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PRODUCT FOCUS

Focus on solifenacin

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Introduction

Overactive bladder syndrome (OAB) is a chronic medical condition that can have a major effect on quality of life. OAB causes a frequent and sudden urge to urinate that may be difficult to control and can also lead to urinary incontinence.[1] First-line treatment starts with behavioural therapies such as bladder training, pelvic floor muscle exercises, and fluid management. After lifestyle interventions, anticholinergic drugs are the next step in treating OAB. Antimuscarinics are the drug class of choice for OAB symptoms and have proven efficacy.[1-3]

Indication

Solifenacin is indicated for the symptomatic treatment of OAB: symptoms of urinary urgency, frequent micturition and/or urinary incontinence.[4]

Mechanism of action

Solifenacin is in the group called urinary antispasmodics and is classified as a cholinolytic or otherwise known as an anticholinergic drug.[4]

Solifenacin is a competitive, specific cholinergic receptor antagonist. In vitro studies demonstrated that solifenacin binds to muscarinic receptors, with high affinity.[4]

Solifenacin works to decrease bladder activity by inhibiting contraction of the smooth muscle wall surrounding the bladder. Micturition normally occurs following stimulation of acetylcholine muscarinic M3 receptors within the detrusor muscle wall.[5]

Efficacy of solifenacin in OAB

In studies where the efficacy and safety of solifenacin was studied in patients with OAB, it was found that solifenacin was significantly more effective than placebo in reducing the mean number of episodes of severe urgency. Episodes of nocturia and incontinence were also significantly reduced when compared to placebo. The most common adverse effects with solifenacin were dry mouth and constipation and these adverse effects were mild to moderate.[6]

In a systematic literature review where the efficacy and tolerability of solifenacin 5 mg/day was compared to other oral antimuscarinic agents for the treatment of OAB, it was found that solifenacin is at least similar to other common antimuscarinics across the spectrum of OAB symptoms analysed and is more effective than tolterodine 4 mg/day in reducing incontinence and urinary urgency incontinence episodes. It was also found that solifenacin 5 mg/day has a lower risk of dry mouth compared with several other antimuscarinic agents.[7]

In an older review it was found that treatment with solifenacin was well tolerated by patients with few discontinuations due to adverse effects. It was also found that there was a high resolution and improvement rate due to the impact that solifenacin has on urgency that could be acknowledged as a key symptom of this syndrome.[8]

Solifenacin's efficacy has clearly been demonstrated in published studies for all symptoms of the OAB complex, with a high degree of tolerability and patient benefit.

Dosing and administration

For adults

The recommended dose is 5 mg once daily, if needed, the dose may be increased to 10 mg once daily.[4,9]

Special populations

Patients with renal impairment

No dose adjustment is necessary for patients with mild to moderate renal impairment (creatinine clearance > 30 ml/min). Patients with severe renal impairment (creatinine clearance > 30 ml/min) should be treated with caution and receive not more than 5 mg once daily.[4,9]

Patients with hepatic impairment

No dose adjustment is necessary for patients with mild hepatic impairment. Patients with moderate hepatic impairment should be treated with caution and receive not more than 5 mg once daily.[4,9]

The use of solifenacin is not recommended in patients with severe hepatic impairment.[9]

Potent inhibitors of cytochrome P450 3A4

The maximum dose of solifenacin should be limited to 5 mg when used simultaneously with ketoconazole or therapeutic doses of potent CYP3A4-inhibitors, e.g. ritonavir, nelfinavir, itraconazole.[4,9]

Method of administration

Solifenacin should be taken orally and should be swallowed whole with liquids. It can be taken with or without food, as is convenient.[4]

Warnings and special precautions

Other causes of frequent urination (heart failure or renal disease) should be addressed before treatment with solifenacin is undertaken. If urinary infection is present, an appropriate antibacterial therapy should be started.[4]

Solifenacin should be used with caution in patients with:

- clinically significant bladder outflow obstruction in the absence of clean intermittent catheterisation due to the risk of urinary retention
- severe renal impairment (creatinine clearance < 30 ml/min)
- moderate hepatic impairment (Child Pugh score 7–9). Not recommended in patients with severe hepatic impairment (Child Pugh score 10–15)[4,10]
- decreased gastrointestinal (GI) motility (severe constipation, ulcerative colitis) or GI obstructive disorders (pyloric stenosis) as it may increase the risk of gastric retention[10]
- hiatus hernia or gastro-oesophageal reflux and/or patients who are concurrently taking medicines (such as bisphosphonates) that can cause oesophagitis[4]
- known history of QT prolongation[4] or other risk factors for QT prolongation (e.g. concomitant use of medications known to prolong QT interval, electrolyte abnormalities).[9,10] QT-prolongation and Torsades de Pointes have been observed in patients with risk factors.[1] The risk for QT prolongation is dose-related.[9,10]
- controlled (treated) narrow-angle glaucoma. The use of solifenacin is contraindicated in uncontrolled narrow-angle glaucoma.[4,9,10]
- concomitant use of a potent CYP3A4 inhibitor, e.g. ketoconazole[4,9]
- autonomic neuropathy[4]
- safety has not been established in pregnancy and lactation[4]

According to the Beers Criteria, use should be avoided in elderly patients with delirium or at high risk of delirium as solifenacin may induce or worsen delirium.[9]

Due to the pharmacological effect of solifenacin, the drug may cause anticholinergic side effects that range from mild to moderate in severity.[4] The frequency and severity of anticholinergic side effects are dose-related.[4] Solifenacin may cause drowsiness and/or blurred vision, which may impair physical or mental abilities and patients must be cautioned about performing tasks that require mental alertness (e.g. operating machinery, driving).[4,10]

Other central nervous system (CNS) effects (e.g. headache, confusion, hallucinations, somnolence), have been reported particularly at treatment initiation or dose increase. Reduce the dose or discontinue if these symptoms persist.[10]

Interactions

Pharmacological interactions

Concomitant administration with other medicines with anticholinergic properties may result in more pronounced therapeutic effects and side effects. An interval of approximately one week should be allowed after stopping treatment with solifenacin before commencing other anticholinergic therapy.[4]

The therapeutic effect of solifenacin may be reduced by concomitant administration of cholinergic receptor agonists.[4,10]

Solifenacin can reduce the effect of medicines that stimulate the mobility of the GI tract, such as metoclopramide and cisapride.[4,10]

Pharmacokinetic interactions

Since solifenacin is metabolised by CYP3A4, pharmacokinetic interactions are possible with other CYP3A4 substrates, inhibitors, and inducers.[4]

Solifenacin showed no effect on the pharmacokinetics of oral contraceptives, warfarin, or digoxin.[4]

In summary

For the treatment of OAB, antimuscarinics have been used successfully for many years. The ideal antimuscarinic agent should effectively relieve the symptoms of OAB, with minimum of side effects, it should be available as a once-daily sustained release formulation and in dosage strengths that allow easy dose titration for most sufferers.[3,11] Solifenacin succinate was launched in 2005 and has been shown in both short- and long-term clinical trials to fulfil these requirements.[11]

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