Pregabalin (Lyrica™) - A new treatment option for neuropathic pain

Neuropathic pain (NP) is a complex condition caused by a lesion of the central nervous system.[1] It may result from various causes that affect the brain, spinal cord and peripheral nerves, including diabetic neuropathy, cancer-related neuropathic pain, postherpetic neuralgia, HIV-related neuropathy, spinal cord injury, trigeminal neuralgia and other pain syndromes.[1]

NP is especially problematic because it is often experienced in parts of the body that otherwise appear normal, it is generally chronic, severe and resistant to over-the-counter analgesics and it is aggravated by allodynia (touch-evoked pain).[1]

Many different medicines have been used for the treatment of NP. These include a wide variety of anti-epileptic medicines (e.g. carbamazepine, phenytoin, oxcarbazepine, lamotrigine, valproic acid, topiramate, gabapentin and pregabalin), opioid analgesics, tricyclic antidepressants, ketamine, lidocaine, amantadine, cannabinoids and several others.[2]

Mechanisms thought to be involved in the development of NP include alterations in peripheral nerves, dorsal root ganglia and the spinal cord. These changes include upregulation and/or downregulation of neuropeptides and neurotransmitters and changes that occur at supraspinal sites and result in facilitation of pain transmission.[2]

Approved indication
Pregabalin is indicated in the treatment of two of the most common causes of neuropathic pain – diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN).[3]

Mode of action
Pregabalin is a gamma-aminobutyric acid (GABA) analogue. Although the mechanism underlying the ability of pregabalin to relieve NP is not understood, available information suggests that it may be binding to high-affinity sites on subunits of voltage-activated calcium channels. This binding is thought to increase calcium influx into nerve terminals and reduce the release of neurotransmitters, including glutamate, noradrenaline and substance P.[2,3] The mechanism of action of pregabalin, therefore, appears to the same as for gabapentin.[2]

Note: Pregabalin does NOT interact with GABA receptors, it is not converted metabolically into GABA or a GABA-agonist and it is not an inhibitor of GABA uptake or degradation.

Dosage
Adults: The recommended starting dose is 75 mg twice daily, taken with food or on an empty stomach. Based on response and tolerability, the dosage may be increased to 150 mg twice daily after an interval of 3 to 7 days.[3]
If treatment is to be discontinued, it is recommended that this should be done gradually over at least one week.

Since pregabalin is eliminated by renal excretion as unchanged drug, dosage reduction is necessary in patients with compromised renal function. The dosage adjustment required is individualized based on creatinine clearance.[3]

Evidence of efficacy
The indication of pregabalin in painful diabetic peripheral neuropathy (DPN) is based on results from three clinical trials that enrolled patients with type 1 or type 2 diabetes and a diagnosis of painful polyneuropathy for 1-5 years. Results from the three trials indicated significant superiority of pregabalin (300 mg daily) over placebo in decreasing mean pain scores.[2]

The efficacy of pregabalin for the treatment of post-herpetic neuralgia (PHN) was established in three studies that enrolled patients with neuralgia persisting for 3 months or more after healing of a herpes zoster rash. The superior efficacy of pregabalin (150-600 mg/day) over placebo was apparent by the first week of treatment and was sustained for the duration of each study.[2]

Precautions
- **General**
  The safety and efficacy of pregabalin has not been established in children below the age of 18 years.
  Patients with reduced renal function may require dose adjustment based on creatinine clearance.
- **Pregnancy & lactation**
  There is no data on the use of pregabalin during pregnancy. It is also not known if pregabalin is secreted into human breast milk. Therefore, the use of pregabalin during pregnancy and lactation is not recommended.

Major adverse effects
The most commonly reported adverse effects reported in placebo-controlled trials were dizziness, somnolence and peripheral oedema.[2,3] Other common adverse effects include: increased appetite, euphoric mood, confusion, decreased libido or sexual function, irritability, ataxia, changes in attention, co-ordination or memory, tremor, dysarthia, paraesthesia, changes in vision, dry mouth, constipation, vomiting, flatulence, fatigue and weight increase.

Drug interactions
Since pregabalin is not metabolised by the liver and is predominantly excreted unchanged in the urine, it is unlikely to be affected by pharmacokinetic interactions. However, the sedative effects of pregabalin may be potentiated by the effects of ethanol and other medicines causing central nervous system depression.

Cost: Single Exit Price (incl VAT)
Lyrica™ 25 (75) (150) mg capsules:
- R118.70/56 capsules (25 mg)
- R296.76/56 capsules (75 mg)
- R445.19/56 capsules (150 mg)

Patient information
Patients should be warned that pregabalin frequently causes dizziness and somnolence. As such, patients should be advised not to drive or use machines until they know how they react to the medication.

Conclusion
Pregabalin is a reasonable alternative for the treatment of painful diabetic neuropathy and post-herpetic neuralgia. Of the available treatments for NP, pregabalin appears to be well tolerated with few drug interactions.

References

1. Gilron I, Watson CPN, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. *CMAJ* 2006;175(3):265-275.
2. Gidal B, Billington R. New and emerging treatment options for neuropathic pain. *Am J Man Care* 2006;12:S269-278.
3. Lyrica package insert.

Tablet identity:
Concerta® 18mg tablet.
This is a controlled-release form of methylphenidate indicated for the treatment of attention-deficit hyperactivity disorder in children over the age of 6 years.

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Introducing the World's first MDI with counter

Research shows that up to two thirds of patients reported feeling anxious not knowing how much medication they have left in their inhaler.[1] This is all about to change.

GlaxoSmithKline is pleased to announce the introduction of the new Seretide® with dose counter. The world's first metered dose inhaler with counter will be available at the same cost as the current inhaler.

This is just another way we remain committed to keeping costs as low as possible.

The counter on the new Seretide® MDI enables patients to see at a glance how many doses of medication remain in the device. This will help aid compliance, improve asthma control and GET your patients BACK OUT THERE. Not only does this improve the management of asthma for everyone but it also gives you peace of mind.

The new Seretide® MDI with counter will be phased in from mid April 2008 and will replace the existing MDI inhaler stock.

The inhaler should be primed before using it for the first time: remove the mouthpiece cover, shake well and release puffs into the air until the counter reads 120. The inhaler is now ready to use. The mouthpiece cover should be replaced after use. A replacement inhaler should be obtained when the counter approaches 020 and not used again once the counter reads 000.

References

1. Hailey M, Rand P, Godfrey J, Cude I, Cox M, Rosenzweig JC. Design and Characteristics of an MDI Counter Device. Abstract 599. J Allergy Clin Immunol 2005:S150.

S3 Seretide 25/50 INHALER – 35/21.5.4/0411, Seretide 25/125 INHALER – 35/21.5.4/0412, Seretide 25/250

INHALER – 35/21.5.4/0413. Applicant: GlaxoSmithKline South Africa (Pty) Ltd. (Co reg. no. 1948/030135/07) Private Bag X173, Bryanston. 2021. Tel: +27 11 745 6000. Fax +27 11 745 7000.

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