

Focus on: Orphenadrine citrate as a muscle relaxant

L Steyn

Amayeza Info Services

The term “skeletal muscle relaxants” represents a broad group of drugs that are structurally and pharmacologically diverse.¹

Skeletal muscle relaxants are used to treat both spasticity and local musculoskeletal spasms.¹ These two conditions differ in their aetiology, with spasticity originating centrally more as a result of a motor neuron disorder, while local musculoskeletal spasms occur peripherally and more as a result of trauma or muscle strain.¹ For this reason, centrally-acting (e.g. baclofen) and peripherally-acting skeletal muscle relaxants (e.g. orphenadrine, cyclobenzaprine) cannot be used interchangeably. Orphenadrine is used to relieve musculoskeletal spasm originating from painful peripheral musculoskeletal conditions.¹

Mechanism of action

Orphenadrine is structurally similar to diphenhydramine, but has less antihistaminic activity.^{2,3} It also has a less sedating effect than diphenhydramine, having a slight euphorogenic effect.^{4,5} The precise mechanism of action of orphenadrine is not known, but it appears to indirectly relieve muscle pain through central atropine-like effects.³ It does not work directly on the muscle to relieve muscle spasm and does not affect normal muscle tone.^{3,5}

Indications

Oral orphenadrine is indicated for use in conditions involving skeletal muscle spasm, such as lower back pain and torticollis, as well as those conditions resulting from trauma, such as whiplash.⁵ The orphenadrine 100 mg tablets are recommended for short-term use.³

Pharmacokinetics

Orphenadrine is 95% bioavailable after oral absorption.² Time to peak concentration after oral administration is 2 to 4 hours.² It is extensively metabolised in the liver through the cytochrome P450 (CYP450) system and the metabolites are primarily eliminated in the urine.^{1,3} The elimination half-life (t_{1/2}) of orphenadrine varies between 13.2 to 20.1 hours.²

Dosing

One tablet of orphenadrine 100 mg may be taken two or three times daily.⁵ The tablets may be taken without regard to meals.⁶

Efficacy

Skeletal muscle relaxants have been found to be more effective than placebo when used for short-term relief of back pain.³ Peak effects occur after two to four hours and can last for up to 6 hours.³ Skeletal muscle relaxants may be used in combination with analgesics for lower back pain. They may also be used as an alternative to nonsteroidal anti-inflammatory drugs (NSAIDs) in patients who are not able to tolerate NSAIDs, or who have renal dysfunction.⁷

Safety of orphenadrine

Adverse effects

The side-effect profile of orphenadrine is mainly related to the anticholinergic effects of the drug.³ These side-effects usually occur at higher doses and may include:

- Dry mouth, nausea, blurring of vision⁸
- Drowsiness⁸
- Increased intraocular pressure⁴
- Urinary retention⁴
- CNS stimulation (especially in elderly people)⁴
- Constipation

For this reason, oral orphenadrine is contraindicated for use in patients with⁶:

- Myasthenia gravis
- Gastrointestinal (GI) obstruction
- Glaucoma
- Bladder obstruction or other urinary tract obstruction
- Prostatic hypertrophy

Oral orphenadrine should also be used with caution in patients with:

- Heart failure (palpitations, tachycardia)⁶
- Gastro-oesophageal reflux⁶
- Hepatic disease, renal impairment, or renal disease⁶
- A history of substance abuse, due its euphoric effects (can occur at therapeutic doses)⁶

Long-term use

Safety and efficacy of long-term use of orphenadrine has not been established.⁶ It is recommended that periodic blood, urine, and liver function tests should be performed if orphenadrine is used long term.⁴ Chronic use of orphenadrine 100 mg should be tapered slowly before discontinuation.³

Use in the elderly

Careful consideration should be taken in recommending orphenadrine to people over 65 years of age, due to the increased risk of anticholinergic side-effects, drowsiness and the associated increased risk for falls.³

Drug interactions

Although metabolised by CYP450, orphenadrine being a minor substrate and weak inhibitor, is less likely to be involved in drug interactions.³ Increased CNS depression may occur when orphenadrine is taken with other CNS depressants, including alcohol.¹

Conclusion

Skeletal muscle relaxants, including orphenadrine are usually recommended for short term use in the treatment of painful musculoskeletal conditions.^{3,6} They are recommended for use in conjunction with other non-drug measures, such as rest and physical therapy.⁶ If orphenadrine preparations are used

in combination with other analgesics such as paracetamol, contraindications and precautions for each individual ingredient should be taken into account.⁴

References:

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