

- ❄ Peripheral neuropathic pain due to lumbar spine disease causes leg pain/numbness, low back pain, sleep disturbance, and reduced quality of life.
- ❄ Current $\alpha 2\delta$ ligands like pregabalin/gabapentin can help neuropathic pain, but CNS adverse effects such as dizziness & somnolence limit use; mirogabalin is a newer selective $\alpha 2\delta$ ligand designed to provide analgesia with fewer CNS effects.
- ❄ This retrospective study evaluated 8 weeks of mirogabalin therapy in patients with neuropathic leg symptoms due to lumbar spinal canal stenosis or lumbar disc herniation.

Study design: Retrospective clinical study

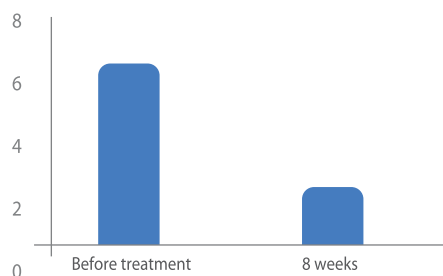
Population	Center	Duration	Intervention	Key outcome
60 patients	5 institutions in Japan	8 weeks	Mirogabalin 10 mg/day initially, titrated weekly as needed; maximum 30 mg/day	Leg symptoms improved from NRS 6.4 ± 1.4 before treatment to 1.8 ± 1.4 at 8 weeks; low back pain, sleep disturbance, and QOL also improved significantly ($p < 0.05$).

Efficacy of Mirogabalin: Leg Symptom NRS

- ⚙ Mirogabalin efficacy on leg symptoms
- ⚙ Mean Numerical Rating Scale (NRS) before & after 8 weeks of treatment.
- ⚙ Before treatment 8 weeks 02468
- ⚙ Lower NRS score indicates less severe symptoms

Mirogabalin efficacy on leg symptom

Mean numerical rating scale (NRS) before & after 8 weeks of treatment



Conclusion

- ❄ Mirogabalin significantly ($p < 0.05$) improved neuropathic leg symptoms in lumbar spine disease.
- ❄ It also improved associated low back pain, sleep disturbance, and quality of life.
- ❄ Benefit appeared greater in patients with symptom duration under 3 months, but larger controlled studies are needed.

Ref: Kim K, Isu T, Kokubo R, Iwamoto N, Morimoto D, Kawauchi M, Morita A. Therapeutic Effect of Mirogabalin on Peripheral Neuropathic Pain due to Lumbar Spine Disease. Asian Spine Journal. 2021;15(3):349–356. doi: 10.31616/asj.2020.0136.

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Peripheral neuropathic pain

- Neuropathic pain (NeP) (central or peripheral) is defined by the International Association for the Study of Pain (IASP) as “pain caused by a lesion or disease of the somatosensory nervous system”¹
- Peripheral neuropathic pain (PNP) in diabetic peripheral neuropathy (DPN) and post herpetic neuralgia (PHN) is a chronic and debilitating condition leading to significant morbidity and poor quality of life.²
- The prevalence of DPN is estimated at ~50% and expected to increase significantly over the next few decades.^{3,4}
- After initial herpes zoster infection subsides, 6.5-18% of patients may develop PHN persists for months to years, significantly impacting quality of life.⁵
- An estimated 50% of patients with NeP achieve 30–50% pain relief due to suboptimal analgesia and poorly tolerated side effects.⁶
- Although pregabalin and gabapentin are effective in managing NeP, its tolerability limits their clinical utility in a substantial proportion of patients. Hence an effective and well-tolerated pharmacotherapy is required to address the concerns in managing NeP, especially in the gabapentinoid class.⁷

Mirogabalin: selective and well tolerated analgesic for DPNP and PHN⁸

- Mirogabalin besylate is a gabapentinoid approved for diabetic neuropathic pain and post-herpetic neuralgia.
- It has a potent pain-modulating effect with a unique, selective, high affinity and prolonged dissociation rate for the $\alpha 2\delta$ -1 subunit of voltage-gated calcium (Ca²⁺) channels (VGCCs) on the dorsal root ganglion resulting in more sustained analgesia compared with traditional gabapentinoids.
- Additionally, mirogabalin has a superior adverse events (AEs) profile due to a rapid dissociation from the $\alpha 2\delta$ -2 subunit of VGCCs potentially implicated in central nervous system specific AEs.

Mirogabalin vs Pregabalin and Gabapentin in peripheral neuropathic pain¹⁰

Feature	Mirogabalin	Pregabalin	Gabapentin
Binding Affinity	Stronger binding to $\alpha 2\delta_1$ & $\alpha 2\delta_2$	Non-selective binding to $\alpha 2\delta_1$ & $\alpha 2\delta_2$	Non-selective binding to $\alpha 2\delta_1$ & $\alpha 2\delta_2$
Dissociation Rate	Slower from $\alpha 2\delta_1$ subunit	Faster dissociation	Faster dissociation
Efficacy	Higher analgesic efficacy	Moderate efficacy	Moderate efficacy
Adverse Effects	Lower incidence of CNS adverse effects	Higher incidence of CNS adverse effects	Higher incidence of CNS adverse effects
Common Side Effects	Dizziness, somnolence, headache	Higher incidence of Dizziness, somnolence, headache	Higher incidence of Dizziness, somnolence, headache
Long-term Tolerability	Well tolerated with minimal safety concerns	Associated with higher adverse effect	Associated with higher adverse effects
Onset of action	Maximum plasma concentration is achieved in less than 1 hour	Maximum plasma concentration is achieved in 1 hour	Maximum plasma concentration is achieved in 3 hours

Ref: 1. Salvatore Caruso, Marco Iraci, Stefano Cianci, et. al. Effects of long-term treatment with Dienogest on the quality of life and sexual function of women affected by endometriosis-associated pelvic pain. Journal of Pain Research, Volume 12, 2019 - Issue 2. R Watanajingchareonchai, S Rattanasi, C Charakorn, et. al. Postoperative hormonal treatment for prevention of endometrioma recurrence after ovarian cystectomy: a systematic review and network meta-analysis. BJOG. 2021 Jan; 128(1): 25–35; 3. Fabio Baira, Antonio Simone Lagana, Carolina Scala, et. al. Pretreatment with dienogest in women with endometriosis undergoing IVF after a previous failed cycle. Reproductive BioMedicine Online, Volume 41, Issue 5, November 2020, Pages 859-868; 4. Paul L. McCormack. Dienogest: A Review of its Use in the Treatment of Endometriosis. Drugs 2010; 70(16): 2073-2088; 5. Adolf E Schindler. Dienogest in long-term treatment of endometriosis. Int J Womens Health. 2011; 3: 175–184; 6. Klaas Heinemann, Bruno Imthurn, Lena Marions, et. al. Safety of Dienogest and Other Hormonal Treatments for Endometriosis in Real-World Clinical Practice (WPOS): A Large Noninterventional Study. Adv Ther. 2020 May;37(5):2528-2537; 7. Thomas Römer. Long-term treatment of endometriosis with dienogest: retrospective analysis of efficacy and safety in clinical practice. October 2018 Archives of Gynecology and Obstetrics 298(4); 8. Andreas D Ebert, Liying Dong, et. al. Dienogest 2 mg Daily in the Treatment of Adolescents with Clinically Suspected Endometriosis: The VSanne Study to Assess Safety in Adolescents. J Pediatr Adolesc Gynecol. Epub 2017 Feb 9; 9. Neil P Johnson, Lone Hummelshøj, et. al. World Endometriosis Society consensus on the classification of endometriosis. December 2016 Human Reproduction.

