Dulcolax®

Composition

1 coated tablet contains 5 mg
4,4'-diacetoxy-diphenyl-(pyridyl-2)-methane (= bisacodyl)

Product Description

Round, beige yellow biconvex, sugar/enteric-coated tablets with a smooth, shiny surface and a white core.

Pharmacological 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 increase 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 the distal part of the gut, bisacodyl is ineffective in altering the digestion or absorption of calories or essential nutrients in the small intestine.

Pharmacokinetics

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.

Indications
For use in patients suffering from constipation.
For preparation of diagnostic procedures, in pre- and postoperative treatment and in conditions, which require defecation to be facilitated.

Dosage and Administration
Short-term treatment for constipation

Adults and children over 10 years: 1 to 2 coated tablets (5 - 10 mg) daily before bedtime, or 1 suppository (10 mg) daily for immediate effect.
Children 4 – 10 years: 1 coated tablet (5 mg) daily before bedtime.
It is recommended to start with the lowest dose. The dose may be adjusted up to the maximum recommended dose to produce regular stools. The maximum daily dose should not be exceeded.

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

For preparation of diagnostic procedures and Preoperatively
For preparation of diagnostic procedures, in pre- and postoperative treatment when defaecation needs to be facilitated, DULCOLAX should be used under medical supervision. The tablets should be combined with suppositories in order to achieve complete evacuation of the intestine.

Adults and children over 10 years: 2 coated tablets (10 mg) in the morning and 2 coated 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 coated tablet (5 mg) in the evening on the following morning is recommended.

Instructions for use
It is recommended to take the coated 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.

Suppositories are usually effective in about 20 minutes (usual range 10 to 30 minutes). Rarely the laxative effect has been reported 45 minutes after administration. They should be unwrapped and inserted into the rectum pointed end first.

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.

Side 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.

<u>Nervous system disorders</u>
Uncommon: Dizziness,
Rare: syncope.
Dizziness and syncope occurring after taking bisacodyl appear to be consistent with a vasovagal response (e.g., to abdominal spasm, defecation).

<u>Gastrointestinal disorders</u>
Uncommon: Haematochezia (blood in stool), vomiting, abdominal discomfort, anorectal discomfort.
Common: Abdominal cramps, abdominal pain, diarrhoea and nausea.
Rare: Colitis including ischaemic colitis.

Special warning and Precautions for use
As with all laxatives, DULCOLAX should not be taken on a continuous daily basis or for extended periods without investigating the cause of constipation.
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 of 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) DULCOLAX should be discontinued and only be restarted under medical supervision.

Stimulant laxatives including DULCOLAX® do not help with weight loss (see Section Pharmacological 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 DULCOLAX. The details available for these cases suggest that the events would be consistent with defecation 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.

One coated tablet contains 33.2 mg lactose, resulting in 66.4 mg lactose per maximum recommended daily dose for treatment of constipation in adults and children over 10 years of age. For radiographic examination this will result in 132.8 mg per maximum recommended daily dose in adults. Patients with rare hereditary conditions of fructose intolerance, galactose intolerance, e.g. galactosaemia, total lactase deficiency, glucose-galactose malabsorption should not take this medicine.

One coated tablet contains 23.4 mg sucrose (saccharose), resulting in 46.8 mg sucrose (saccharose) per maximum recommended daily dose for treatment of constipation in adults and children over 10 years of age. For radiographic examination this will result in 93.6 mg per maximum recommended daily dose in adults. Patients with the rare hereditary condition of fructose intolerance, or sucrase-isomaltase insufficiency should not take this medicine.

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 (bis- (p-hydroxyphenyl)-pyridyl-2-methane) nor its glucuronides are excreted into the milk of healthy lactating human females.

Nevertheless, as with all medicines, DULCOLAX 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.

Effects on ability to drive and use machines
No studies on the effects of DULCOLAX 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.

Contraindications
DULCOLAX 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 severe conditions.

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

In case of rare hereditary conditions that may be incompatible with an excipient of the product (please refer to "Special Precautions") the use of the product is contraindicated.

Interactions
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 DULCOLAX 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 DULCOLAX®

Overdosage

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

Availability of pack sizes
Dulcolax Tablet 5mg: Box of 30 or 200 coated tablets.
Not all pack sizes may be marketed.

Storage condition
Store below 30°C.

Please consult your doctor or pharmacist for further information.
Please refer to packaging for information on shelf-life.

Name and address of manufacturer
Mfd. by
Delpharm Reims
10, Rue Colonel Charbonneaux, Reims, 51100, France

Product license holder:
In Malaysia:
DKSH Malaysia Sdn Bhd
B-11-01, The Ascent, Paradigm
No. 1, Jalan SS7/26A, Kelana Jaya
47301 Petaling Jaya
Selangor Darul Ehsan
Malaysia

Product registrant
In Singapore:
Opella Healthcare Singapore Pte Ltd

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Store in a safe place out of the reach of children!