

Summary Public Assessment Report

Macrovic Junior, Macrovic (macrogol 3350, sodium chloride, sodium hydrogen carbonate, potassium chloride)

SE/H/1855/01-02/E/01

This module reflects the scientific discussion for the approval of Macrovic Junior, Macrovic. The Summary Public Assessment Report was written in November 2016 by the previous RMS UK after initial procedure UK/H/6090/01-02/DC. RMS transfer from UK to SE was completed on 7 November 2018.



Medicines & Healthcare products
Regulatory Agency



Public Assessment Report

Decentralised Procedure

STRIGOL Paediatric 6.86 g powder for oral solution
STRIGOL 13.72 g powder for oral solution

(Macrogol, sodium chloride, sodium bicarbonate and potassium chloride)

Procedure No: UK/H/6090/001-002/DC

UK Licence No: PL 28176/0175-0176

Strides Arcolab International Ltd

LAY SUMMARY

STRIGOL Paediatric 6.86 g powder for oral solution

STRIGOL 13.72 g powder for oral solution

(Macrogol, sodium chloride, sodium bicarbonate and potassium chloride)

This is a summary of the Public Assessment Report (PAR) for STRIGOL Paediatric 6.86 g powder for oral solution (PL 28176/0175; UK/H/6090/001/DC) and STRIGOL 13.72 g powder for oral solution (PL 28176/0176; UK/H/6090/002/DC). It explains how STRIGOL Paediatric 6.86 g powder for oral solution and STRIGOL 13.72 g powder for oral solution were assessed and their authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as STRIGOL oral solution throughout this lay summary for ease of reading.

For practical information about using STRIGOL oral solution, patients should read the package leaflets or contact their doctor or pharmacist.

What is STRIGOL oral solution and what is it used for?

STRIGOL oral solution is a 'generic medicine'. This means that this product is similar to 'reference medicines' already authorised in the European Union (EU) called Movicol Paediatric Plain 6.9 g sachet, powder for oral solution (Norgine Pharmaceuticals Limited) and Movicol 13.8 g sachet, powder for oral solution (Norgine Limited).

STRIGOL Paediatric and STRIGOL powder for oral solution are laxatives.

STRIGOL Paediatric 6.86 g powder for oral solution is used for the treatment of chronic constipation in children aged 2 to 11 years, and for the treatment of very bad constipation (called faecal impaction) in children aged 5 to 11 years. STRIGOL Paediatric also prevents re-impaction after successful disimpaction in children 2 to 11 years of age.

STRIGOL 13.72 g powder for oral solution is used for the treatment of chronic constipation in adults, adolescents and elderly, and for the treatment of very bad constipation (called faecal impaction). It is not recommended for children below 12 years of age.

STRIGOL oral solution helps patients to have a comfortable bowel movement even if they have been constipated for a long time.

How does STRIGOL oral solution work?

STRIGOL oral solution contains the active ingredients macrogol, sodium chloride, sodium bicarbonate and potassium chloride. STRIGOL oral solution works by making the stools (faeces) softer and easier to pass, therefore, providing relief from constipation.

How is STRIGOL oral solution used?

STRIGOL oral solution is taken orally. This medicine can be given at any time with or without food or drink.

The patient should always take this medicine exactly as the patient's doctor or pharmacist has told them. The patient must check with their doctor or pharmacist if they are not sure.

The recommended dose is:

STRIGOL Paediatric 6.86 g powder for oral solution:**Chronic constipation:**

The dose of STRIGOL Paediatric depends on the age of the child and the response to treatment. As a starting dose, children aged 2 to 6 years should be given 1 sachet each day. Children aged 7 to 11 should be given 2 sachets each day.

The patient's doctor may increase the number of sachets taken until the child has a soft bowel movement. If the dose does need increasing, this should be done every other day. Normally, no more than four sachets are required to be taken in one day. It is not necessary to take all of the drink at one time, if the child prefers it, half the drink can be taken in the morning and half in the evening.

The duration of treatment with this medicine needs to be for a prolonged period of time at least 6-12 months.

Faecal impaction:

Before a patient (child) takes this medicine for faecal impaction, the patient's doctor must check to confirm that the child has this condition. The treatment course lasts up to 7 days.

A course of treatment with STRIGOL Paediatric is as follows:

	Number of STRIGOL Paediatric sachets						
Age (years)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
5-11	4	6	8	10	12	12	12

The daily number of sachets should be taken in divided doses, all taken within 12 hours (e.g. 8am – 8pm). Treatment can be stopped when the medicine has worked. This is shown by the child passing large volumes of stool and/or watery diarrhoea.

STRIGOL 13.72 g powder for oral solution**Chronic constipation:**

The recommended dose for adults, adolescents and the elderly is one sachet, 1–3 times a day according to the severity of constipation.

Treatment with STRIGOL oral solution usually lasts for about 2 weeks. If patients need to take this medicine for longer, they should get advice from their doctor. If constipation is caused by an illness such as Parkinson's disease or multiple sclerosis (MS), or if patients take medicines that cause constipation, they may be advised by a doctor to take STRIGOL oral solution for longer than 2 weeks. Usually for long term treatment the dose can be lowered to either 1 or 2 sachets a day.

Faecal impaction:

Before a patient takes STRIGOL oral solution for faecal impaction, a doctor must check to confirm that a patient has this condition. The recommended dose for adults, adolescents and the elderly is 8 sachets a day. All the 8 sachets should be taken within 6 hours, and for up to 3 days if required. Patients with heart conditions should not take more than 2 sachets per hour.

How to mix STRIGOL Paediatric 6.86 g powder for oral solution:

- Open the sachet and pour the contents into a glass
- Add ¼ glass (about 62.5ml) of water
- Stir until all the powder has dissolved and the solution is clear or slightly hazy, before drinking.

How to mix STRIGOL 13.72 g powder for oral solution:

- Open the sachet and pour the contents into a glass
- Add ½ glass (about 125ml) of water
- Stir until all the powder has dissolved and the solution is clear or slightly hazy, before drinking

For faecal impaction it may be easier to dissolve 8 sachets of STRIGOL in a litre of water.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

STRIGOL Paediatric 6.86 g powder for oral solution can only be obtained with a prescription.

STRIGOL 13.72 g powder for oral solution can be obtained without a prescription.

What benefits of STRIGOL oral solution have been shown in studies?

No additional studies were needed as STRIGOL oral solution is a generic medicine that is given as an oral solution and contains the same active substances as the reference medicines, Movicol Paediatric Plain 6.9 g sachet, powder for oral solution and Movicol 13.8 g sachet, powder for oral solution.

What are the possible side effects of STRIGOL oral solution?

Because STRIGOL oral solution is a generic medicine, its benefits and possible side effects are taken as being the same as the reference medicines.

For the full list of all side effects reported with STRIGOL oral solution, see section 4 of the package leaflets available on the MHRA website.

Why was STRIGOL oral solution approved?

It was concluded that, in accordance with EU requirements, STRIGOL oral solution has been shown to have comparable quality and is comparable to Movicol Paediatric Plain 6.9 g sachet, powder for oral solution and Movicol 13.8 g sachet, powder for oral solution. Therefore, the MHRA decided that, as for Movicol Paediatric Plain 6.9 g sachet, powder for oral solution and Movicol 13.8 g sachet, powder for oral solution, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of STRIGOL oral solution?

A risk management plan (RMP) has been developed to ensure that STRIGOL oral solution is used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflets for STRIGOL oral solution including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about STRIGOL oral solution

Belgium, Germany, Sweden, The Netherlands and the UK agreed to grant Marketing Authorisations for STRIGOL oral solution on 01 September 2016. Marketing Authorisations were granted in the UK on 22 September 2016.

The full PAR for STRIGOL oral solution follows this summary.

For more information about treatment with STRIGOL oral solution, read the package leaflets, or contact your doctor or pharmacist.

This summary was last updated in November 2016.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Member States considered that the applications for STRIGOL Paediatric 6.86 g powder for oral solution (PL 28176/0175; UK/H/6090/001/DC) and STRIGOL 13.72 g powder for oral solution (PL 28176/0176; UK/H/6090/002/DC), are approvable.

STRIGOL Paediatric 6.86 g powder for oral solution is a prescription only medicine (POM) used to treat the following indications:

- For the treatment of chronic constipation in children 2 to 11 years of age.
- For the treatment of faecal impaction in children from the age of five years, defined as refractory constipation with faecal loading of the rectum and/or colon.
- For the prevention of re-impaction after successful disimpaction in children 2 to 11 years of age.

STRIGOL 13.72 g powder for oral solution is a pharmacy (P) medicine used for the treatment of chronic constipation in adults and children above 12 years. STRIGOL 13.72 g powder for oral solution is also effective in resolving faecal impaction, defined as refractory constipation with faecal loading of the rectum and/or colon in adults and children above 12 years.

These applications were submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS), and Belgium, Germany, Sweden and The Netherlands as Concerned Member States (CMS). The applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic applications. The applicant has cross-referred to Movicol Paediatric Plain 6.9 g sachet, powder for oral solution which was originally granted to Norgine Limited (PL 00322/0083) on 24 September 2003 and to Movicol 13.8 g sachet, powder for oral solution which was originally granted to Norgine Limited (PL 00322/0070) on 18 December 1995. Movicol Paediatric Plain 6.9 g sachet, powder for oral solution underwent a change of ownership procedure to the current Marketing Authorisation Holder, Norgine Pharmaceuticals Limited (PL 20011/0005), on 26 March 2008.

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 defecation. 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.

No new non-clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

No new clinical data have been submitted and none are required for applications of this type. A bioequivalence study was not necessary to support these applications as both test and reference products are aqueous oral solutions at the time of administration and given that the products act locally in the gastrointestinal tract.

A summary of the pharmacovigilance system and a detailed risk management plan have been provided with these applications and these are satisfactory.

The RMS has been assured that acceptable standards of Good Manufacturing Practice are in place for this product type at all sites responsible for the manufacture, assembly and batch release of these products.

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.

All Member States agreed to grant Marketing Authorisations for the above products at the end of the procedure (01 September 2016). After a subsequent national phase, the UK granted Marketing Authorisations (PL 28176/0175-0176) for these products on 22 September 2016.

II QUALITY ASPECTS

II.1 Introduction

One sachet of STRIGOL Paediatric 6.86 g powder for oral solution contains the following active ingredients

- Macrogol 3350, 6.563 g
- Sodium chloride, 175.4 mg
- Sodium bicarbonate, 89.3 mg
- Potassium chloride, 23.30 mg

One sachet of STRIGOL 13.72 g powder for oral solution contains the following active ingredients:

- Macrogol 3350, 13.125 g
- Sodium chloride, 350.7 mg
- Sodium bicarbonate, 178.5 mg
- Potassium chloride, 46.6 mg

Other ingredients consist of the following pharmaceutical excipients acesulfame potassium and lemon flavour. The excipient acesulfame potassium complies with its respective European Pharmacopoeia monograph. The flavouring agent, lemon flavour, is controlled by a suitable in-house specification. In addition, confirmation has been provided that the lemon flavour complies with Directive 88/388/EEC. Satisfactory Certificates of Analysis have been provided for both excipients.

None of the excipients contain materials of animal or human origin.

No genetically modified organisms (GMO) have been used in the preparation of these products.

The finished product is packed into a sachet comprised of a four-layer laminate film consisting of aluminium, low density polyethylene (LDPE) and paper. The product is available in pack sizes of 6, 8, 10, 20, 30, 40, 50, 60 or 100 sachets. Not all pack sizes may be marketed.

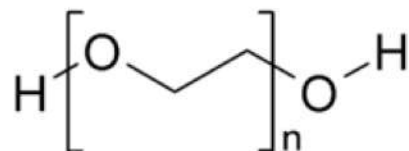
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components.

II.2. Drug Substances

INN: Macrogol 3350

Chemical name: N-2(2-diethylaminoethyl)-1-benzothiophene-2-carboxamide

Structural Formula:



Molecular formula: $\text{H}-(\text{OCH}_2\text{-CH}_2)_n\text{-OH}$

Molecular mass: 3350 g/mol

Appearance: A white or almost white solid with a waxy or paraffin-like appearance.

Solubility: It is very soluble in water and in methylene chloride, very slightly soluble in alcohol, practically insoluble in fatty oils and in mineral oils.

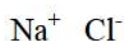
Macrogol 3350 is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, macrogol 3350, are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

INN: Sodium chloride

Chemical name: Sodium chloride

Structural Formula:



Molecular formula: NaCl

Molecular mass: 58.44 g/mol

Appearance: A white or almost white crystalline powder, colourless crystals or white or almost white pearls.

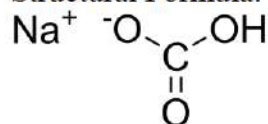
Solubility: It is freely soluble in water and practically insoluble in anhydrous ethanol.

The active substance, sodium chloride, is neither covered by a Certificate of Suitability nor an Active Substance Master File (ASMF). It is a well-established simple inorganic substance that is sufficiently well-defined by the European Pharmacopoeia. Only a very brief description of its manufacture has been submitted. This is acceptable.

INN: Sodium bicarbonate

Chemical name: sodium bicarbonate

Structural Formula:

Molecular formula: NaHCO₃

Molecular mass: 84.01 g/mol

Appearance: A white or almost white crystalline powder.

Solubility: It is soluble in water and practically insoluble in ethanol (96%).

The active substance, sodium bicarbonate, is neither covered by a Certificate of Suitability nor an Active Substance Master File (ASMF). It is a well-established simple inorganic substance that is sufficiently well-defined by the European Pharmacopoeia. Only a very brief description of its manufacture has been submitted. This is acceptable.

INN: Potassium chloride

Chemical Name: Potassium chloride

Structural Formula:



Molecular formula: KCl

Molecular mass: 74.55 g/mol

Appearance: A white or almost white crystalline powder or colourless crystals.

Solubility: It is freely soluble in water and practically insoluble in anhydrous ethanol.

Potassium chloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, potassium chloride, are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3. Medicinal Product

Pharmaceutical Development

The objective of the development programme was to formulate a safe, efficacious, powder for oral solution that is comparable in performance to the originator products Movicol Paediatric Plain 6.9 g sachet, powder for oral solution (Norgine Pharmaceuticals Limited) and Movicol 13.8 g sachet, powder for oral solution (Norgine Limited).

A satisfactory account of the pharmaceutical development has been provided.

Manufacture of the products

Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing processes. The manufacturing processes have been validated at commercial-scale batch size and shown satisfactory results.

Finished Product Specifications

The finished product specifications proposed are acceptable. The test methods have been described and have been adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Stability of the Products

Finished product stability studies were performed in accordance with current guidelines on batches of finished product in the packaging proposed for marketing. The data from these studies support a shelf-life of 4 years for the unopened sachet with no special storage conditions. Once the solution is reconstituted, it should be covered and kept in a refrigerator (2°C to 8°C), and should be used within 24 hours. These proposals are satisfactory.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

There are no objections to the approval of these applications from a pharmaceutical viewpoint.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of macrogol 3350, sodium chloride, sodium bicarbonate and potassium chloride are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant's non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology

Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.3 Pharmacokinetics

Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.4 Toxicology

Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)

Since these products are intended for generic substitution, their use will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

No new non-clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

There are no objections to the approval of these applications from a non-clinical viewpoint.

IV CLINICAL ASPECTS

IV.1 Introduction

As per the guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**), “bioequivalence studies are generally not required if the test product is to be administered as an aqueous oral solution containing the same active substances as the currently approved products.” In addition, the excipients do not affect the gastrointestinal transit, the absorption, solubility or *in vivo* stability of the active substances.

No new efficacy or safety studies have been performed and none are required for this type of application. A comprehensive review of the published literature has been provided by the applicant, citing the well-established clinical pharmacology, efficacy and safety of macrogol 3350, sodium chloride, sodium bicarbonate and potassium chloride.

IV.2 Pharmacokinetics

In line with the guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**), the test products are to be administered as an aqueous oral solution containing the same active substances as the currently approved products. No results from a bioequivalence study have been submitted with these applications and none are required.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted and none were required for applications of this type.

IV.4 Clinical efficacy

No new efficacy data were submitted and none were required for applications of this type.

IV.5 Clinical safety

No new safety data were submitted and none were required for these applications.

IV.6 Risk Management Plan (RMP)

The marketing authorisation holder (MAH) has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to STRIGOL Paediatric 6.86 g powder for oral and STRIGOL 13.72 g powder for oral solution.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, is listed below:

Safety concern	Routine risk minimization measures	Additional risk minimization measures
Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia	<i>For Compound Macrogol 6.86 g Paediatric powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u> Listed in <i>Section 4.4 Special warnings and precautions for use</i> Rare symptoms indicating shifts of fluid/electrolytes, e.g. oedema, shortness of breath, increasing fatigue, dehydration, and cardiac failure have been reported in adults when using preparations containing Macrogol. If this occurs Macrogol 3350 should be stopped immediately, electrolytes measured, and any abnormality should be treated appropriately. Listed in <i>Section 4.8 Undesirable effects Metabolism and nutrition disorders:</i> - Not known: Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia. <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section 4 Possible side effects</i> Like all medicines, Macrogol can have side effects. Other side effects reported include: - High or low levels of potassium in the blood	None proposed

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	<i>For Compound Macrogol 13.72 g powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u> Listed in <i>Section 4.4 Special warnings and precautions for use</i> Mild adverse drug reactions are possible, as indicated in „Section 4.8 Undesirable effects“. If patients develop any symptoms indicating shifts of fluids/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure), Macrogol 3350 should be stopped immediately and electrolytes measured, and any abnormality should be treated appropriately. Listed in <i>Section 4.8 Undesirable effects</i> The frequency of the adverse effects is not known as it cannot be estimated from the available data. • <i>Metabolism and nutrition disorders:</i> Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia. <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section What you need to know before you take Compound Macrogol</i> Warning and precautions: If you develop any symptoms indicating shifts of fluids/electrolytes (e.g. oedema, shortness of breath, increasing fatigue,	

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	dehydration, cardiac failure), consult your doctor. Listed in <i>Section 4 Possible side effects</i> Like all medicines, Macrogol can have side effects. Other side effects reported include: • High or low levels of potassium in the blood Other routine risk minimization measures Legal Status: Prescription only product.	
•Hypersensitivity (including anaphylactic reactions)	<i>For Compound Macrogol 6.86 g Paediatric powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u> Listed in <i>Section 4.3 Contraindications</i> Hypersensitivity to the active substances. Tabulated in <i>Section 4.8 Undesirable effects</i> Immune system disorders: Rare: Anaphylaxis. Not known: Angioedema, dyspnoea, rash, erythema, urticaria and pruritus. <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section 2 What you need to know before you give Compound Macrogol Paediatric to your child</i> Do not give Macrogol if your doctor has told you that your child is:	None proposed

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	Allergic to Macrogol 3350, sodium chloride, sodium hydrogen carbonate, potassium chloride, or any of the other ingredients in this medicine Listed in <i>Section 4 Possible side effects</i> Other side effects include: Allergic reactions which may cause a skin rash, itching, reddening of the skin or a nettle rash, swollen hands, feet or ankles, headaches, and high and low levels of potassium in the blood. <i>For Compound Macrogol 13.72 g powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u> Listed in <i>Section 4.3 Contraindications</i> Hypersensitivity to the active ingredients or to any of the excipients. Tabulated in <i>Section 4.8 Undesirable effects</i> <u>Immune system disorders:</u> <u>Allergic reactions, including anaphylaxis, angioedema, dyspnoea, rash, erythema, urticaria, and pruritus.</u> <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section 2 What you need to know before you take Compound Macrogol</i>	

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	Do not take Macrolog if your doctor has told you that you are allergic (hypersensitive) to Macrolog 3350, sodium chloride, sodium hydrogen carbonate, potassium chloride or acesulfame potassium Listed in <i>Section 4. Possible side effects</i> Other side effects include: Allergic reactions which may cause a skin rash, itching, reddening of the skin or a nettle rash, swollen hands, feet or ankles, headaches, and high and low levels of potassium in the blood. Other routine risk minimization measures Legal Status: Prescription only product.	
Decreased efficacy with some concomitantly administered medicinal products	<i>For Compound Macrolog 6.86 g Paediatric powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u> Listed in <i>Section 4.4 Special warnings and precautions for use</i> The absorption of other medicinal products could be transiently reduced due to an increase in gastro-intestinal transit rate induced by Macrolog 3350. Listed in <i>Section 4.5 Interaction with other medicinal products and other forms of interaction</i> Medicinal products in solid dose form taken within one hour of administration of large volumes of Macrolog	None proposed

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	preparations (as used when treating faecal impaction) may be flushed from the gastrointestinal tract and not absorbed. Macrogol raises the solubility of medicinal products that are soluble in alcohol and relatively insoluble in water. There is a possibility that the absorption of other medicinal products could be transiently reduced during use with Macrogol 3350. There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products, e.g. anti-epileptics. <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section 2 What you need to know before you give Compound Macrogol Paediatric to your child</i> Taking other medicines Some medicines, e.g. anti-epileptics, may not work as effectively during use with Macrogol. Tell your doctor about any other medicines your child is taking. When taking large volumes of Macrogol (e.g. for faecal impaction), your child should not take other medicines within one hour of taking Macrogol. <i>For Compound Macrogol 13.72 g powder for oral solution in sachet:</i> <u>Risk minimization activities described in the relevant section of the SPC:</u>	

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	Listed in <i>Section 4.4 Special warnings and precautions for use</i> The absorption of other medicinal products could be transiently reduced due to an increase in gastro-intestinal transit rate induced by Macrogol 3350 Listed in <i>Section 4.5 Interaction with other medicinal products and other forms of interaction</i> Macrogol raises the solubility of medicinal products that are soluble in alcohol and relatively insoluble in water. There is a possibility that the absorption of other medicinal products could be transiently reduced during use with Macrogol 3350. There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products, e.g. anti-epileptics. <u>Risk minimization activities described in the relevant section of the PL:</u> Listed in <i>Section 2. What you need to know before you take Compound Macrogol</i> Taking other medicines Some medicines, e.g. anti-epileptics, may not work as effectively during use with Macrogol. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicines,	

Safety concern	Routine risk minimization measures	Additional risk minimization measures
	including medicines obtained without a prescription Other routine risk minimization measures Legal Status: Prescription only product.	

No new risks have been identified for these generic products, which are not recognised for the reference products. Overall, the proposed RMP has adequately captured the important identified and potential risks associated with the drug substances.

IV.7 Discussion on the clinical aspects

No new clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

A bioequivalence study was not necessary to support these applications as both test and reference products are aqueous oral solutions at the time of administration and given that the products act locally in the gastrointestinal tract.

The grant of Marketing Authorisations is recommended for these applications.

V User consultation

The package leaflet has been evaluated via a user consultation study, in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.

The results show that the package leaflet meets the criteria for readability, as set out in the *guideline on the readability of the label and package leaflet of medicinal products for human use*.

VI Overall conclusion, benefit/risk assessment and recommendation

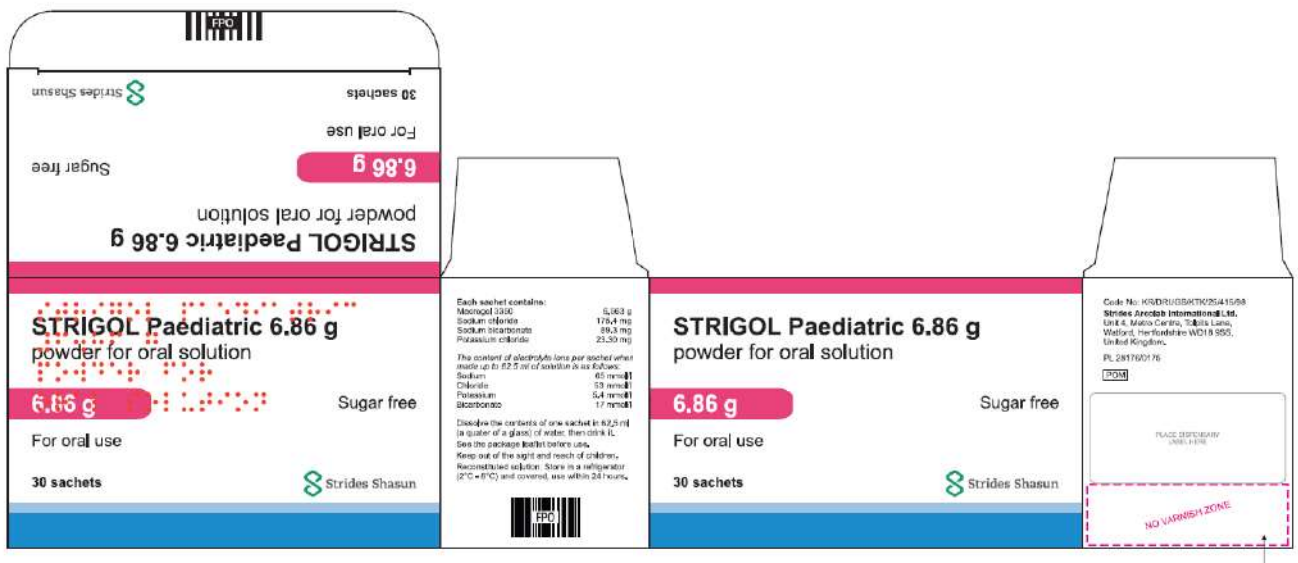
The quality of the products is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with macrogol 3350, sodium chloride, sodium bicarbonate and potassium chloride is considered to have demonstrated the therapeutic value of the compounds. The benefit-risk is, therefore, considered to be positive.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for STRIGOL Paediatric 6.86 g powder for oral solution and STRIGOL 13.72 g powder for oral solution is presented below:





STRIGOL 13.72 g

powder for oral solution

13.72 g

For oral use

Sugar free

 Strides Shasun

Each sachet contains:

Macrogol 3350

Sodium chloride

Sodium bicarbonate

Potassium chloride

13.125 g

350.7 mg

178.5 mg

46.6 mg

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

Bicarbonate

17 mmol/l

For oral use.

Dissolve the contents of one sachet in 125 ml of water, then drink it.

See the package leaflet before use.

Keep out of the sight and reach of children.

Reconstituted solution: Store in a refrigerator (2°C - 8°C) and covered, use within 24 hours.

Code No: KRD/DRUGS/KTK/25/415/98

Strides Arcolab International Ltd.

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PL 28176/0176



Batch & Expiry Date

Over Printed Area

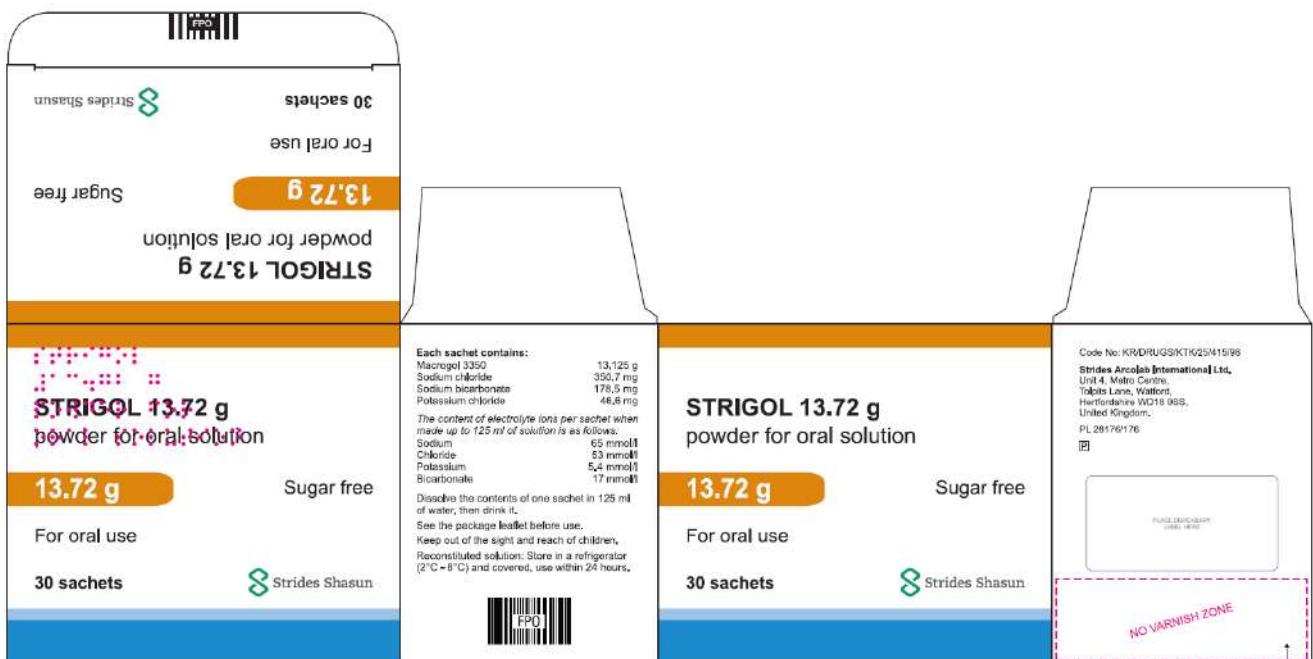


Table of content of the PAR update for MRP and DCP

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval/non approval	Assessment report attached Y/N (version)