Front

Gabiro™

(Mirogabalin)

Tablet

گیبیرو

COMPOSITION:

Gabiro Tablet 2.5 mg:
Each film coated tablet contains:
Mirogabalin Besylate equivalent to
Mirogabalin ..... 2.5 mg.

Product Specs.: Innovator

Gabiro Tablet 5 mg:
Each film coated tablet contains:
Mirogabalin Besylate equivalent to
Mirogabalin ..... 5 mg.

Product Specs.: Innovator

Gabiro Tablet 10 mg:
Each film coated tablet contains:
Mirogabalin Besylate equivalent to
Mirogabalin ..... 10 mg.

Product Specs.: Innovator

Gabiro Tablet 15 mg:
Each film coated tablet contains:
Mirogabalin Besylate equivalent to
Mirogabalin ..... 15 mg.

Product Specs.: Innovator

INDICATIONS:
Mirogabalin, a gamma-aminobutyric acid (GABA) derivative. It is a potent and specific ligand of the α2δ 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.

POSOLOGY:
Adults:
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.

SPECIAL POPULATIONS:
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 > Clcr)
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.

METHOD OF ADMINISTRATION: For oral use. Mirogabalin can be taken with or without food.

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

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, diarrhea, decreased ap petite). 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 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

DRUG INTERACTIONS:
Co-administration with OAT1, OAT3, OCT2, 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 OAT1, OAT3, OCT1, OCT2, OATP1B1, OATP1B3, MATE1, MATE2-K, P-gp, and BCRP). However, consulting with a healthcare provider before using Mirogabalin with other medications is recommended.

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FERTILITY, PREGNANCY & LACTATION:
Women of childbearing potential: As the potential risk for humans is unknown, effective contraception must be used in women of child bearing potential.
Pregnancy: For pregnant women Mirogabalin should be administered only if the expected therapeutic benefits outweigh the possible risks associated with treatment.
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.
Fertility: There are no clinical data on the effects of Mirogabalin on female fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Mirogabalin may impair the ability to drive or operate machinery. Elderly people should be aware of falling and fracture.

ADVERSE EFFECTS:

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.

OVERDOSE:
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.

PHARMACOLOGICAL PROPERTIES:
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 path way in the descending pain inhibitory system.

PHARMACOKINETIC PROPERTIES:
Absorption: Mirogabalin was rapidly absorbed in adults. Following the administration of Mirogabalin at a single oral dose of 3, 5, 10, and 30 mg in healthy adults, plasma Mirogabalin concentrations reached the maximum concentration (C_{max}) 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 healthy adults, administration in the fed state resulted in a decrease of C_{max} by approximately 18% and a delay of T_{max} 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 (AUC_{inf}) 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 ^{14}C-Mirogabalin at a single oral dose of 30 mg (150 μCi) 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 ($t_{½}$) 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 ^{14}C-Mirogabalin at a single oral dose of 30 mg (150 μCi) 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, C_{max} 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.

INSTRUCTIONS:
– Store below 30°C.
– Protect from heat, sunlight & moisture.
– Keep out of the reach of children.
– To be sold on the prescription of a registered medical practitioner only.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

PRESENTATION:

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Gabiro Tablet 10 mg	:	Pack of 1 x 10 tablets.
Gabiro Tablet 15 mg	:	Pack of 1 x 10 tablets.

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL
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