

PART VI SUMMARY OF THE RMP

Active substance	Bisacodyl
Product concerned	Dulcolax
Name of MAH or applicant	Boehringer Ingelheim International GmbH, Ingelheim, Germany
DLP for this module	15 Jun 2015
Version number of RMP when this module was last updated	1.0

PART VI.1 ELEMENTS FOR SUMMARY TABLES IN THE EPAR

PVI.Table 1 Summary table of the safety concerns

Important identified risks	Syncope Hypersensitivity
Important potential risks	None
Missing information	Use in pregnancy

PVI.Table 2 Table of ongoing and planned studies in the post-authorisation PV development plan

Study/activity ¹	Objectives	Safety concerns addressed	Status ²	Date for submission of interim or final reports ³
None				

¹ Type, title, and category (1-3).

² Planned or started.

³ Planned or actual.

PVI.Table 3 Summary table of the post-authorisation efficacy development plan

Study (type and study number)	Objectives	Efficacy uncertainties addressed	Status (planned/started)	Date for submission of interim or final reports
None				

PVI.Table 4 Summary table of risk minimisation measures

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
<i>Important identified risks</i>		
Syncope	Product information	None
Hypersensitivity	Product information	None
<i>Missing information</i>		
Use in pregnancy	Product information	None

PART VI.2 ELEMENTS FOR A PUBLIC SUMMARY

Part VI.2.1 Overview of disease epidemiology

Constipation

Constipation is a common problem that may affect up to 1 in every 3 people in Europe at least occasionally. It is more frequent in the elderly, in women and during pregnancy. Many factors can contribute to developing constipation, including: lack of fibre, fluids or exercise, some medical conditions, and certain medicines.

Constipation is usually mild, but in some patients can become severe. Complications can arise, often due to straining, which may be painful and difficult to treat. Initially, treatment usually involves advice to increase fibre and fluid intake and exercise, although these lifestyle changes are not always sufficient. In those cases, several types of medicine are available, including: laxatives that soften stools, increase stool size, or help stools move through the bowels.

Diagnostic procedures, before and after surgery and in conditions which require defecation to be facilitated

Oral laxatives such as Dulcolax are also frequently used to cleanse the colon of fecal contents, prior to surgery. One survey of 1082 patients from 295 hospitals in the European Union (EU) and the United States (US) reported that bowel clearance was used in 85% of patients prior to colorectal surgery.

Endoscopy

Laxatives are commonly used in preparation for colonoscopy, a procedure that allows physicians to examine the inner lining of the large intestine. In the US, colonoscopy is recommended for adults 50 to 75 years of age. A review of numerous studies suggest that screening endoscopic procedures such as colonoscopy could help in the prevention of cancer of the large intestine and deaths by 40% to 60%.

Inability to tolerate full-laxative bowel preparation is considered to be the most inconvenient aspect of screening procedures (e.g. radiological procedure to examine a person's digestive

tract), but reducing or eliminating the laxative component can affect examination and make detection more difficult.

Part VI.2.2 Summary of treatment benefits

Constipation

The efficacy of Dulcolax in treating constipation has been confirmed in several modern, well-designed studies.

In the most recent study, adults with constipation received Dulcolax tablets or a dummy medication in a blinded fashion, meaning that neither the patient nor the physician knew which treatment was being given. After 4 weeks of treatment, the average number of complete spontaneous bowel movements increased from 1 per week for both groups to more than 5 per week in the Dulcolax group compared to only around 2 per week in the group receiving the dummy medication. The difference was statistically significant in favour of Dulcolax. Other constipation symptoms (like stool consistency, straining), as well as quality of life were also significantly improved in the Dulcolax group.

In another study, Dulcolax was as effective as another laxative (Laxoberal) in increasing the number of bowel movements and in softening stools.

For preparation of diagnostic procedures

For colon cleansing, Dulcolax is used under medical guidance alone or in combination with other laxatives. The efficacy of Dulcolax as a colon cleansing agent has been demonstrated in several studies and confirmed in clinical practice over many decades.

Lately, efforts have been undertaken to improve the quality of colonoscopies and patient acceptability of the bowel preparation regimens. In particular, the addition of Dulcolax was demonstrated as an effective way of reducing the volume of other bowel cleansing preparations used at the same time (2L preparations vs. 4L preparations) thus improving patient acceptance.

In pre- and post-operative treatment

Due to its laxative effect, Dulcolax is used before surgery for bowel cleansing (e.g. before surgery of the belly and rectum) and after surgery for treatment of constipation thus contributing to earlier bowel movements and accelerated recovery.

Part VI.2.3 Unknowns relating to treatment benefits

The studies covered a wide selection of patients with constipation including children, the elderly, and pregnant and lactating women. Although most patients were white Caucasians, Dulcolax has been used worldwide for several decades and there is no evidence that it is less effective for other racial groups.

Part VI.2.4 Summary of the safety concerns

PVI.Table 5 Important identified risks

Risk	What is known	Preventability
Fainting (Syncope)	<p>Fainting was reported in only a few patients participating in studies using Dulcolax. In cases where information was available, the events were of moderate intensity and the patients recovered. None of the cases was considered serious.</p> <p>Fainting in association with Dulcolax use has also been reported in patients outside of clinical studies.</p> <p>Some patients react to abdominal spasms or passing stools with fainting. The details available for these cases suggest that these fainting events might be caused by passing stool or straining at stool, or an abnormal response to severe abdominal pain. These reactions may be related to the constipation, and not necessarily to the use of Dulcolax.</p>	<p>Dizziness may be a first sign of fainting.</p> <p>Knowing that dizziness and/or fainting due to an abnormal reaction to abdominal spasm or defaecation may occur, patients should avoid potentially hazardous tasks or act with caution when feeling dizzy or experiencing abdominal cramps as described in several sections of the prescribing information and the patient information leaflet.</p>
Allergic reactions (Hypersensitivity)	<p>Allergic reactions can occur with the use of any medicine.</p> <p>No allergic reactions have been reported during the use of Dulcolax in patient studies.</p> <p>However, allergic reactions have been reported in patients who were not taking part in clinical studies. These were mostly skin reactions such as rashes with or without swelling and itching.</p> <p>This includes serious allergic reactions, which may cause swelling of the face or throat.</p>	<p>Drug allergies are unpredictable.</p> <p>Avoidance of substances the patient is allergic to and immediate help from a physician is of importance in dealing with allergic reactions in order to reduce the likelihood of progression to potentially serious outcomes. As a common problem, allergic reactions are well known to doctors and other medical staff, which can be treated when necessary.</p> <p>The doctor's prescribing information and the patient information leaflet contain information and warnings relating to the risk of allergic reactions linked to the use of Dulcolax.</p>

PVI.Table 6 Missing information

Risk	What is known
Use in pregnancy	There are no adequate and well-controlled studies in pregnant women. Lengthy experience, however, has shown no evidence of undesirable or damaging effects during pregnancy.

Part 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 health care 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 (PL). The measures in these documents are known as routine risk minimisation measures.

The SmPC and the PL for Dulcolax can be found on the Dulcolax EPAR page.

This medicine has no additional risk minimisation measures.

Part VI.2.6 Planned post-authorisation development plan

No studies are planned as this medicine is already well characterised and has been available for many years.

Part VI.2.7 Summary of changes to the RMP over time

There have been no changes to the RMP over time as this is the first version.

PART VI.3 ABBREVIATIONS

DLP	Data lock point
EPAR	European public assessment report
EU	European Union
MAH	Marketing authorisation holder
PL	Package leaflet
RMP	Risk management plan
SmPC	Summary of product characteristics
US	United States