prucalopride (Resolor®) and chronic constipation in men

Avoid in both men and women

In a placebo-controlled trial in 374 men, prucalopride was only effective in a minority of cases, as previously observed in women. In addition to its cardiovascular harms, there is evidence that prucalopride may cause depression and suicidal ideation.

When a patient presents with chronic constipation, the first step is to rule out an underlying disease that requires specific treatment, or a drug-related cause. When dietary, lifestyle and behavioural measures are inadequate, bulk laxatives and osmotic laxatives (with the exception of saline osmotic laxatives) are the drugs of first choice. There is no standard treatment for patients who find laxatives inadequate (1). Lubricant laxatives, oral stimulant laxatives and rectal laxatives are best avoided, or should only be used for short periods because of their potentially disproportionate adverse effects (1).

Prucalopride (Resolor®, Shire), a serotonin 5-HT4 receptor agonist first authorised in the European Union for use in women when other laxatives fail, has an unfavourable harm-benefit balance (1). Three 12-week trials were provided in support of marketing authorisation, but the very modest efficacy, safety, and tolerability of prucalopride in men with chronic constipation "Am J Gastroenterol 2015; 110: 741-748 + annex: 9 pages.

During the trial, depression occurred in two men in the prucalopride group and none in the placebo group (4). The Uppsala pharmacovigilance centre of the World Health Organization (WHO) has reported 3 cases of suicidal ideation among prucalopride-treated patients with no history of psychiatric disorders, with a favourable outcome after drug withdrawal. This adverse effect has also been reported with tegaserod, another 5HT-4 agonist that was authorised to treat constipation in some countries, before it was withdrawn from the market (7).

In practice. For men presenting with constipation, a troublesome but usually benign disorder, prucalopride carries a disproportionate risk of cardiovascular disorders, depression and suicidal ideation. As in women, it is better to optimise the use of standard laxatives, and to avoid prucalopride altogether.

prucalopride tablets

Resolor®

• 1 mg or 2 mg of prucalopride per tablet

laxative; serotonin 5-HT4 agonist

New indication: "(…) symptomatic treatment of chronic constipation in adults in whom laxatives fail to provide adequate relief."

[AU centralised authorisation]