Public Assessment Report

Mutual Recognition Procedure

Movicol Plain 13.7g sachet, powder for oral solution

Macrogol 3350, Potassium chloride, Sodium chloride, Sodium hydrogen carbonate

UK/H/0131/05/MR

UK licence no: PL 20142/0004

Applicant: Norgine B.V.

LAY SUMMARY

On 13th May 2008, the MHRA granted Norgine B.V a Marketing Authorisation (licence) for the medicinal product Movicol Plain 13.7g sachet, powder for oral solution (PL 20142/0004). This is a product to be supplied through pharmacy and promoted to healthcare professionals only (P) that act as a laxative for the treatment of constipation in adults, adolescents and the elderly.

Movicol Plain helps you to have a comfortable bowel movement even if you have been constipated for a long time. Movicol Plain also works in very bad constipation called faecal impaction.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Movicol Plain sachet, powder for oral solution outweigh the risks, hence a Marketing Authorisation has been granted.

TABLE OF CONTENTS

Module 1

Product Name	Movicol Plain 13.7g sachet, powder for oral solution
Type of Application	Article 8.3
Active Substance	Macrogol 3350, Potassium chloride, Sodium chloride, Sodium hydrogen carbonate
Form	Powder for oral solution
Strength	13.7g sachet
MA Holder	Norgine B.V., Hogehilweg 7, 1101 CA Amsterdam ZO, The Netherlands.
RMS	UK
CMS	Austria, Belgium, Finland, Republic of Ireland, Italy, Spain, Sweden
Procedure Number	UK/H/0131/05/MR
Timetable	Day 90 - 13/05/2008

Module 2

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

MOVICOL Plain 13.7g sachet, powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of MOVICOL Plain contains the following active ingredients:

Macrogol 3350	13.1250 g
Sodium Chloride	0.3508 g
Sodium Hydrogen Carbonate	0.1786 g
Potassium Chloride	0.0502 g

The content of electrolyte ions per sachet when made up to 125 ml of solution is as follows:

Sodium	65 mmol/l
Chloride	53 mmol/l
Potassium	5.4 mmol/l
Hydrogen Carbonate	17 mmol/l

For excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution. Free flowing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of chronic constipation. MOVICOL Plain is also effective in resolving faecal impaction, defined as refractory constipation with faecal loading of the rectum and/or colon.

4.2 Posology and method of administration

Chronic Constipation

A course of treatment for constipation with MOVICOL Plain does not normally exceed two weeks, although this can be repeated if required.

As for all laxatives, prolonged use is not usually recommended. Extended use may be necessary in the care of patients with severe chronic or resistant constipation, secondary to multiple sclerosis or Parkinson's Disease, or induced by regular constipating medication, in particular opioids and antimuscarinics.

Adults, adolescents and the elderly: 1-3 sachets daily in divided doses, according to individual response.

For extended use, the dose can be adjusted down to 1 or 2 sachets daily.

Children (below 12 years old): Not recommended. Alternative MOVICOL products are available for children.

Faecal impaction

A course of treatment for faecal impaction with MOVICOL Plain does not normally exceed 3 days.

Adults, adolescents and the elderly: 8 sachets daily, all of which should be consumed within a 6 hour period.

Children (below 12 years old): Not recommended. Alternative MOVICOL products are available for children.

Patients with impaired cardiovascular function: For the treatment of faecal impaction the dose should be divided so that no more than two sachets are taken in any one hour.

Patients with renal insufficiency: No dosage change is necessary for treatment of either constipation or faecal impaction.

Administration
Each sachet should be dissolved in 125ml water. For use in faecal impaction 8 sachets may be dissolved in 1 litre water.

4.3 Contraindications
Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, ileus, severe inflammatory conditions of the intestinal tract, such as Crohn's disease and ulcerative colitis and toxic megacolon.

Hypersensitivity to the active ingredients or to any of the excipients.

4.4 Special warnings and precautions for use
Diagnosis of impaction/faecal loading of the rectum should be confirmed by physical or radiological examination of the abdomen and rectum.

Mild adverse drug reactions are possible as indicated in Section 4.8. If patients develop any symptoms indicating shifts of fluid/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure) MOVICOL Plain should be stopped immediately and electrolytes measured, and any abnormality should be treated appropriately.

4.5 Interaction with other medicinal products and other forms of interaction
No clinical interactions with other medicinal products have been reported. Macrogol raises the solubility of medicinal products that are soluble in alcohol and relatively insoluble in water. There is therefore a theoretical possibility that the absorption of such medicinal products could be transiently reduced.

4.6 Pregnancy and lactation
There is no experience of the use of MOVICOL Plain during pregnancy and lactation and it should only be used if considered essential by the physician.

4.7 Effects on ability to drive and use machines
MOVICOL Plain has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Abdominal distension and pain, borborygmi and nausea, attributable to the expansion of the contents of the intestinal tract can occur. Mild diarrhoea which usually responds to dose reduction. Allergic reactions are a possibility.

4.9 Overdose
Severe pain or distension can be treated by nasogastric aspiration. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Osmotically acting laxatives.

ATC code: A06A D65

Macrogol 3350 acts by virtue of its osmotic action in the gut, which induces a laxative effect. Macrogol 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is an improved propulsive colonic transportation of the softened stools and a facilitation of the defaecation. Electrolytes combined with macrogol 3350 are exchanged across the intestinal barrier (mucosa) with serum electrolytes and excreted in faecal water without net gain or loss of sodium, potassium and water.

For the indication of faecal impaction controlled comparative studies have not been performed with other treatments (e.g. enemas). In a non-comparative study in 27 adult patients, MOVICOL cleared the

faecal impaction in 12/27 (44%) after 1 day's treatment; 23/27 (85%) after 2 days' treatment and 24/27 (89%) at the end of 3 days.

Clinical studies in the use of MOVICOL in chronic constipation have shown that the dose needed to produce normal formed stools tends to reduce over time. Many patients respond to between 1 and 2 sachets a day, but this dose should be adjusted depending on individual response.

5.2. Pharmacokinetic properties

Macrogol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastro-intestinal tract Any macrogol 3350 that is absorbed is excreted via the urine.

5.3 Preclinical safety data

Preclinical studies provide evidence that macrogol 3350 has no significant systemic toxicity potential, although no tests of its effects on reproduction or genotoxicity have been conducted.

There are no long-term animal toxicity or carcinogenicity studies involving macrogol 3350, although there are toxicity studies using high levels of orally administered high molecular macrogols that provide evidence of safety at the recommended therapeutic dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

None are known.

6.3 Shelf life

3 years.
Reconstituted solution: 6 hours.

6.4 Special precautions for storage

Sachet: Do not store above 25°C.
Reconstituted solution: Store at 2-8ºC (in a refrigerator and covered)

6.5 Nature and contents of container

Each sachet contains 13.7 g of powder.
Sachet: laminate consisting of four layers: low density polyethylene, aluminium, low density polyethylene and paper.
Pack sizes: boxes of 6, 8, 10, 20, 30, 40, 50, 60 or 100 sachets.
Not all pack sizes may be marketed

6.6 Special precautions for disposal

Any unused solution should be discarded within 6 hours

7 MARKETING AUTHORISATION HOLDER

Norgine BV
Hogehilweg 7
1101 CA Amsterdam ZO
The Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

PL 20142/0004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 September 2006

10 DATE OF REVISION OF THE TEXT

05/11/2008

Module 3
Patient Information Leaflet

Patient Information Leaflet

MOVICOL® Plain

13.7 g sachet, powder for oral solution

Please read all of this leaflet carefully before taking your medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What is MOVICOL Plain and what is it used for?

The name of this medicine is MOVICOL Plain 13.7g sachet, powder for oral solution. It is a laxative for the treatment of constipation in adults, adolescents and elderly. It is not recommended for children below 12 years of age.

MOVICOL Plain helps you to have a comfortable bowel movement even if you have been constipated for a long time. MOVICOL Plain also works in very bad constipation called faecal impaction.

2. Before you take MOVICOL Plain

Do not take MOVICOL Plain if your doctor has told you that you have:
- a blockage of your intestine (gut obstruction, paralysis of the intestine (ileus))
- a perforated gut wall
- severe inflammatory bowel disease like ulcerative colitis, Crohn's disease, or toxic megacolon
- an allergy to the active substances or any of the other ingredients of MOVICOL Plain

Heart conditions

Follow the special instructions in section 3 if you are taking MOVICOL Plain for faecal impaction.

Pregnancy and breast feeding

If you are pregnant or breast feeding, talk to your doctor before taking MOVICOL Plain.

Taking other medicines

Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicines, including medicines obtained without a prescription.

Driving and using machines

MOVICOL Plain does not affect your ability to drive or use machines.

3. How to take MOVICOL Plain

This medicine can be taken any time with or without food or drink.

Constipation

A dose of MOVICOL Plain is 1 sachet.
Take this 1–3 times a day according to the severity of your constipation.

Faecal impaction

Before you take MOVICOL Plain for faecal impaction, it should be confirmed that you have this condition.

A dose of 8 sachets a day of MOVICOL is needed for the treatment faecal impaction. The 8 sachets should be taken within 6 hours for up to 3 days if required. If you have a heart condition do not take more than 2 sachets in any one hour.

How to mix:

Open the sachet and pour the contents into a glass. Add about 125ml or 1/4 pint of water to the glass. Stir well until all the powder has dissolved and the MOVICOL Plain solution is clear or slightly hazy, then drink it. If you are taking MOVICOL Plain for faecal impaction it may be easier to dissolve 8 sachets in 1 litre of water.

Duration of treatment

Constipation

Treatment with MOVICOL Plain usually lasts for about 2 weeks. If you need to take MOVICOL Plain for longer, please see your doctor.

If your constipation is a caused by an illness such as Parkinson's disease or multiple sclerosis (MS), or if you take medicines that cause constipation your doctor may recommend that you take MOVICOL Plain for longer than 2 weeks. If you need to take MOVICOL Plain for longer, please see your doctor.
Usually for long term treatment the dose can be lower to either 1 or 2 sachets a day.

Faecal impaction

Treatment with MOVICOL Plain can be for up to 3 days.

If you take more MOVICOL Plain than you should

You may develop diarrhoea. Stop taking MOVICOL Plain until it clears, and then start again at a lower dose. If you are worried contact your doctor or pharmacist.

If you forget to take MOVICOL Plain

Take the dose as soon as you remember to take it.

4. Possible side effects

Like all medicines, MOVICOL Plain can have side effects.

Tell your doctor immediately and stop taking MOVICOL Plain if:
- You feel weak, increasingly tired, breathless, very thirsty with a headache or get puffy ankles.
- You have a skin rash or itching which may be signs of an allergic reaction. Other possible signs of an allergic reaction include difficulty in breathing or dizziness.

Sometimes people have stomach ache or rumbles, or feel bloated or sick. You may have mild diarrhoea when starting to take MOVICOL Plain.

If any of the above are troublesome or last more than a few days or if you notice any side effects not mentioned in this leaflet, please inform you doctor or pharmacist.

5. How to store MOVICOL Plain

Keep all medicines out of the reach and sight of children

Do not use MOVICOL Plain after the expiry date on the sachet and carton.

Do not store above 25°C.

Once you have made up MOVICOL Plain in water, if you cannot drink it straight away keep it covered and in the fridge (2 – 8°C). Throw away any solution not used in a 6 hour period.

Medicines should not be disposed of via wastewater or household waste. Ask you pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further Information

Each 13.7g sachet of MOVICOL Plain contains the following:

Macrogol 3350	13.125 g
Sodium chloride	0.3508 g
Sodium hydrogen carbonate	0.1786 g
Potassium chloride	0.0502 g

When it is made into a drink with 125 millilitres of water each sachet gives the equivalent of:

Sodium	65	millimoles/litre
Chloride	53	millimoles/litre
Hydrogen carbonate	17	millimoles/litre
Potassium	5.4	millimoles/litre

What MOVICOL Plain looks like and contents of the pack

MOVICOL Plain is a powder for oral solution. MOVICOL Plain is available in boxes of 6, 8, 10, 20, 30, 40, 50, 60 or 100 sachets.
Not all pack sizes may be marketed.

UK Marketing authorisation holder:

Norgine BV, Hoegilweg 7, 1101 CA Amsterdam ZO, The Netherlands.

IE Marketing authorisation holder:

Norgine Ltd, Moorhall Road, Harefield, Middx, UB9 6NS UK

Manufacturer:

Norgine Ltd, New Road, Hengoed, Mid Glamorgan, CF82 8SJ, U.K.

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	MOVICOL Aromafrei
Belgium	MOVICOL Neutral
Finland	MOVICOL Plain
Ireland	MOVICOL Plain
Italy	MOVICOL Dearoma
Netherlands	MOVICOLon Naturel
Spain	MOVICOL Sabor Neutro
Sweden	MOVICOL Neutral
Switzerland	MOVICOL Aromafrei
United Kingdom	MOVICOL Plain

This leaflet was last approved in June 2008.

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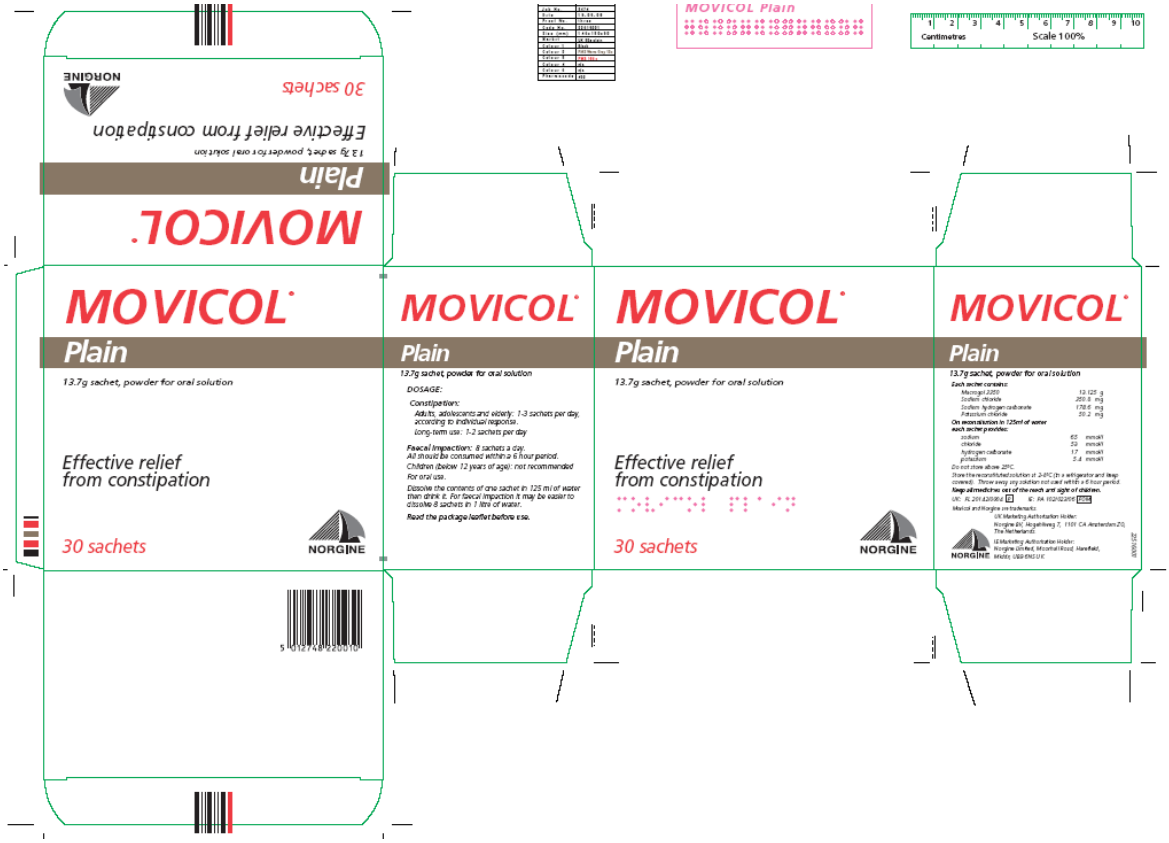
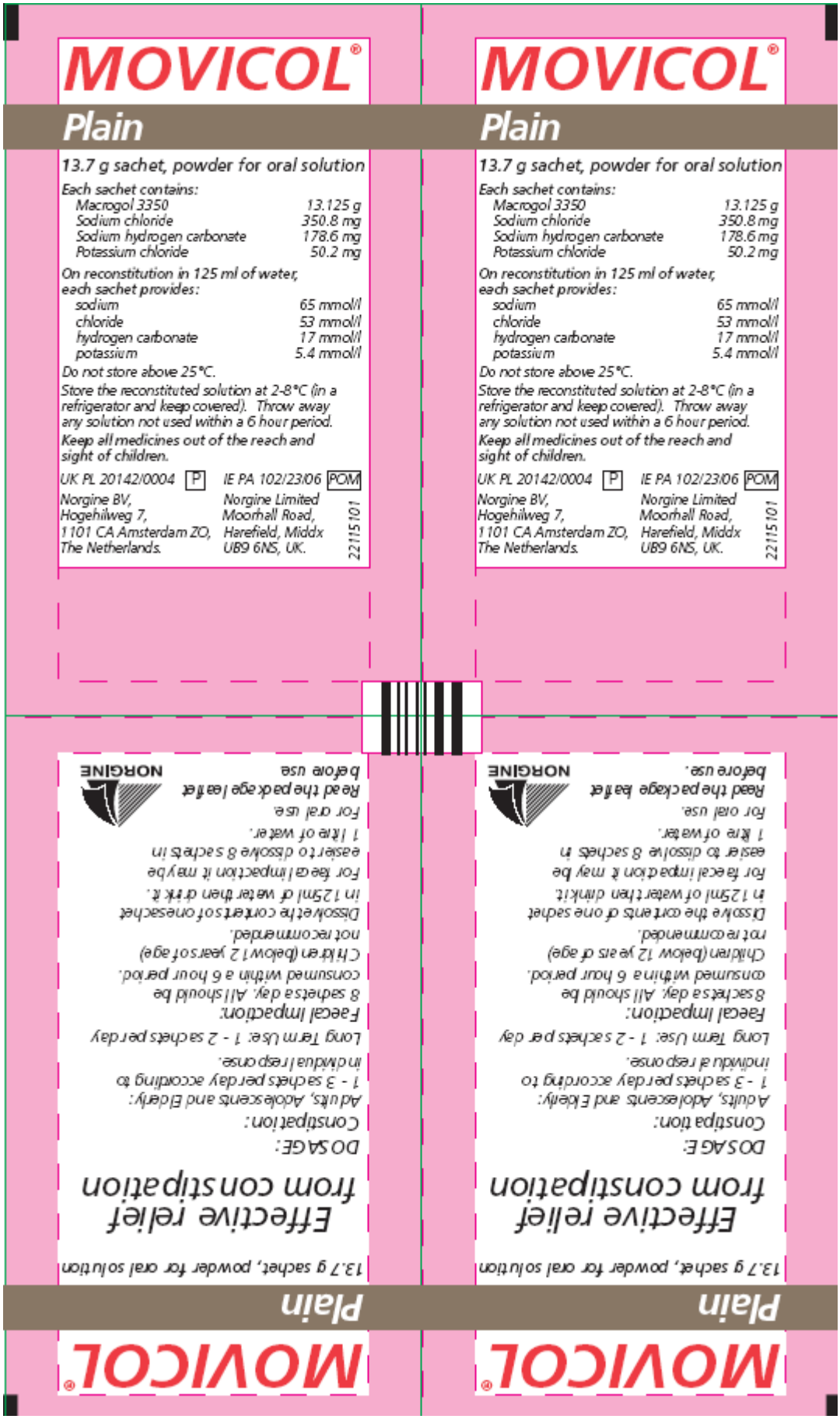
Module 4

Labelling




MOVICOL®
Plain
13.7 g sachet, powder for oral solution
Each sachet contains:
Macrogol 3350 13.125 g
Sodium chloride 350.8 mg
Sodium hydrogen carbonate 178.6 mg
Potassium chloride 50.2 mg
On reconstitution in 125 ml of water, each sachet provides:
sodium 65 mmol/l
chloride 53 mmol/l
hydrogen carbonate 17 mmol/l
potassium 5.4 mmol/l
Do not store above 25°C.
Store the reconstituted solution at 2-8°C (in a refrigerator and keep covered). Throw away any solution not used within a 6 hour period.
Keep all medicines out of the reach and sight of children.
UK PL 20142/0004 P
IE PA 102/23/06 POM
Norgine BV, Hogehilweg 7, 1101 CA Amsterdam ZO, The Netherlands.
Norgine Limited Moorhall Road, Harefield, Middx UB9 6NS, UK.
22115101
MOVICOL®
Plain
13.7 g sachet, powder for oral solution
Effective relief from constipation
DOSAGE:
Constipation:
Adults, Adolescents and Elderly:
1 - 3 sachets per day according to individual response.
Long Term Use: 1 - 2 sachets per day
Faecal Impaction:
8 sachets a day. All should be consumed within a 6 hour period.
Children (below 12 years of age) not recommended.
Dissolve the contents of one sachet in 125ml of water then drink it.
For faecal impaction it may be easier to dissolve 8 sachets in 1 litre of water.
For oral use.
Read the package leaflet before use
NORGINE

Module 5

Scientific discussion during initial procedure

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the RMS considered that the application for Movicol Plain 13.7g sachet, powder for oral solution in the treatment of chronic constipation and faecal impaction, could be approved. A national marketing authorisation was granted on 13th January, 2006.

II EXECUTIVE SUMMARY

II.1 Problem statement

This mutual recognition application, submitted under Article 8.3 of Directive 2001/83/EC (as amended), considers Movicol Plain 13.7g sachet, powder for oral solution (PL 20142/0004, formerly 00322/0085), a line extension of the product Movicol (PL 00322/0070). The originator product is Movicol (PL 00322/0070 - Marketing Authorisation Holder: Norgine Limited, UK). Reference is made to Movicol (PL 00322/0070) and Movicol Paediatric (PL 00322/0082) during the application.

The product was granted a marketing authorisation in the UK on 13th January 2006 (PL 00322/0085). With the UK as the Reference Member State in this Mutual Recognition Procedure (MRP), the Marketing Authorisation Holder, Norgine B.V., is applying for a marketing authorisation for Movicol Plain 13.7g sachet, powder for oral solution in Austria, Belgium, Spain, Finland, Republic of Ireland, Italy, and Sweden (UK/H/0131/05/MR).

User testing has been performed on the PIL, which is in compliance with the new requirements, set out in Article 59(1) of Directive 2001/83/EC, as amended. Results from this have been submitted to the MHRA.

II.2 About the product

Movicol (PL 00322/0070) is currently licensed and actively marketed in over 40 countries worldwide, including nine countries within the European Union in which marketing authorisation was granted via the mutual recognition procedure in July 1996, and subsequent MR renewals granted in June 2001 and April 2007, with the UK as the reference member state.

Movicol Plain is identical in terms of safety, efficacy and quality to Movicol. The difference between Movicol Plain and Movicol is in the excipients. The recommended dosage administered to the patient remains the same.

Movicol Plain was originally granted to Norgine Limited under a different tradename on 13th January 2006 (PL 00322/0085). A subsequent variation granted in June 2006 removed the flavouring, and the product was renamed Movicol Plain. The licence underwent a Change of Ownership in September 2006, to change the marketing authorisation holder to Norgine B.V. (PL 20142/0004).

The main active ingredient of Movicol Plain is Macrogol 3350. This high molecular weight polyethylene glycol has been shown to exert an osmotic effect that influences fluid transfer

through the colon mucosa. Macrogol 3350 maintains an iso-osmotic liquid flow throughout the length of the gastrointestinal tract. The other active ingredients are potassium chloride, sodium chloride and sodium hydrogen carbonate. These electrolytes serve to ensure that there is no net gain or loss of water, sodium ions or potassium ions from the body. All the active substances are established pharmacapoeial products with good safety profiles.

II.3 The development programme

The objective of the development programme was to produce a “flavourless” and “sweetener less” Movicol product, that was essentially identical to the lemon and lime flavoured originator Movicol product in all other respects.

II.4 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

No new preclinical studies were conducted, which is acceptable given that the actives used are well-known substances and in the case of potassium chloride, sodium chloride and sodium hydrogen carbonate are relatively simple compounds.

No new clinical data were submitted, which is acceptable given that the actives used are well-known substances and in the case of potassium chloride, sodium chloride and sodium hydrogen carbonate are relatively simple compounds.

The actives used have been used in other products, including Movicol, which was granted a national licence in January 1996.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product prior to granting its national authorisation.

For manufacturing sites within the community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

Nomenclature

INN:
Macrogol
Sodium Chloride
Sodium Hydrogen Carbonate (Sodium Bicarbonate)
Potassium Chloride

Structure

Macrogol = H-(OCH_2-CH_2)$_n$-OH where *n* represents the average number of oxyethylene groups (N=3350).

The other active substances are all simple compounds:

Sodium Chloride	-	NaCl
Sodium Hydrogen Carbonate	-	$NaHCO_3$
Potassium Chloride	-	KCl

General Properties

Macrogol is an osmotic agent.
Sodium Chloride, Sodium hydrogen carbonate and Potassium chloride act to maintain electrolyte and water balance.

Macrogol is a white to off white powder soluble in water.
Sodium chloride and Potassium chloride are both apparent as an odourless white crystalline powder freely soluble in water.
Sodium hydrogen carbonate is an odourless white crystalline powder.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

All Actives are stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Acceptable justification of the proposed specifications are provided.

Satisfactory certificates of analysis have been provided by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been provided for all manufacturers of actives.

DRUG PRODUCT

Other Ingredients
There are no excipients used for this product.

Manufacture
A description and flow-chart of the manufacturing method has been provided and is satisfactory.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches. The results are satisfactory.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
Product is packaged in laminate sachets. Specifications and certificates of analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with solutions for parenteral and ophthalmic use Directive 2002/72/EC (as amended).

Stability
Finished product stability studies have been conducted in accordance with current guidelines. The shelf-life of 3 years with storage condition ‘Do not store above 25 degree C’ has been set. This is satisfactory.

All results obtained were within specification

Conclusion
It is recommended that Marketing Authorisation is granted for this application.

PRECLINICAL ASSESSMENT

This mutual recognition application is made under Article 8.3 of Directive 2001/83/EC (as amended). All the drug substances in the formulation are well established products and simple compounds. Therefore, new preclinical data is deemed not necessary. No new preclinical data has been supplied with this application and none is required.

CLINICAL ASSESSMENT

1. INTRODUCTION

This is a mutual recognition application for Movicol Plain for the treatment of chronic constipation and faecal impaction. The application is submitted under article 8.3 of the EEC directive 2001/83 (as amended). Movicol Plain is a line extension of the product Movicol (PL 00322/0070) which was granted UK approval in December 1995. Movicol is currently licensed and actively marketed in over 40 countries worldwide, including nine countries within the European Union in which marketing authorisation was granted via the mutual recognition procedure in July 1996, and subsequent MR renewals granted in June 2001 and April 2007, with the UK as the reference member state.

Movicol Plain was originally granted under a different tradename to Norgine Limited on 13th January 2006 (PL 00322/0085). A subsequent variation granted in June 2006 removed the flavouring, and the product was renamed Movicol Plain. The licence underwent a Change of Ownership in September 2006, to change the marketing authorisation holder to Norgine B.V. (PL 20142/0004).

Movicol Plain is identical in terms of safety, efficacy and quality to Movicol. The only difference between Movicol Plain and Movicol is in excipient. The recommended dosage administered to the patient remains the same.

2. BACKGROUND

The main active ingredient of Movicol Plain is Macrogol 3350. This high molecular weight polyethylene glycol has been shown to exert an osmotic effect that influences fluid transfer through the colon mucosa. Macrogol 3350 maintains an iso-osmotic liquid flow throughout the length of the gastrointestinal tract. The other active ingredients are potassium chloride, sodium chloride and sodium hydrogen carbonate. These electrolytes serve to ensure that there is no net gain or loss of water, sodium ions or potassium ions from the body.

3. INDICATIONS

For the treatment of chronic constipation. MOVICOL Plain is also effective in resolving faecal impaction, defined as refractory constipation with faecal loading of the rectum and/or colon.

4. DOSE & DOSE SCHEDULE

Chronic Constipation

A course of treatment for constipation with MOVICOL Plain does not normally exceed two weeks, although this can be repeated if required.
As for all laxatives, prolonged use is not usually recommended. Extended use may be necessary in the care of patients with severe chronic or resistant constipation, secondary to multiple sclerosis or Parkinson's Disease, or induced by regular constipating medication, in particular opioids and antimuscarinics.

Adults, adolescents and the elderly: 1-3 sachets daily in divided doses, according to individual response.

For extended use, the dose can be adjusted down to 1 or 2 sachets daily.

Children (below 12 years old): Not recommended. Alternative MOVICOL products are available for children.

Faecal impaction
A course of treatment for faecal impaction with MOVICOL Plain does not normally exceed 3 days.

Adults, adolescents and the elderly: 8 sachets daily, all of which should be consumed within a 6 hour period.

Children (below 12 years old): Not recommended. Alternative MOVICOL products are available for children.

Patients with impaired cardiovascular function: For the treatment of faecal impaction the dose should be divided so that no more than two sachets are taken in any one hour.

Patients with renal insufficiency: No dosage change is necessary for treatment of either constipation or faecal impaction.

Administration
Each sachet should be dissolved in 125ml water. For use in faecal impaction 8 sachets may be dissolved in 1 litre water.

5. TOXICOLOGY

All the drug substances in the formulation are well established products and simple compounds. Therefore, no formal data is provided under this heading and none are required for this application.

6. CLINICAL PHARMACOLOGY

6.1 Pharmacodynamics

The high molecular weight macrogols are long linear polymers which retain water molecules by means of hydrogen bonds. When administered by the oral route, they lead to an increase in the volume of intestinal fluids. It is the volume of unabsorbed intestinal fluid, which accounts for the laxative properties of the solution.

6.2 Pharmacokinetics

Following oral ingestion, Macrogol 3350 undergoes virtually no absorption from the gastrointestinal tact and passes unchanged through the gut. Any macrogol that may be absorbed is excreted via the urine.

6.3 Bioequivalence

Not applicable.

7. EFFICACY

No new efficacy data are submitted or required.

8. SAFETY

No new safety data are submitted or required.

9. EXPERT REPORT

A satisfactory clinical expert report has been written by an appropriately qualified person and his CV has been provided.

10. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

This is satisfactory and consistent with the SPC for Movicol.

11. PATIENT INFORMATION LEAFLET (PIL)

The PIL is an accurate reflection of the SPC and complies with the appropriate guidelines. It is consistent with the PIL for Movicol.

12. LABELLING

This is satisfactory.

13. MAA

The MAA is satisfactory.

14. DISCUSSION

Osmotic laxatives, including macrogols (Polyethylene glycols), have been available in the European Union, including the UK for much more than 10 years. Their use is well-established with recognised efficacy and acceptable safety.

15. CONCLUSION

A Marketing authorisation can be granted.

Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

Date submitted	Application type	Scope	Outcome
20/07/2007	Type 1A	To register a new certificate of suitability	Approved 24/07/2007
09/08/2007	Type IB	To replace the manufacturing site for Sodium Chloride	Approved 30/10/2007