SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Bisacodyl Laxative Tablets
Entrolax Constipation Relief

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Bisacodyl BP 5.00 mg
See 6.1 for excipients

3. PHARMACEUTICAL FORM

Enteric sugar-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term relief of constipation.

Constipation either chronic or recent onset, whenever a stimulant laxative is required.

Bowel clearance before surgery, labour or radiological investigation. Replacement of the evacuant enema in all its indications.

4.2 Posology and method of administration

Children aged 10 years or younger with chronic or persistent constipation should only be treated under the guidance of a physician. Bisacodyl should not be used in children aged 4 years or younger.

Short-term treatment for constipation:

Adults and children over 10 years:
1 to 2 tablets (5 - 10 mg) daily before bedtime.

Children 4 – 10 years:
1 tablet (5 mg) daily before bedtime.

For preparation of diagnostic procedures and preoperatively

Should only be used under medical supervision.

Adults and children over 10 years:
2 tablets (10 mg) in the morning and 2 tablets (10 mg) in the evening and 1 suppository (10 mg) on the following morning is recommended.

Children aged 4 -10 years of age:
1 tablet (5 mg) in the evening and one suppository (5 mg) on the following morning is recommended.

When using Bisacodyl Laxative tablets to prepare the patient for radiographic examination of the abdomen or employing it preoperatively, tablets should be combined with suppositories in order to achieve complete evacuation of the intestine.

In the management of constipation, once regularity has been restarted dosage should be reduced and can usually be stopped.

It is recommended to take the tablets at night to have a bowel movement the following morning. They should be swallowed whole with an adequate amount of fluid.

The coated tablets should not be taken together with products which reduce the acidity of the upper gastrointestinal tract, such as milk, antacids or proton pump inhibitors, in order not to prematurely dissolve the enteric coating.

.
No specific information on the use of this product in the elderly is available. Clinical trials have included patients over 65 years and no adverse reactions specific to this age group have been reported.

4.3 Contraindications

Bisacodyl is contraindicated in patients with ileus, intestinal obstruction, acute abdominal conditions including appendicitis, acute inflammatory bowel diseases, and severe abdominal pain associated with nausea and vomiting which may be indicative of the aforementioned severe conditions.

Bisacodyl is also contraindicated in severe dehydration and in patients with known hypersensitivity to bisacodyl or any other component of the product.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Patients with rare hereditary problems of fructose intolerance or sucrase-isomaltase insufficiency should not take this medicine

4.4 Special warnings and precautions for use

As with all laxatives, Bisacodyl should not be taken on a continuous daily basis for more than five days without investigating the cause of constipation.

Prolonged excessive use may lead to fluid and electrolyte imbalance and hypokalaemia.

Intestinal loss of fluids can promote dehydration. Symptoms may include thirst and oliguria. In patients suffering from fluid loss where dehydration may be harmful (e.g. renal insufficiency, elderly patients) Bisacodyl should be discontinued and only be restarted under medical supervision.

Patients may experience haematochezia (blood in stool) that is generally mild and self-limiting.

Dizziness and or syncope have been reported in patients who have taken Bisacodyl The details available for these cases suggest that the events would be consistent with defaecation syncope (or syncope attributable to straining at stool), or with a vasovagal response to abdominal pain related to the constipation, and not necessarily to the administration of bisacodyl itself.

There have been isolated reports of abdominal pain and bloody diarrhoea occurring after taking bisacodyl. Some cases have been shown to be associated with colonic mucosal ischaemia.

Bisacodyl should not be taken by children under 10 years without medical advice.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The tablets should not be crushed or chewed but swallowed whole. Antacids should not be given one hour after taking the tablets.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of antacids and milk products may reduce the resistance of the coating of the tablets and result in dyspepsia and gastric irritation.

The concomitant use of diuretics or adreno-corticosteroids may increase the risk of electrolyte imbalance if excessive doses of Bisacodyl are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

4.6 Fertility, Pregnancy and lactation

There are no adequate and well-controlled studies in pregnant women. Long experience has shown no evidence of undesirable or damaging effects during pregnancy.

Clinical data show that neither the active moiety of bisacodyl (BHPM or bis-(p-hydroxyphenyl)-pyridyl-2-methane) nor its glucuronides are excreted into the milk of healthy lactating females.

Nevertheless, as with all medicines, Bisacodyl should not be taken in pregnancy, especially the first trimester, and during breast feeding unless the expected benefit is thought to outweigh any possible risk and only on medical advice

No studies on the effect on human fertility have been conducted.

4.7 Effects on ability to drive and use machines

No studies on the effects of Bisacodyl on the ability to drive and use machines have been performed.

However, patients should be advised that due to a vasovagal response (e.g. to abdominal spasm) they may experience dizziness and / or syncope. If patients experience abdominal spasm they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

The most commonly reported adverse reactions during treatment are abdominal pain and diarrhoea.

Adverse events have been ranked under headings of frequency using the following convention: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1000, <1/100); rare (≥ 1/10000, <1/1000); very rare (<1/10000).

<u>Immune system disorders</u>

Rare: anaphylactic reactions, angioedema, hypersensitivity.

<u>Metabolism and nutrition disorders</u>

Rare: dehydration.

Nervous system disorders

Uncommon: dizziness.

Rare: Syncope.

Dizziness and syncope occurring after taking bisacodyl appear to be consistent with a vasovagal response (e.g. to abdominal spasm, defaecation).

Gastrointestinal disorders

Uncommon: haematochezia (blood in stool), vomiting, abdominal discomfort, anorectal discomfort.

Common: abdominal cramps, abdominal pain, diarrhoea and nausea.

Rare: colitis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms: If high doses are taken watery stools (diarrhoea), abdominal cramps and a clinically significant loss of fluid, potassium and other electrolytes can occur.

Laxatives when taken in chronic overdose may cause chronic diarrhoea, abdominal pain, hypokalaemia, secondary hyperaldosteronism and renal calculi. Renal tubular damage, metabolic alkalosis and muscle weakness secondary to hypokalaemia have also been described in association with chronic laxative abuse.

Therapy: After ingestion of oral forms of Bisacodyl, absorption can be minimised or prevented by inducing vomiting or gastric lavage. Replacement of fluids and correction of electrolyte imbalance may be required. This is especially important in the elderly and the young. Administration of antispasmodics may be of value.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Bisacodyl is a locally acting laxative from the diphenylmethane derivatives group having a dual action. As a contact laxative, for which also antiresorptive hydragogue effects have been described, bisacodyl stimulates after hydrolysis in the large intestine, the mucosa of both the large intestine and of the rectum. Stimulation of the mucosa of the large intestine results in colonic peristalsis with promotion of accumulation of water, and consequently electrolytes, in the colonic lumen. This results in a stimulation of defecation, reduction of transit time and softening of the stool. Stimulation of the rectum causes increased motility and a feeling of rectal fullness. The rectal effect may help to restore the “call to stool” although its clinical relevance remains to be established.

5.2 Pharmacokinetic properties

Following either oral or rectal administration, bisacodyl is rapidly hydrolyzed to the active principle bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM), mainly by esterases of the enteric mucosa.

Administration as an enteric coated tablet was found to result in maximum BHPM plasma concentrations between 4 – 10 hours post administration whereas the laxative effect occurred between 6 – 12 hours post administration. In contrast, following the administration as a suppository, the laxative effect occurred on average approximately 20 minutes post administration; in some cases it occurred 45 minutes after administration. The maximum BHPM-plasma concentrations were achieved 0.5 – 3 hours following the administration as a suppository. Hence, the laxative effect of bisacodyl does not correlate with the plasma level of BHPM. Instead, BHPM acts locally in the lower part of the intestine and there is no relationship between the laxative effect and plasma levels of the active moiety. For this reason, bisacodyl coated tablets are formulated to be resistant to gastric and small intestinal juice. This results in a main release of the drug in the colon, which is the desired site of action.

After oral and rectal administration, only small amounts of the drug are absorbed and are almost completely conjugated in the intestinal wall and the liver to form the inactive BHPM glucuronide. The plasma elimination half-life of BHPM glucuronide was estimated to be approximately 16.5 hours. Following the administration of bisacodyl coated tablets, an average of 51.8% of the dose was recovered in the faeces as free BHPM and an average of 10.5% of the dose was recovered in the urine as BHPM glucuronide. Following the administration as a suppository, an average of 3.1% of the dose was recovered as BHPM glucuronide in the urine. Stool contained large amounts of BHPM (90% of the total excretion) in addition to small amounts of unchanged bisacodyl.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, maize starch, magnesium stearate, pregelatinised maize starch, cellulose acetate phthalate, diethylphthalate, sucrose, povidone, talc, E171 titanium dioxide, E104 dispersed quinoline yellow, methanol, dichloromethane & purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years for containers and blister packs.

6.4 Special precautions for storage

Do not store above 25°C. Keep in original container.

6.5 Nature and contents of container

Cylindrical polypropylene containers with polythene lids and polyurethane or polythene inserts or PVC/Aluminium blister packs.
Pack sizes: 8, 10, 20, 28, 30, 50, 56, 60, 84, 100, 250, 500 & 1000.

Not all pack sizes may be Marketed.

6.6 Special precautions for disposal

No special instructions.

7. MARKETING AUTHORISATION HOLDER

Dr. Reddy's Laboratories (UK) Ltd.
6 Riverview Road,
Beverley,
East Yorkshire, HU17 0LD
U.K.

8. MARKETING AUTHORISATION NUMBER(S)

PL 08553/0200

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/12/2004 / 04/02/2010

10. DATE OF REVISION OF THE TEXT

23/08/2013