



AWMSG Secretariat Assessment Report – Limited submission Prucalopride succinate (Resolor[®]) 1 mg and 2 mg film-coated tablets

Company: Shire Pharmaceutical Contracts Ltd

Licensed indication under consideration:

Prucalopride (Resolor[®]) for the symptomatic treatment of chronic constipation in men in whom laxatives fail to provide adequate relief.

Marketing authorisation date: 27 May 2015

Comparator(s):

The comparator included in the company submission was lubiprostone (Amitiza[®]).

Limited submission details:

The limited submission criteria were met based on minor licence extension (to include men) and the anticipated usage of prucalopride (Resolor[®]) in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness:

- Prucalopride was previously licensed for use only in women, due to a lack of supportive data for use in men from clinical trials. The National Institute for Health and Care Excellence (NICE) Technology Appraisal 211 recommends prucalopride as a treatment option in women with chronic constipation who have tried at least two different types of laxatives at the highest possible recommended doses, for at least six months, in whom invasive treatment for constipation is being considered.
- The license extension for use in men was supported by a phase III, randomised, double-blind, placebo-controlled trial conducted in men only. This had a similar design and inclusion criteria as the earlier trials that supported the use of prucalopride in women, and enrolled patients with \leq two spontaneous complete bowel motions (SCBM) per week for at least six months.
- Prucalopride significantly increased the primary endpoint of the proportion of men achieving a mean of \geq three SCBMs per week over a 12-week treatment period compared with placebo (37.9% vs. 17.7%, $p < 0.0001$; Number Needed Treat (NNT) = 5).
- The European Public Assessment Report includes a pooled analysis across six phase III or IV trials, including the above trial in men, which suggests comparable efficacy in men and women.
- The Committee for Medicinal Products for Human Use (CHMP) concluded that prucalopride was generally well tolerated; common adverse events were consistent with previous clinical trials and no new safety concerns were identified in men.
- There are no direct comparative data for prucalopride and other agents used to treat constipation, and the company considers indirect treatment comparisons are limited by trial heterogeneity. The NICE technology appraisal of lubiprostone (NICE TA 318) concluded lubiprostone and prucalopride (at that time only licensed for use in women) were similarly effective.
- The Summary of Product Characteristics notes that, if prucalopride is not effective after four weeks of treatment, the benefit of continuing treatment should be

reconsidered. It also notes that efficacy has not been demonstrated beyond three months in placebo-controlled studies, and in case of prolonged treatment, the benefit should be reassessed at regular intervals.

Budget impact:

- Based on incidence figures from the NICE costing template for TA211, the company estimates there are 574 women eligible for prucalopride in NHS Wales in the first year. In earlier prucalopride trials, approximately 12% of enrolled patients were male, which the company assumes reflects the proportion of male patients in practice. The company therefore estimates the number of men eligible for prucalopride treatment to be 78, of which it anticipates uptake will be 10% in the first year, rising to 50% by year five. The company assumes population growth of 1% per annum, and also assumes that a third of patients discontinue prucalopride each year.
- The budget impact analysis is based on prucalopride displacing use of lubiprostone, on the basis that their respective NICE recommendations (NICE TA211 and NICE TA318) position them similarly in the care pathway.
- The net budget impact is estimated as £394 in year one based on five male patients being treated with prucalopride. This rises to £2,054 in year five, based on 27 male patients.
- There are several points to note: prucalopride is assumed to be dosed at 2 mg per day in all patients, which may overestimate its net costs; the costs for the third of patients who discontinue treatment are not included, which would potentially underestimate the net costs of prucalopride; and treatment with both prucalopride and lubiprostone is assumed to last for one year in patients who do not discontinue, although the NICE costing template for use of prucalopride in women assumed a treatment duration of 220 days. There is also the assumption that prucalopride and lubiprostone are similarly effective.

Additional information:

- AWTTTC is of the opinion that, if recommended, prucalopride (Resolor[®]) for the indication under consideration may be appropriate for use within NHS Wales prescribed by clinicians with experience of treating chronic constipation and in line with existing NICE recommendations for prucalopride use in women.
- The company does not anticipate that prucalopride (Resolor[®]) will be supplied by a home healthcare provider.

Evidence search:

Date of evidence search: 3 and 5 November 2015

Date of range of evidence search: No date limits were applied to database searches.

AWMSG review

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTTC at AWTTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Prucalopride (Resolor[®]) 1mg and 2 mg film-coated tablets. Reference number: 918. February 2015.