VI.2 ELEMENTS FOR A PUBLIC SUMMARY

VI.2.1 Overview of Disease Epidemiology

Chronic constipation is a common complaint seen in clinical practice; approximately 13-14% of the general population of adults meets strict clinical criteria. Constipation is more common in people older than 65 years, especially those living in nursing homes. Constipation is also more common in women than men across all age groups. People with higher education and income are less often affected than people with lower education and income. Risk factors for constipation include anxiety, depression, low physical activity, obesity. A low fibre diet, family history and stressful life events have also been linked to constipation. Chronic constipation is rarely fatal but can cause impairment of physical and emotional wellbeing and other serious medical conditions. Changes in lifestyle and diet is usually recommended as the first line of treatment, however, several treatment options available include the use of bulk-forming agents, osmotic/contact laxatives, pelvic floor physiotherapy, enemas and prokinetics.

VI.2.2 Summary of Treatment Benefits

Prucalopride is a medicine that is used to treat symptoms of chronic constipation in women for whom laxatives (medicines that trigger bowel movements) do not work well enough.

Prucalopride has been shown to be an effective and well tolerated treatment for women with chronic constipation. An overall analysis of the results from 6 large studies confirmed the effectiveness of prucalopride when taken up to 12 weeks. Patients in the studies were given either prucalopride or placebo (a pill that contains no medicine). The main measure of effectiveness was the number of patients who completely emptied their bowels at least three times a week over a 12 week period without the help of laxatives. The results of this analysis of these studies showed that prucalopride was more effective than placebo at treating chronic constipation.

VI.2.3 Unknowns Relating to Treatment Benefits

The main studies excluded people with severe heart and blood vessel disorder, severe reduced liver function and pregnant and breast-feeding women. Therefore, there is limited knowledge with prucalopride in these types of patients.

VI.2.4 Summary of Safety Concerns

Table 1: Important Identified Risks

Risk	What is Known	Preventability
Heart beating too hard or too fast, skipping a beat, or fluttering (palpitations)	In clinical studies palpitations were reported more frequently in patients on prucalopride than patients on placebo. The majority of events of palpitations	Patients should discuss new onset of palpitation with their physician.

Table 1: Important Identified Risks		
Risk	**What is Known**	**Preventability**
	were not serious, and majority of patients continued to use prucalopride.	

Table 2: Important Potential Risks	
Risk	**What is Known**
Heart and blood vessel problems resulting from reduced blood supply (Cardiovascular and cerebrovascular ischaemic events)	Cardiovascular ischaemic events have been associated with drugs in similar drug class. However, the mechanism by which prucalopride would cause cardiovascular and cerebrovascular ischaemic events is not known.
Inflammation of the large intestine resulting from reduced blood supply (Ischaemic colitis)	Although ischaemic colitis has been associated with drugs in similar drug class, how prucalopride can cause ischaemic colitis is not known.
Abnormal heart rhythms, fainting (QT prolongation, related ventricular arrhythmias, and syncope)	QT prolongation and related ventricular arrhythmias are known to occur with similar drug class.

Table 3: Missing Information	
Risk	**What is Known**
Safety in pregnant women	Experience with prucalopride during pregnancy is limited. Therefore, women of childbearing potential should use effective contraception during treatment. Prucalopride is not recommended during pregnancy.
Safety in patients with severe reduced liver function (Safety in patients with severe hepatic impairment)	Experience with prucalopride in patients with reduced liver function is limited. The concentration of prucalopride in patients with moderate and severe reduced liver function was higher than in patients with normal liver function.after a single oral dose of 2mg.
Safety in patients with severe and unstable disease of the heart and blood vessels (Safety in patients with severe and unstable cardiovascular disease)	Patients with severe and unstable cardiovascular disease have not been studied. Therefore physicians have to take caution when prescribing prucalopride to patients with these conditions.

VI.2.5 Summary of Risk Minimisation Measures by Safety Concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, the risks

and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet. The measures in these documents are known as routine risk minimisation measures.

The SmPC and the package leaflet for RESOLOR can be found in the RESOLOR'S European public assessment report (EPAR) page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned Post-authorisation Development Plan

Table 4: List of Studies in Post-authorisation Development Plan

Study/Activity (including study number)	Objectives	Safety Concerns/Efficacy Issue Addressed	Status	Planned Date for Submission of (Interim and) Final Results
M0001-EPI-1 (FUM006) Drug utilisation study (a study looking at the real-life use of a medicine)	To estimate the risk of stillbirths, foetal death, malformations and spontaneous abortions that result in medical attention among prucalopride-exposed pregnancies. To provide a detailed description of patients that are prescribed prucalopride for the first time and compare them with the general population and estimate how it is being prescribed in real-life use To estimate the occurrence of heart related problems and/or death in patients who take prucalopride and compare the frequency of these events to the general population.	**Important potential risks:** Heart and blood vessel problems resulting from reduced blood supply Abnormal heart rhythms, fainting **Missing information:** Safety in pregnant women	In progress	Annual reports will be submitted for 5 years. Interim report (first report): September 2011 Interim report (second report (September 2012) Third study report: October 2014; Fourth study report: December 2014 Final study report: December 2017

VI.2.6.1 Studies which are a Condition of the Marketing Authorisation.

None of the above studies are conditions of the MA.