Translated from *Rev Prescrire* May 2016; 36 (391): 336-337

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-HT 4 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 of *prucalopride* in these studies was not confirmed in a subsequent trial that lasted 24 weeks (1,2). *Prucalopride* carries a risk of cardiovascular adverse effects given its relationship with *cisapride*, a neuroleptic that was withdrawn from the market (2).

In 2015, *prucalopride* was also authorised for use by men in whom other laxatives have proven ineffective.

Effective in only a minority of men. Clinical evaluation of *prucalopride* in men is based on a randomised, double-blind trial in 374 men, few of whom were severely constipated (3,4).

After 12 weeks, 47% of men in the *prucalopride* group experienced a marked improvement, compared to 30% of those in the placebo group; this corresponds to a benefit in only about one in six men (4).

Possible depression and suicidal ideation, in addition to cardiovascular harms. The adverse effect profile of *prucalopride* mainly includes cardiovascular disorders (palpitations, ischaemic cardiovascular events, possible QT prolongation), gastrointestinal disorders (nausea, diarrhoea, abdominal pain), headache and dizziness (5).

In the trial in men, gastrointestinal disorders and headache were more frequent in the *prucalopride* group (3,4). The frequency of cardiac disorders was similar in the two groups, but it should be noted that patients with a history of cardiovascular disease were excluded from the trial (4). In France, a 3-year post-marketing study identified 7 cases of palpitations and tachycardia in patients taking *prucalopride* (6). As part of the risk management plan, a study is underway in the UK to better document cardiovascular adverse effects (3).

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.

©Prescrire

Selected references from Prescrire's literature search.

In response to our request for information, Shire provided us with no documentation on its product.

1- Prescrire Editorial Staff "Prucalopride. In chronic constipation: poorly documented risks" *Prescrire Int* 2011; **20** (116): 117-120.

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*".
[EU centralised authorisation]

2- European Commission "SPC-Resolor" 27 May 2015: 21 pages.
3- EMA - CHMP "Public assessment report for Resolor. EMEA/H/C/001012/II/0034" 23 April 2015: 38 pages.
4- Yiannakou Y et al. "A randomized, double-blind, placebo-controlled, phase 3 trial to evaluate the efficacy, safety, and tolerability of prucalopride in men with chronic constipation" *Am J Gastroenterol* 2015; **110**: 741-748 + annex: 9 pages.
5- Prescrire Rédaction "6-2-10. Patients sous prucalopride" *Rev Prescrire* 2015; **35** (386 suppl. interactions médicamenteuses).
6- ANSM "Réunion du comité technique de pharmacovigilance - CT012015043" 17 April 2015: 16 pages
7- Gasparotto A and Chandler RE "Prucalopride and suicidal ideation" *Who Pharmaceuticals Newsletter* 2015; **3**: 22-26.

Downloaded from english.prescrire.org on 18/10/2025
Copyright(c)Prescrire. For personal use only.