SUMMARY OF PRODUCT CHARACTERISTICS

LAXADIN®

1 NAME OF THE MEDICINAL PRODUCT

LAXADIN®

Film coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: Bisacodyl 5mg.

Excipients with known effect:

Each Tablet contains 40 mg of lactose monohydrate.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets for oral administration.

White, round biconvex film coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

All types of constipation in ambulatory and bedridden in patients over the age of 6 years.

Preparation of patients for abdominal radiography and proctoscopy.

4.2 Posology and method of administration

The tablets should not be chewed or crushed, but swallowed whole.

Adults

1-3 tablets at bedtime.

Children 6 Years of Age and Over

1 tablet or alternatively 0.3 mg/kg/body weight at bedtime.

4.3 Contraindications

Laxadin 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.

Laxadin is also contraindicated in severe dehydration and in patients with known hypersensitivity to bisacodyl or to any of the excipients listed in section 6.1.

In case of rare hereditary conditions that may be incompatible with an excipient of the product (please refer to “Special warnings and special precautions for use”) the use of the product is contraindicated.

4.4 Special warnings and precautions for use

Should not be used in children under the age of 6 years.

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.

Frequent or prolonged use may cause dependence on laxatives.

Long term everyday use of stimulant laxatives may harm the intestinal function and should be avoided. If laxatives are needed every day the cause of the constipation should be investigated. This product should only be used if a therapeutic effect cannot be achieved by a change in diet or the administration of bulk forming agents,

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.

Stimulant laxatives including bisacodyl do not help with weight loss (see section 5.1 Pharmacodynamic properties).

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

If the symptoms worsen during the use of the medicinal product, a doctor or pharmacist should be consulted.

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 diarrhea occurring after taking bisacodyl. Some cases have been shown to be associated with colonic mucosal ischemia.

Patients should be advised to drink liberally when using laxatives to aid stool softening.

Laxadin Tablets contain a small amount of lactose (40 mg) in each tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or

glucose-galactose malabsorption should not take this medicine.

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 Laxadin are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

The concomitant use of other laxatives may enhance the gastrointestinal side effects of Laxadin.

Laxative-induced diarrhea may interfere with the full absorption of many drugs. It would therefore be prudent to ensure an adequate interval of time (at least 2 hours), between the ingestion of laxatives and other drugs.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Lactation

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, Laxadin 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.

Fertility

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).

Immune system disorders

Rare: anaphylactic reactions, angioedema, hypersensitivity.

Metabolism and nutrition disorders

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 including ischemic 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

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

ATC code: A06AB02

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. Bisacodyl showed improvements in constipation-related symptoms like straining, stool consistency, abdominal discomfort and bloating compared with placebo, based on patient self- assessment questionary. Normalization of evacuatory function by bisacodyl treatment was accompanied by a relative normalization of the microflora.

The results of two-phase IV clinical trials with a total of 29 patients treated by low dose (5mg) of bisacodyl indicate that the transit through the colon, assessed through MRI, is promoted by stimulating propulsive colon motor activity with bisacodyl. In addition, repeated doses of bisacodyl 5mg during three consecutive days showed an increased in the water content in the gut. These trials demonstrated that there was no change in the underlying physiology which showed to return to baseline values 24 hours after ceasing treatment with bisacodyl.

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.

As a laxative that acts on the colon, bisacodyl specifically stimulates the physiological natural evacuation process in the lower region of the gastrointestinal tract.

Because its main effect is on distal part of the gut, bisacodyl is ineffective in altering the digestion or absorption of calories essential nutrients in the small intestine.

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 (sometimes up to 24 hours). 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 Monohydrate, Microcrystalline Cellulose, Methacrylic Acid Copolymer

Dispersion, Talc, Esma Spreng, Starch, Gelatin, Povidone, Magnesium Stearate, Triethyl Citrate, Polyethylene Glycol 4000, Simethicone, Methyl Cellulose 400, Sorbic Acid.

6.2 Incompatibilities

None stated.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a dry place, below 25ºC.

6.5 Nature and contents of container

Packs of 10, 20, 30, 50 and 1000 tablets in PVC/aluminium blisters.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None stated.

7 LICENCE HOLDER AND MANUFACTURER

Teva Israel Ltd.

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8 REGISTRATION NUMBER

018.16.24419

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