Gabaqol Tablet 2.5mg, 5mg, 10mg & 15mg Leaflet

English

Gabaqol Tablet 2.5mg, 5mg, 10mg & 15mg

COMPOSITION:

Gabaqol Tablet 2.5mg

Each film coated tablet contains:
Mirogabalin Besylate Eq. to
Mirogabalin.....2.5mg

Gabaqol Tablet 5mg

Each film coated tablet contains:
Mirogabalin Besylate Eq. to
Mirogabalin. . . ,..... 5mg

Gabaqol Tablet 10mg

Each film coated tablet contains:
Mirogabalin Besylate Eq. to
Mirogabalin 10mg

Gabaqol Tablet 15mg

Each film coated tablet contains:
Mirogabalin Besylate Eq. to
Mirogabalin 15mg

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Mechanism Of Action

Mirogabalin is considered to exhibit its analgesic effect by reducing calcium current via binding to the $\alpha_2\sigma$ 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 path way in the descending pain inhibitory system.

PHARMACOKINETICS

Absorption: Mirogabalin was rapidly absorbed in adults. Following the administration of Mirogabalin at a single oral dose of 3, 5, 10, and 30mg in healthy adults, plasma Mirogabalin concentrations reached the maximum concentration (C) at 1h post-dose. Following the administration of Mirogabalin at a single oral dose of 15 mg in the fasted and fed states in 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 AUC 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, of the population mean exposure (AUCmax) of the oral suspension to the tablet is approximately 45%.

Distribution:

Adults: Following the administration of Mirogabalin at a single oral dose of 3, 5, 10, and 30 mg, the apparent volume of distribution based on the terminal phase was 78.01 to 87.97 L.

Biotransformation: Following the administration of C-Mirogabalin at a single oral dose of 30 mg (150 **µ** Ci) in healthy male adult, 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 Min 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.

Adults: Following the administration of Mirogabalin at a single oral dose of 3, 5, 10. and 30 mg in healthy adults, the apparent total body clearance ranged between 16.50 and 18.24 L/h with a half-life (t'/J 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 ''C-Mirogabalin at a single oral dose of 30 mg (150 µ Ci) in healthy male adults, a cumulative excretion rate of radio activity up to 168 h post-dose was ≥98%; radioactivity recovered in urine and faeces was approximately 97% and 1%, respectively.

Elderly population: Following the administration of Mirogabalin at multiple oral doses of 5, 10, and 15 mg twice daily in healthy elderly subjects between 55 years and 75 years of age for 14 days, steady state was reached by Day 3, with t ½ of 3.58 to 4.55 h on Day 14. The AUC0- 12h on Day 14 was 1.13 times to 1.24 times of that on Day 1.

The pharmacokinetics of Mirogabalin in the healthy elderly subjects did not differ significantly from those observed in healthy non-elderly subjects.

Renal impairment: Following the administration of Mirogabalin at a single oral dose of 5 mg in 30 subjects with normal renal function or renal impairment, AUC last increased in association with decreased creatinine clearance. In patients with end-stage renal disease requiring hemodialysis, 15.3% of dosed Mirogabalin was re moved from blood during 4-hour hemodialysis.

Hepatic impairment: Following the administration of Mirogabalin at a single oral dose of 15 mg with mild or moderate hepatic impairment, Cmax with mild and moderate hepatic impairment was 1.0 and 0.8 times, respectively, higher, and AUC with mild and moderate hepatic impairment was 0.9 and 1.1 times, respectively, greater than that in healthy subjects.

SPECIAL POPULATION

Renal impairment. No dose adjustment is recommended in mild renal impairment. Reduce to 50% dose in moderate renal impairment. Reduce to 75% dose in severe renal impairment and End-Stage Renal Disease (ESRD) patients.

		Degree of Renal Dysfunction (CLcr mL/min)		
		Mild (90 > CLcr ≥ 60)	**Moderate (60 > CLcr ≥ 30)**	**Severe (including hemodialysis patients) (30 > C'lcr)**
Daily dose		10- 30mg	5 - 15mg	2.5 - 7.5mg
Initial dose		5 mg twice a day	2.5 mg twice a day	2.5 mg once a day
Effective Dose	**Minimum dose**	10mg twice daily	5 mg twice a day	5 mg once a day
	Recommended dose	15mg twice daily	7.5 mg twice a day	7.5 mg once a day

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 Impairment: No dose adjustment is required for patients with hepatic impairment.

Missed dose: If you miss a dose, take the missed dose as soon as possible. If it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. You should never take two doses at

one time. If you accidentally take more than your prescribed dose, consult with your doctor or pharmacist. Do not stop taking this medicine unless your doctor instructs you**.**

THERAPEUTIC INDICATIONS

Mirogabalin. a gamma-aminobutyric acid (GABA) derivative. It is a potent and specific ligand of the $\alpha_2\sigma$ subunit of voltage-dependent Ca2+ channels that inhibits calcium ions influx and suppresses the release of neurotransmitters in the nervous system to reduce pain. It is usually used for treating:

- Diabetic Peripheral Neuropathic Pain
- Postherpetic Neuralgia.

DOSAGE & ADMINISTRATION

POSOLOGY

Adult:

In general, for adults, the initial dose of Mirogabalin is 5 mg orally twice daily, and then the dose is gradually increased by 5 mg at intervals of 1 week or longer to 15 mg orally twice daily. Depending on age and symptoms, the dosage may be adjusted appropriately within the range of 10 to 15 mg at a time, and the dose should be administered twice daily.

METHOD OF ADMINISTRATION

For oral use. Mirogabalin can be taken with or without food.

ADVERSE REACTIONS

System Organ Class	**Very common (≥1/10)**	**Common (≥1/100 to ≤1/10)**	**Uncommon (≥1 /1,000 to <1/100)**	**Rare / Not known (≥1/10,000 to ≤1/1,000)**
Nervous system disorders	Somnolence, Dizziness	Headache	Loss of consciousness, Disturbance in attention	Seizure (rare). Withdrawal symptoms (not known
Eye disorders	-	-	Blurred vision	-
General disorders and administration site conditions	-	Fatigue	-	-
Infections and infestations	-	Nasopharyngitis	-	-
Metabolism and nutrition disorders	-	Weight gain	Increased appetite	-
Vascular disorders	-	-	Peripheral oedema	-
Injury, poisoning and procedural complications	-	-	Falls (particularly in elderly)	-
Immune system disorders	-	-	-	Hypersensitivity reactions (rash, pruritus,

				angioedema) - not known
Cardiac disorders	-	Nausea	Constipation	-

- In clinical trials most, adverse events occurred early in treatment (within 2 weeks) and resolved spontaneously or after dose reduction.
- Elderly patients and those with renal impairment are at greater risk of adverse CNS effects (somnolence, dizziness, falls).
- Abrupt discontinuation may result in withdrawal symptoms such as headache, anxiety, sweating, insomnia, nausea, and diarrhea.

CONTRAINDICATIONS

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

PRECAUTIONS

Dizziness, somnolence, loss of consciousness: Dizziness, somnolence, and loss of consciousness, which may cause fails 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, diarrhea, decreased appetite). Treatment 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 ex aminations including careful history taking.

Other precautions: It should he 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.

DRUG INTERACTIONS

Co-administratipn with 0AT1, 0AT3, 0CT2, MATE1, MATE2-K, or UGT inhibitors may increase Mirogabalin exposure, so it should be used with caution. Mirogabalin did not inhibit or induce major human CYP molecular species and did not inhibit activities of drug transporters (including 0AT1, OATS. OCTI.OCT2. 0ATP1B1. OATP1B3, MATE1. MATE2-K. P-gp, and BCRP). However, consulting with a healthcare provider before using Mirogabalin with other medications is recommended.

OVERDOSAGE

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.

PRESENTATION

Gabaqol Tablet 2.5mg available in blister pack of 1x10's

Gabaqol Tablet 5mg available in blister pack of 1x10's Gabaqol Tablet 10mg available in blister pack of 1x10's Gabaqol Tablet 15mg available in blister pack of 1x10's
INSTRUCTIONS: Store below 30°C. Protect from sunlight & moisture. Keep out of the reach of children. To be dispensed on the prescription of a registered medical practitioner only.
Manufactured by: **Kaizen Pharmaceuticals (Pvt.) Ltd.** E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.