BISACODYL 5MG TABLETS
PL 06464/2353

UKPAR

TABLE OF CONTENTS

Lay Summary Page 2
Scientific discussion Page 3
Steps taken for assessment Page 11
Summary of Product Characteristics Page 12
Product Information Leaflet
Labelling
On 30th July 2010, the MHRA granted Waymade PLC a Marketing Authorisation (licence) for the medicinal product Bisacodyl 5mg Tablets (PL 06464/2353). This is a General Sale Licence (GSL).

Bisacodyl 5mg Tablets contain the active ingredient bisacodyl. Bisacodyl is a laxative used to provide short term relief from constipation.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Bisacodyl 5mg Tablets outweigh the risks; hence a Marketing Authorisation has been granted.
BISACODYL 5MG TABLETS
PL 06464/2353

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction Page 4
Pharmaceutical assessment Page 5
Preclinical assessment Page 8
Clinical assessment (including statistical assessment) Page 9
Overall conclusions and risk benefit assessment Page 10
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted a marketing authorisation for the medicinal product Bisacodyl 5mg Tablets (PL 06464/2353) to Waymade PLC on the 30th July 2010. This is a General Sale Licence (GSL) used for the short term use in cases of constipation.

This application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, cross-referring to Bisacodyl 5mg Tablets (PL 06464/0186) also held by Waymade PLC, which was granted a marketing authorisation on 8th March 1994.

No new data were submitted nor were they necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated.

The Marketing Authorisation Holder has submitted a commitment to update the pharmacovigilance system in the due course through a variation procedure following the grant of the licence.

No environmental risk assessment has been undertaken, as this is not considered necessary. This is justified as it is not anticipated that the grant of this new marketing authorisation will result in an increase in the environmental exposure of the drug.

The applicant’s justification for absence of ERA is satisfactory.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 06464/2353
PROPRIETARY NAME: Bisacodyl 5mg Tablets
COMPANY NAME: Waymade PLC
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: GSL

1 INTRODUCTION
This is a simple, informed consent application for Bisacodyl 5mg Tablets, submitted under Article 10c of Directive 2001/83/EC. The application cross-refers to Bisacodyl 5mg Tablets (PL 06464/0186), approved on 8th March 1994 to the marketing authorisation holder Waymade PLC. The current application is considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)
2.1 Name(s)
The proposed name of the product is Bisacodyl 5mg Tablets. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains the active ingredient bisacodyl.

The tablets are packed in Polyvinylchloride/Aluminium blister strips. The pack sizes are 10, 20 and 40 tablets. Specification and Certificate of Analysis for all packaging components used have been provided and are satisfactory. The packaging and pack size are the same as those for the reference product.

The proposed shelf life is 36 months, with the storage conditions ‘Do not store above 25°C’, ‘Keep the container tightly closed’ and ‘Store in the original containers’. The shelf-life and storage conditions are identical to those for the reference product and are satisfactory.

2.3 Legal status
The product is a General Sale Licence (GSL).

2.4 Marketing authorisation holder/Contact Persons/Company
The proposed Marketing Authorisation holder is Waymade PLC trading as Sovereign Medical, Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FR, United Kingdom

The Qualified Person (QP) responsible for pharmacovigilance is stated and a Curriculum Vitae (CV) is included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the reference product and evidence of Good Manufacturing Practice compliance has been provided.
2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specifications
The proposed finished product and shelf-life specifications are in line with the details registered for the reference product.

2.9 Drug substance specification
The proposed drug substance specification conforms to the current British Pharmacopoeia monograph for bisacodyl, and is in-line with that for the reference product.

European Directorate for the Quality of Medicines (EDQM) Certificates of Suitability for the manufacturer of bisacodyl has been provided. The active substance manufacturer is in line with that for the reference product.

2.10 TSE Compliance
No materials of human or animal origin have been used in the manufacture of this product. This is consistent with the reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the reference product Bisacodyl 5mg Tablets (PL 06464/0186).

3 EXPERT REPORT
The applicant has included detailed expert reports of the application. Signed declarations and copies of the experts’ CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to that of the reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING
The patient information leaflet has been prepared in line with the details registered for the reference product.

The applicant has submitted results of PIL user testing. The results indicate that the PIL is well-structured and organised, easy to understand and written in a
comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

The proposed artwork complies with the relevant statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with the application is acceptable. The grant of a marketing authorisation is recommended.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.
OVERALL CONCLUSION AND BENEFIT RISK ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the reference product and, as such, have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
This application is identical to the previously granted application for Bisacodyl 5mg Tablets (PL 06464/0186), granted to Waymade PLC on the 8th March 1994.

Pharmaceutical preclinical and clinical expert statements have been provided, together with CVs showing the experts are appropriately qualified. The experts confirm that the product is identical in composition, manufacture and pharmaceutical characteristics to the respective reference product and that there are no toxicological or clinical issues.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the reference product. Extensive clinical experience with bisacodyl is considered to have demonstrated the therapeutic values of the compounds. The risk benefit is, therefore, considered to be positive.
**STEPs TAKEN FOR ASSESSMENT**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 13\textsuperscript{th} December 2005</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 6\textsuperscript{th} January 2006</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 6\textsuperscript{th} June 2006 and 3\textsuperscript{rd} March 2008</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 29\textsuperscript{th} January 2008 and 30\textsuperscript{th} April 2010</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 30\textsuperscript{th} July 2010</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Bisacodyl 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Bisacodyl 5mg

   For excipients, see 6.1

3 PHARMACEUTICAL FORM
Gastro-resistant Tablets

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
For the short term use in cases of constipation.

4.2 Posology and method of administration
   For oral use.

   **Adults & children over 10 years old:**
   1 to 2 tablets taken at ‘night’.

   Children under 10 years should not take bisacodyl tablets without medical advice

   **Children aged 4-10 years:**
   1 tablet taken at ‘night’.

   Children under 4 years, not recommended.

   **Elderly:**
   As in adults but in some cases not more than 1 tablet should be taken.

4.3 Contraindications
1. Hypersensitivity or previous allergic reaction to bisacodyl or any of the products excipients.

2. Undiagnosed painful abdominal symptoms that may be due to acute appendicitis and/or other acute surgical conditions such as intestinal obstruction or acute inflammatory bowel disease.

3. Ileus.

4. In severe dehydration states with water and electrolyte imbalance.

4.4 Special warnings and precautions for use
1. If laxatives are needed every day the cause of the constipation should be investigated.

2. Excessive and prolonged use is dangerous and may result in diarrhoea leading to electrolyte imbalance and hypokalaemia.

3. Prolonged and daily use may precipitate the onset of rebound constipation.

4. Excessive and prolonged use may precipitate the onset of an atonic non-functioning colon.

5. Patients with rare hereditary problems of galactose or fructose intolerance, Lapp lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
6. 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.

7. Dizziness and/or syncope have been reported in patients during defecation, consistent with defecation syncope (or syncope attributable to straining at stool), or with a vasovagal response to abdominal pain which may be related to the constipation that prompted these patients to resort to the use of laxatives.

4.5 Interaction with other medicinal products and other forms of interaction
The concomitant use of diuretics, cardiac glycosides or adrenal corticosteroids may enhance electrolyte imbalance, particularly potassium. As a consequence cardiac glycoside toxicity may be increased.
The concomitant use of antacids and milk containing products may reduce the resistance of the tablet coating and result in dyspepsia and gastric irritation.

4.6 Pregnancy and lactation
For bisacodyl, no clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Caution should be exercised when prescribing to pregnant women.
It is advisable not to breast-feed when taking bisacodyl as small amounts of the compound pass into the breast milk.

4.7 Effects on ability to drive and use machines
On the basis of the product’s pharmacodynamic profile and reported adverse events, bisacodyl has no known effect on an individual’s ability to drive or operate machinery.

4.8 Undesirable effects
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). Not known – incidence cannot be estimated from the available data.

Immune system disorders
Not known: anaphylactic reactions, angioneurotic oedema and other hypersensitivity.

Gastrointestinal disorders
Uncommon: vomiting.
Common: Abdominal discomfort, abdominal pain, abdominal cramps, nausea and diarrhoea.
Not known: colitis (see section 4.4).

4.9 Overdose
Symptoms of overdose include, colicky lower abdominal pain with possible signs of dehydration particularly in the elderly and the very young.

Gastric lavage should be performed where appropriate. Adequate hydration must be maintained, and electrolyte imbalances, particularly in the serum potassium, corrected. Antispasmodics may be of some value.

Particular care should be taken regarding fluid balance in the elderly and the very young.
5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
In common with other stimulant laxatives bisacodyl (which has a related structure to phenolphalein) stimulates accumulation of water and electrolytes in the colonic lumen, and enhances intestinal motility. It may be intestinal Na\(^+\), K\(^-\)ATPase which may account for at least a portion of it’s laxative activity. It may also increase the synthesis of prostaglandins and cyclic AMP, and this may contribute to increased secretion of water and electrolytes.

5.2 Pharmacokinetic properties
Bisacodyl is rapidly converted by intestinal and bacterial enzymes to it’s active desacetyl metabolite. As much as 5% of an oral dose is absorbed and excreted in the urine as the glucuronide. This inactive metabolite is also excreted in the bile and may be hydrolysed to active drug in the colon.

5.3 Preclinical safety data
There are no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Lactose
Polyvinyl acetate phthalate
Stearic acid
Maize starch
Magnesium stearate
Liquid paraffin
Opadry®
Carnauba Wax

6.2 Incompatibilities
None known.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 25°C. Keep the container tightly closed. Store in the original containers.

6.5 Nature and contents of container
The tablets are available in packs of 10, 20 and 40 in PVC/Aluminium blister strips. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
The tablets should not be chewed or crushed.

7 MARKETING AUTHORISATION HOLDER
Waymade PLC trading as Sovereign Medical
Sovereign House
Miles Gray Road
Basildon
Essex
SS14 3FR
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 06464/2353

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
30/07/2010
DATE OF REVISION OF THE TEXT
30/07/2010
PATIENT INFORMATION LEAFLET

Patient Information Leaflet:  GBR 726-4203-APIL

Bisacodyl 5 mg Tablets

Bisacodyl

Read all of this leaflet carefully before you start taking this medicine.
- Please keep this leaflet.
- You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects becomes severe, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Bisacodyl 5 mg Tablets are and what they are used for.
2. Before you take Bisacodyl 5 mg Tablets.
3. How to take Bisacodyl 5 mg Tablets.
4. Possible side effects.
5. How to store Bisacodyl 5 mg Tablets.
6. Further information.

1. WHAT BISACODYL 5 MG TABLETS ARE AND WHAT THEY ARE USED FOR
The name of your medicine is Bisacodyl 5 mg Tablets. The active ingredient is bisacodyl. Bisacodyl is a laxative used to provide short term relief from constipation.

BEFORE YOU TAKE BISACODYL 5 MG TABLETS
Do not take this medicine if:
- You have ever had an allergic reaction to any of the ingredients of Bisacodyl Tablets or any other medicines that you may have taken to treat constipation (allergic reactions include mild symptoms such as itching and/or rash. More severe symptoms include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing)
- You have recently had undiagnosed stomach pains (as this can be the result of acute appendicitis, a bowel obstruction or acute inflammatory bowel disease)
- You have ileus (paralysis of the bowel)
- You are severely dehydrated following sickness or diarrhoea.

Take special care with this medicine and tell your doctor or pharmacist if:
- you are taking bisacodyl on a daily basis as this medicine should not be used for long periods of time. Prolonged or excessive use may lead to diarrhoea or cause the constipation to return and could also result in the onset of a condition known as non-functioning colon (large intestine)
- you find that you are still constipated after a long period of time. Your doctor will investigate the cause of the constipation.

Talk to your doctor or pharmacist before taking this medicine if you have been told that you have an intolerance to some sugars. This is because Bisacodyl Tablets contain lactose which is a type of sugar.

Taking other medicines
Please tell your doctor or pharmacist if you are taking any of the following:
- medicines for heart problems, e.g. digoxin;
- medicines for high blood pressure or water retention, e.g. diuretics;
- a group of medicines collectively known as 'steroids';
- medicines to treat heartburn, e.g. antacids;
- milk containing products.

Pregnancy and breast-feeding
Tell your doctor or pharmacist if you become pregnant, are planning to become pregnant or if you are breast-feeding. It is advisable not to breast-feed when taking bisacodyl as small amounts of the compound pass into breast milk.

Driving and using machines
This medicine should not affect your ability to drive or operate machinery, provided that it is used only as recommended.

3. HOW TO TAKE BISACODYL 5 MG TABLETS
If this medicine is from your doctor or pharmacist, do exactly as they have told you. You should check with your doctor or pharmacist if you are not sure. He or she will tell you how many to take and how often to take them. The tablet should be swallowed with water. This medicine must not be chewed or crushed.
The usual doses of Bisacodyl 5 mg Tablets are as follows:

**Adults and the elderly**
5 – 10 mg taken at night. Not more than 5 mg may be advised if you are elderly.

**Children**
For children over 10 years of age, 5-10 mg to be taken at night.
For children under 10 years of age, Bisacodyl should NOT be taken without medical advice.
For children between 4-10 years of age, 5 mg to be taken at night.

**Bisacodyl is not recommended for children under 4 years of age.**

If you take more tablets than you should
If you accidentally take too much of your medicine, tell your doctor at once or contact your nearest hospital casualty department immediately. Take your medicine and this leaflet with you.

If you forget to take your medicine
If you forget to take a dose, just take the next dose at the usual time, DO NOT take a double dose.

**4. POSSIBLE SIDE EFFECTS**
Like all medicines, Bisacodyl 5 mg Tablets can cause side effects in some people, although it is generally well tolerated. If you start to suffer from rashes, itching or any other problems with your skin or breathing STOP taking your medicine and see a doctor. These may be symptoms of an allergy or the early symptoms of more serious skin/allergic reactions to your medicine. You are unlikely to get any of the following, but if you do, tell your doctor immediately;

**Common side effects (affect less than 1 in 10 people)**
- abdominal discomfort, cramps or pain
- nausea
- diarrhoea (in rare instances this may contain blood).

**Uncommon side effects (affect less than 1 in 100)**
- vomiting.

Unknown (incidence of side effect cannot be estimated from the available data)
- colitis (inflammation of the large intestine)
- dizziness or fainting while straining due to constipation or while having a bowel movement.

If any of the side effects becomes severe, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist immediately.

5. **HOW TO STORE BISACODYL 5 MG TABLETS**
Store the tablets in original package in order to protect from moisture.
Do not store above 25°C.
Do not use after the expiry date that is stated on the carton or label.

**KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN**
Return any unused medicine to your pharmacist.

6. **FURTHER INFORMATION**
What Bisacodyl 5 mg Tablets contain:
Each tablet contains 5 mg of the active substance bisacodyl.
The other ingredients are lactose, maize starch, liquid paraffin, magnesium stearate, polyvinyl acetate phthalate, stearic acid, Opadry® and Carnauba Wax.

What Bisacodyl 5 mg Tablets look like and the contents of the pack
Bisacodyl 5 mg Tablets are yellow, shiny, round tablets with no markings. They are packed in foil blister packs and available in packs of 10, 20 and 40 tablets.

Not all pack sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer**
Waymade Plc trading as Sovereign Medical, Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FR.

This leaflet does not contain all the available information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

The information in this leaflet applies only to Bisacodyl 5 mg Tablets.

Date of preparation of the leaflet: March 2010
LABELLING

For gentle and effective overnight relief from constipation

Dosage:
Adults and children over 10 years: 1-2 tablets taken at night or as directed by your doctor.
Children under 10 years: Consult your doctor.
To be swallowed whole. Do not crush or chew.
Do not exceed the stated dose.
If symptoms persist, seek medical advice.
If laxatives are needed everyday or if you have a persistent abdominal pain, consult your doctor.
Do not take milk-containing products within an hour before or after Bisacodyl Tablets 5 mg.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Ingredients: Each tablet contains Bisacodyl 5 mg
Also contains lactose, sucrose and tartarazine (E102).
Do not store above 25°C.
Store in the original container in order to protect from moisture.
Further information is provided in the Patient Information Leaflet.

Marketing Authorisation Holder:
Waymade Plc trading as Sovereign Medical,
Sovereign House, Miles Gray Road, Basildon, Essex. SS14 3FR.

GSL
For gentle and effective overnight relief from constipation

Dosage:
- Adults and children over 10 years: 1-2 tablets taken at night or as directed by your doctor.
- Children under 10 years: Consult your doctor.
- To be swallowed whole. Do not crush or chew.
- Do not exceed the stated dose.
- If symptoms persist, seek medical advice.
- If localised pain is needed everyday or if you have a persistent abdominal pain, consult your doctor.
- Do not take milk-containing products within an hour before or after Bisacodyl Tablets 5 mg.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Ingredients: Each tablet contains Bisacodyl 5 mg.
- Also contains butene, sucrose and tartrazine (E102).
- Do not store above 25°C.
- Store in the original container in order to protect from moisture.
- Further information is provided in the Patient Information Leaflet.

Marketing Authorisation Holder:
Waymade Plc trading as Sovereign Medical,
Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FL

Bisacodyl 5 mg Tablets
Constipation relief
- Gentle and effective overnight relief from constipation

20 gastro-resistant tablets