# GLYCEROL SUPPOSITORIES B.P. (GLYCEROL)

## PL 00156/0120-1

## UKPAR

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# GLYCEROL SUPPOSITORIES B.P.
# (GLYCEROL)

# PL 00156/0120-1

## LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Martindale Pharmaceuticals Limited Marketing Authorisations (licences) for the medicinal product Glycerol Suppositories B.P. (PL 00156/0120-1) on 13th July 2009. This is a medicine available on the General Sales List (GSL), and can be purchased at pharmacies, supermarkets and other retail outlets without the supervision of a pharmacist.

Glycerol belongs to a group of medicines called laxatives. A laxative is a medicine which is used for the treatment of constipation. Glycerol Suppositories act as a stimulant laxative for short term treatment of constipation and for emptying of the bowels. Glycerol Suppositories B.P. are for rectal administration and are presented in 3 strengths – 1g, 2g, and 4g, for use in infants, children, and adults respectively.

These applications are duplicates of a previously granted application for Glycerol Suppositories B.P. (PL 00156/0053), held by Martindale Pharmaceuticals Limited, and originally authorised to Cromford Group Limited on 29th March 1985. The test and reference products are identical.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of using Glycerol Suppositories B.P. outweigh the risk; hence Marketing Authorisations have been granted.

# GLYCEROL SUPPOSITORIES B.P.
# (GLYCEROL)

## PL 00156/0120-1

## SCIENTIFIC DISCUSSION

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# INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Martindale Pharmaceuticals Limited Marketing Authorisations for the medicinal product Glycerol Suppositories B.P. (PL 00156/0120-1) on 13th July 2009. The product is available through general supply (GSL).

These applications were submitted as simple abridged 'informed consent' applications according to article 10c of Directive 2001/83/EC (as amended), cross-referring to Glycerol Suppositories B.P. (PL 00156/0053) authorised to Martindale Pharmaceuticals Limited on 6th June1997. This reference product, Glycerol Suppositories B.P. (PL 00156/0053), was originally authorised to Cromford Group Limited on 29th March 1985.

Glycerol Suppositories B.P. are indicated as a stimulant laxative for the treatment of constipation.

Glycerol is an osmotic dehydrating agent with hygroscopic and lubricating properties. Glycerol acts by promoting peristalsis and evacuation of the lower bowel by virtue of a mild irritant effect.

Glycerol is readily absorbed from the intestine and undergoes extensive metabolism principally in the liver, it may be used in the synthesis of lipid, metabolised to glucose or glycogen, or oxidised to carbon dioxide and water. It may also be excreted in the urine unchanged.

No new data were submitted nor was it necessary for these simple applications, 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 PAR was generated for it.

# PHARMACEUTICAL ASSESSMENT

| | |
|---|---|
| **LICENCE NUMBER:** | PL 00156/0120-1 |
| **PROPRIETARY NAME:** | Glycerol Suppositories B.P. |
| **ACTIVE INGREDIENT/S:** | Glycerol |
| **COMPANY NAME:** | Martindale Pharmaceuticals Limited |
| **E.C. ARTICLE:** | Article 10c of Directive 2001/83/EC (as amended) |
| **LEGAL STATUS:** | GSL |

## 1. INTRODUCTION

These are simple abridged applications, submitted under Article 10c of Directive 2001/83/EC (as amended) for Glycerol Suppositories B.P. The proposed MA holder is 'Martindale Pharmaceuticals Limited'.

The reference product is Glycerol Suppositories B.P. (PL 00156/0053), held by Martindale Pharmaceuticals Limited. The test and reference products are identical.

## 2. MARKETING AUTHORISATION APPLICATION FORM

### 2.1 Name(s)

The approved name of the product is Glycerol Suppositories B.P. The product name is acceptable.

### 2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Glycerol Suppositories B.P. are for rectal administration, and come in 3 strengths – 1g, 2g, and 4g. The 1g suppository contains 700mg glycerol and is for use in infants. The 2g suppository contains 1400mg glycerol and is for use in children. The 4g suppository contains 2800mg glycerol and is for use in adults.

The suppositories are licensed for marketing in heat sealed polyethylene lined polyvinyl chloride cavities each containing 1x 1g, 2g or 4g suppository, in strips of 6. The strips and a patient leaflet are packed into cardboard outer cartons. Pack sizes available are 12 x 1g (for infants), 12 x 2g (for children) and 12 x 4g (for adults)**.**

The approved shelf-life (3 years) and storage conditions ('Store below 25$^{o}$C in a dry place') are consistent with the details registered for the cross-reference product.

### 2.3 Legal status

The product is a GSL licensed medicine, available by supply through pharmacies, supermarkets and other retail outlets without the need for supervision by a pharmacist.

### 2.4 Marketing authorisation holder / Contact Persons / Company

The proposed Marketing Authorisation holder is 'Martindale Pharmaceuticals Ltd., Bampton Road, Romford, RM3 8UG, United Kingdom'.

The QP responsible for pharmacovigilance was stated and their CV included.

### 2.5 Manufacturers

The proposed manufacturing site is consistent with that registered for the cross-reference product and evidence of GMP compliance has been provided.

### 2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

### 2.7 Manufacturing process

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

### 2.8 Finished product / shelf-life specification

The proposed finished product specification is in line with the details registered for the cross-reference product.

### 2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

### 2.10 TSE Compliance

The only excipient used that contains material of animal or human origin is gelatin. Satisfactory documentation has been provided by the gelatin supplier stating that the gelatin they provide complies with the criteria described in the current version of the monograph ‘Products with risk of transmitting agents of animal spongiform encephalopathies’.

## 3. EXPERT REPORTS

Satisfactory expert reports and curriculum vitae of experts were provided.

## 4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product name. The appearance of the product (amber coloured suppository) is consistent with that of the cross-reference product.

## 5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The approved SmPCs are consistent with the details registered for the cross-reference product.

## 6. PATIENT INFORMATION LEAFLET (PIL) / CARTON

PIL

The patient information leaflets have been prepared in the user tested format and in line with the details registered for the cross-reference product. The approved PILs are satisfactory.

Labelling

Colour mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has included the name of the products in Braille on the outer packaging.

## 7. CONCLUSIONS

The grounds for these applications are considered adequate. Marketing Authorisations were, therefore, granted.

# PRECLINICAL ASSESSMENT

These applications were submitted as simple abridged applications according to article 10c of Directive 2001/83/EC (as amended).

No new preclinical data have been supplied with these applications and none are required for applications of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.

# CLINICAL ASSESSMENT

These applications were submitted as simple abridged applications according to article 10c of Directive 2001/83/EC (as amended).

As these are duplicate applications for PL 00156/0053, no new clinical data have been supplied with the applications, and none are required for applications of this type. A clinical expert report has been written by a suitably qualified person and is satisfactory.

# OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

## QUALITY

The data for these applications are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

## PRECLINICAL

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

## EFFICACY

Medicinal products containing the active ingredient; glycerol, in the stated dosage form have been available in the UK for much more than ten years. Their use is well established with recognised efficacy and acceptable safety.

This application is identical to the previously granted application for Glycerol Suppositories B.P. (PL 00156/0053, Martindale Pharmaceuticals Limited).

No new or unexpected safety concerns arise from this application.

## PRODUCT LITERATURE

The approved SmPCs, PILs and labelling are satisfactory and consistent with that for the cross-reference product.

Package leaflets have been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflets are well-structured and organised, easy to understand and written in a comprehensive manner. The testing shows that patients/users are able to act upon the information that the leaflets contain.

Colour mock-ups of the labelling have been provided and are satisfactory. The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging.

## 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 cross-reference product. Extensive clinical experience with glycerol is considered to have demonstrated the therapeutic value of this product. The risk: benefit is, therefore, considered to be positive.

# GLYCEROL SUPPOSITORIES B.P.
# (GLYCEROL)

# PL 00156/0120-1

## STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation applications on 5th August 2008

2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 8th August 2008

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 21st August 2008 and 4th June 2009

4 The applicant responded to the MHRA's request, providing further information for the quality sections on 27th January 2009 and 11th June 2009 respectively

5 The applications were determined on 13th July 2009

# GLYCEROL SUPPOSITORIES B.P.
# (GLYCEROL)

# PL 00156/0120-1

## STEPS TAKEN AFTER AUTHORISATION

Not applicable

# SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Glycerol Suppositories B.P. (PL 00156/0120 & 0121) is as follows. The only difference is the PL number:

## 1 NAME OF THE MEDICINAL PRODUCT

Glycerol Suppositories BP

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g suppository contains 700mg Glycerol

Each 2 g suppository contains 1400mg Glycerol

Each 4 g suppository contains 2800mg Glycerol

For full list of excipients, see 6.1.

## 3 PHARMACEUTICAL FORM

Amber coloured suppository, of nominal weight 1g (Infants), 2g (Children) and 4g (Adults) intended for rectal administration.

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

A stimulant laxative used for the treatment of constipation.

### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

For rectal use

Infants
One 1g suppository, to aid insertion the suppository tip should be moistened with water before use.

Children
One 2g suppository, to aid insertion the suppository tip should be moistened with water before use.

Adults and the elderly
One 4g suppository, to aid insertion the suppository tip should be moistened with water before use. No reduction in adult dosage is necessary for elderly patients.

### 4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance(s) or to any of the excipients.
- The product is contraindicated if there is intestinal obstruction or blockage.

### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The product is intended for occasional use only. Prolonged use of the product is not recommended as it can cause diarrhoea and related effects such as hypokalaemia. However, prolonged use may be justifiable in some cases. Use of this product may interfere with glucose control in diabetic patients who may additionally develop hyperglycaemia and glycosuria following metabolism of glycerol. Glycerol must be used with caution in patients with hypervolaemia, cardiac failure, or renal disease. If symptoms persist consult a doctor.

## 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed

## 4.6 PREGNANCY AND LACTATION

No evidence of harmful affects available. However, best avoided during the first trimester of pregnancy. May be used during breast feeding.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None stated

## 4.8 UNDESIRABLE EFFECTS

Use of the product may occasionally cause abdominal cramps. The adverse effects of glycerol are primary due to its dehydrating action. Glycerol increases plasma osmolality resulting in the withdrawal of water from the extravascular spaces. The consequent expansion of extracellular fluid, especially if sudden, can lead to circulatory overload, pulmonary oedema, and heart failure. Glycerol can cause irritation when given rectally. Severe dehydration can occur and Glycerol should be used cautiously in dehydrated patients. Nonketotic hyperosmolar hyperglycaemic coma is rare, but fatalities have been reported.

## 4.9 OVERDOSE

Overdosage via rectal route is unlikely. However, if ingested treat symptomatically.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

ATC code A06AX01

Glycerol is an osmotic dehydrating agent with hygroscopic and lubricating properties.

Glycerol acts by promoting peristalsis and evacuation of the lower bowel by virtue of a mild irritant effect.

## 5.2 PHARMACOKINETIC PROPERTIES

Glycerol is readily absorbed from the intestine and undergoes extensive metabolism principally in the liver, it may be used in the synthesis of lipid, metabolised to glucose or glycogen, or oxidised to carbon dioxide and water. It may also be excreted in the urine unchanged.

## 5.3 PRECLINICAL SAFETY DATA

There are no preclinical data of relevance to the prescriber, which are additional to those already included in other sections of the SmPC

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

Gelatin
Purified Water

## 6.2 INCOMPATIBILITIES

Not applicable

## 6.3 SHELF LIFE

3 years

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C in a dry place

## 6.5 NATURE AND CONTENTS OF CONTAINER

Heat sealed polyethylene lined Poly Vinyl Chloride cavities each containing 1x 1g, 2g or 4g suppository in strips of 6. The strips and a patient leaflet are packed into cardboard cartons. Pack sizes available 12 x 1g (for infants), 12 x 2g (for children) and 12 x 4g (for adults)**.**

## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Wash hands before opening individual packaging. The suppository is shaped for rectal insertion, ensure the tip of the suppository is inserted first. The tip should be moistened with a little cold water to aid insertion.

## 7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Ltd.
Bampton Road,
Romford,
RM3 8UG
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00156/0120
PL 00156/0121

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/07/2009

## 10 DATE OF REVISION OF THE TEXT

13/07/2009

# PRODUCT INFORMATION LEAFLET

(only difference is the PL number)

PACKAGE LEAFLET: INFORMATION FOR THE USER C*****

## Glycerol Suppositories BP 1g, 2g and 4g

Glycerol

**Read all of this leaflet carefully before you start using Glycerol Suppositories.**
- 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 gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

## In this leaflet:



## 1. What Glycerol Suppositories are and what they are used for

Glycerol belongs to a group of medicines called laxatives. A laxative is a medicine which is used for the treatment of constipation.

Glycerol Suppositories act as a stimulant laxative for short term treatment of constipation and for emptying the bowels.

## 2. Before you use Glycerol Suppositories

**Do not use Glycerol Suppositories if:**
- you suffer from a blocked bowel or an abdominal problem for which you have not obtained a medical opinion.
- you are allergic (hypersensitive) to glycerol or any of the other ingredients of Glycerol Suppositories, listed in section 6 of this leaflet.

**Take special care with Glycerol Suppositories. Tell your doctor if:**
- you are diabetic
- you know you have an increase in the volume of blood in your circulation
- you have kidney disease
- you have suffered from heart failure
- you are suffering from dehydration

If any of the above applies to you or your child, please contact your doctor or pharmacist.

It is not recommended that you use Glycerol Suppositories for long periods of time. If you need laxatives every day you should see your doctor.

**Pregnancy and breast-feeding**
Glycerol Suppositories should not be used in the first three months of pregnancy. Glycerol Suppositories can be used during breast-feeding. Ask your doctor or pharmacist for advice before taking any medication.

## 3. How to use Glycerol Suppositories

Always use Glycerol Suppositories exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

1. Wash hands before opening individual packaging. If the suppository is too soft, it may be chilled in the refrigerator or under cold running water before unwrapping
2. To remove a suppository, tear one from the strip along the perforations then peel it from the plastic wrapping by grasping the two halves of the wrapping at the tip of the suppository and pulling them gently apart. The tip should be moistened with a little cold water to aid insertion


3. Lie on your left side (if you are right handed) and draw your knees up towards your chest, with the right leg drawn up more than the left.
4. Using your index finger or middle finger, whichever you find easier, gently push the suppository into the rectum. The suppository is shaped for rectal insertion, ensure the tip of the suppository is inserted first.

*Continued overleaf*

5. The suppository should be inserted as far as possible, pushing the end of the suppository sideways to ensure contact with the wall of the bowel.
6. Lower your legs to a comfortable position to help you to hold the suppository in place.
7. Retain the suppository in place for at least 15 to 20 minutes if possible. If you feel the suppository must come out immediately, it has not been inserted high enough.
8. You may feel an immediate urge to go to the toilet. Try to ignore this as the suppository will not work for at least 15 minutes.

**Glycerol Suppositories should not be swallowed**

**Adults including the elderly**
One 4g suppository

**Children**
One 2g suppository

**Infant**
One 1g suppository

As with all laxatives, the suppositories should not be used on a continuous daily basis for long periods. If you need laxatives every day you should see your doctor.

**If Glycerol Suppositories are swallowed**
If you suspect someone may have swallowed Glycerol Suppositories contact your doctor or pharmacist taking this leaflet with you.

## 4. Possible side effects

Like all medicines, Glycerol Suppositories can cause side effects, although not everybody gets them.These include:

- abdominal cramps
- irritation in or around the rectum (back passage)
- an increase in the amount of fluid in your blood
- water on the lungs
- heart failure
- diabetic coma

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

## 5. How to store Glycerol Suppositories

Keep out of the reach and sight of children.

Do not use Glycerol Suppositories after the expiry date printed on the carton. The expiry date refers to the last day of that month.

Store in a dry place below 25°C.

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

## 6.Further Information

**What Glycerol Suppositories contain**
The active substance is Glycerol BP.
The other ingredients are gelatin and purified water.

**What Glycerol Suppositories look like and contents of the pack**
Gycerol Suppositories are amber topedo shaped suppositories. Each pack contains either 12 x 1g suppositories, 12 x 2g suppositories or 12 x 4g suppositories.

**Marketing Authorisation Holder and Manufacturer**
Martindale Pharmaceuticals,
Bampton Road,
Harold Hill,
Romford, RM3 8UG,
United Kingdom

If you would like any more information, or would like the leaflet in a different format, please contact Medical Information at the above address

**Product Licence number:** PL 00156/0120
**Date of approval:** PL 00156/0121

MARTINDALE Pharmaceuticals

Bampton Road, Harold Hill
Romford, RM3 8UG
United Kingdom

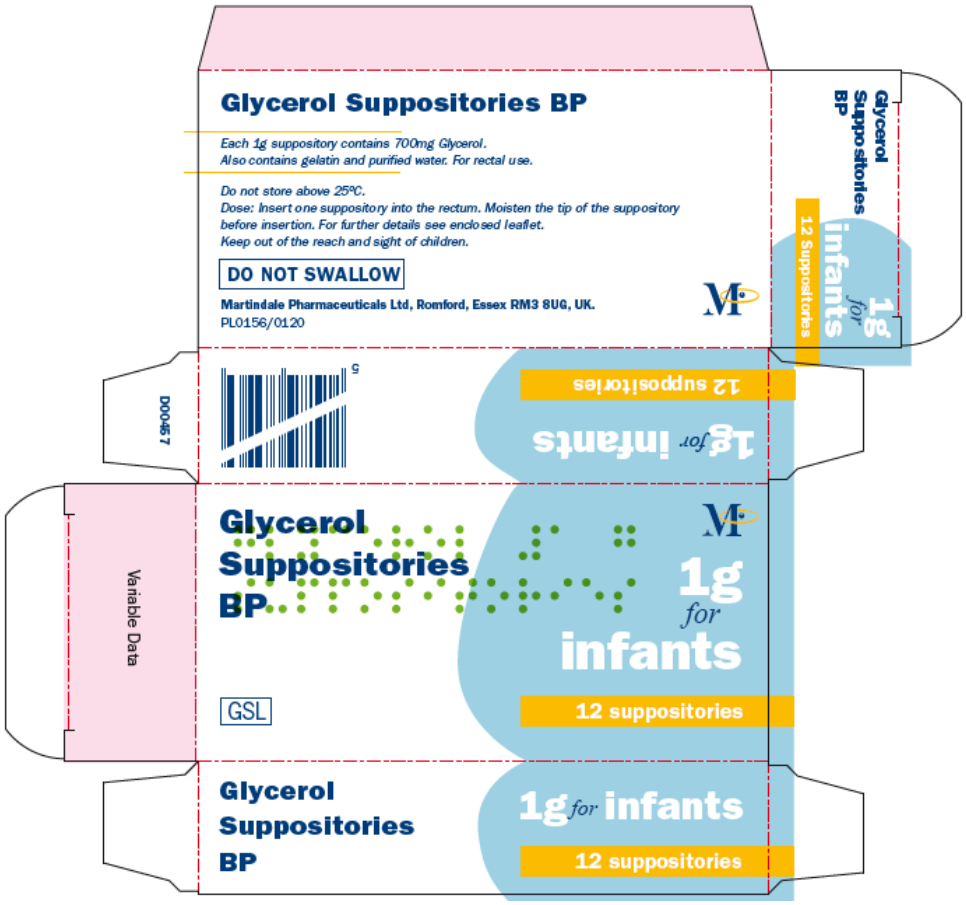
C*****

# LABELLING

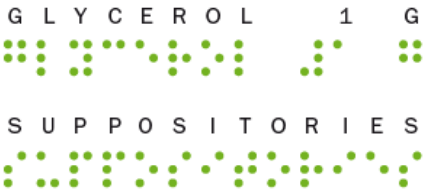
(only difference is the PL number)

## Gycerol 1g Suppositories (infants)

Carton




Braille

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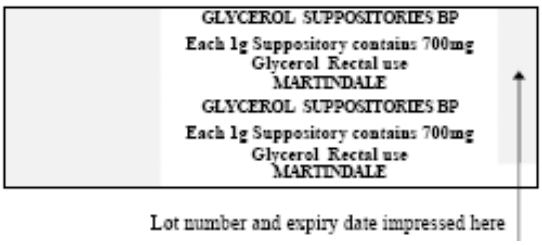
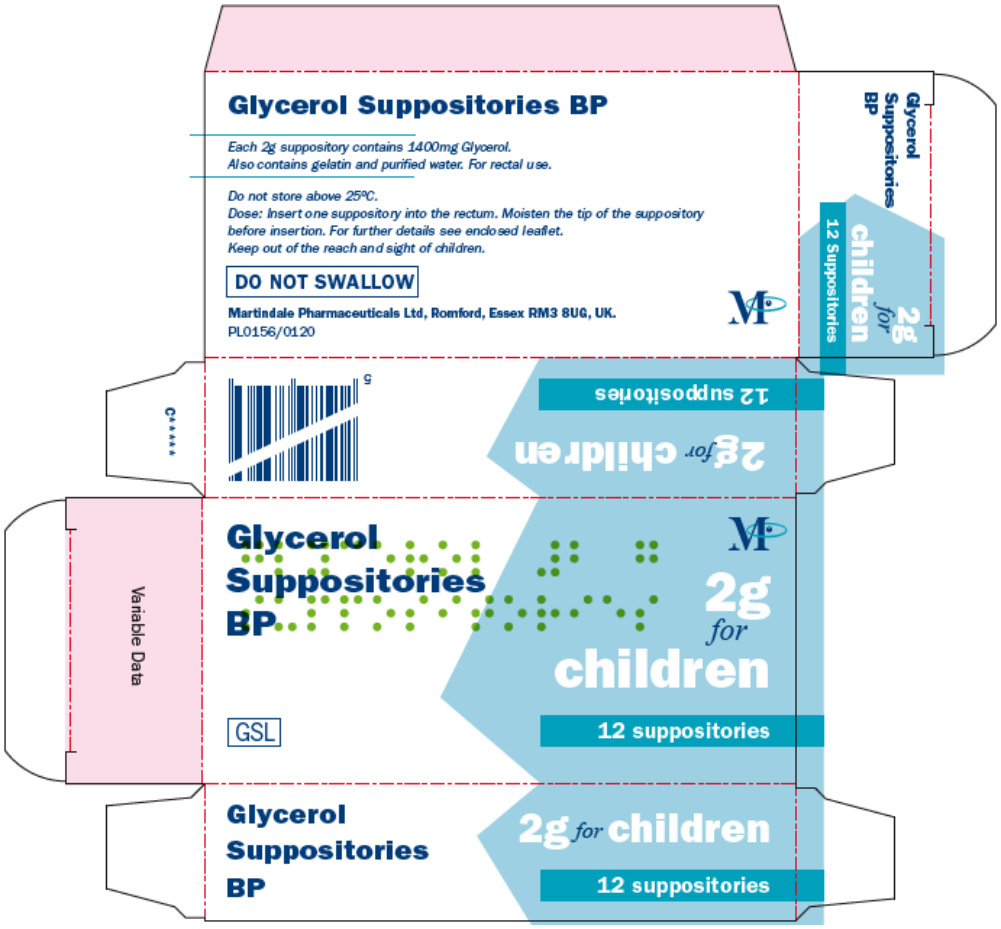


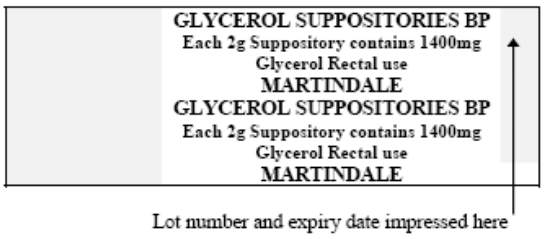
## Gycerol 2g Suppositories (children)

Carton



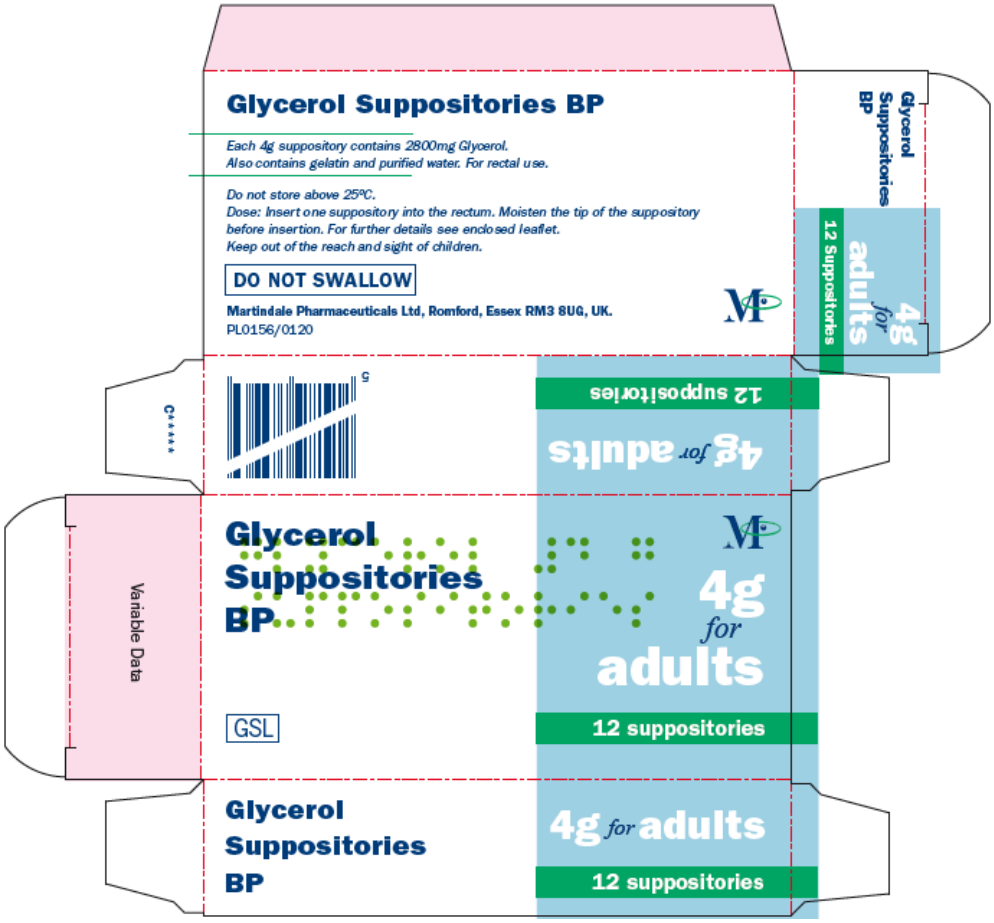

Braille


Blister strip



## Gycerol 4g Suppositories (adults)

Carton

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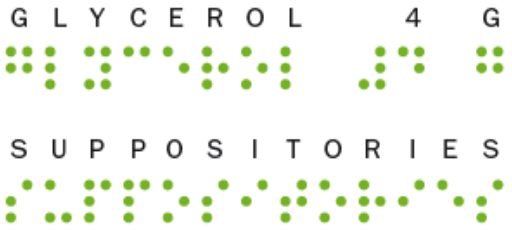


Blister strip