monkeys, mirogabalin besylate was well tolerated at clinically relevant doses. In repeated-dose toxicity studies, the dose-limiting toxicity was central nervous system depression (prone position, hypoactivity, staggering gait, ataxia) reflecting exaggerated pharmacological action; the AUC at the no-observed-adverse-effect level (NOAEL) in the most sensitive species (rat) was about 4.7 times the exposure at the maximum recommended clinical dose.

Mirogabalin was not teratogenic in rats or rabbits and did not impair male fertility or early embryonic development; prolonged pro-oestrus and oestrus were seen in females and prolongation of the pregnancy period at high doses, with a reduced live birth index in the F1 generation. It was not genotoxic in the standard battery of tests. Two-year carcinogenicity studies showed no tumours in mice; in male rats, an increased incidence of urinary bladder transitional cell papilloma occurred only at the highest dose, considered of very low relevance to humans. No environmental impact is anticipated from the clinical use of mirogabalin.

6. Pharmaceutical particulars

6.1 List of excipients

- Carmellose calcium
- Magnesium aluminometasilicate
- Mannitol
- Alpha-tocopherol
- Iron oxide red

- Citric acid
- Hydroxypropyl cellulose
- Silicified microcrystalline cellulose
- Crospovidone
- Colloidal silicon dioxide
- Magnesium stearate
- Hypromellose (6 cps)
- Titanium dioxide
- Talc
- Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

6.5 Nature and contents of container

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

Helix Pharma (Pvt.) Limited

Hakimsons House, A-56, S.I.T.E., Manghopir Road, Karachi, Pakistan.

8. Marketing Authorisation Number

CTD10258

9. Date of first authorisation / renewal of the authorisation

03.07.2026

10. Date of revision of the text

03.07.2026