0.1% W/W POLYSORBATE 80 IN WATER FOR INJECTION
PL 10673/0026

UKPAR

TABLE OF CONTENTS

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LAY SUMMARY

The MHRA granted Octapharm Limited a Marketing Authorisation (licence) for the product 0.1% w/w Polysorbate 80 in Water for Injection on 21st September 2007. This product, to be available by prescription only (POM), contains polysorbate 80 and water for injections, and is intended as a diluent for the reconstitution of freeze-dried human plasma preparation Wilate. There are no specific active ingredients in this product.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of using 0.1% w/w Polysorbate 80 in Water for Injection outweighed the risks, hence a Marketing Authorisation has been granted.

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SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the products 0.1% w/w Polysorbate 80 in Water for Injection on 21st September 2007. The product is a prescription-only product.

This was submitted as an abridged application according to Article 10a of Directive 2001/83/EC, a bibliographic application.

The product contains no active ingredient and is to be used as a solvent for reconstitution of the freeze-dried human plasma preparation Wilate (Factor VIII/von Willebrand factor concentrate).

WILATE is supplied as a powder for reconstitution and intravenous injection. Originally, WILATE was reconstituted with water for injection. However, the high von Willebrand factor content of WILATE impaired the solubility of the lyophilisate and the appearance of the solution was not optimal.

To provide a convenient reconstitution of the product, 0.1 % (weight to weight) Polysorbate 80 in water for injection is used as solvent.

Unfavourable creation of foam is prevented by the reduced surface tension because of Polysorbate 80 presence. The concentration of Polysorbate 80 is balanced between physiological tolerability and effectiveness. 0.1% (w/w) Polysorbate 80 is as low as possible to display sufficient solubility. Reconstitution time is significantly reduced due to the improved way of moistening the lyophilised product even in the presence of high VWF concentrations. The reconstituted product shows excellent short-time stability in solution.

Polysorbate 80 is a well-known substance with a very short half-live of about 15 minutes only. Haemodynamic effects have been observed in dogs after doses of about 5 to 10mg per kg body weight, but such high amounts are unlikely to be given.

After reconstitution with the supplied solvent, WILATE may be administered intravenously.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Not applicable

DRUG PRODUCT

Other ingredients

Other ingredients consist of water for injections and polysorbate 80. Both are controlled to their respective Ph Eur monograph. Satisfactory certificates of analysis have been provided for each ingredient.

None of the excipients used contain material of animal or human origin.

Pharmaceutical development

A suitable pharmaceutical development section has been provided.

Manufacture

A description and flow-chart of the manufacturing method has been provided. A satisfactory batch formula has been provided for the manufacture of the maximum batch size.

In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of each strength. The results appear satisfactory.

Finished product specification

The proposed product complies with the general requirements of the Ph Eur monograph. Batch data have been provided and show compliance with the release specification.

Container Closure System

The finished product is stored in a glass vial, with a bromobutyl rubber stopper and an aluminium closure, in pack sizes of 2.5, 5 and 10ml. Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. The packaging materials have been shown to comply with current guidelines concerning contact with products for parenteral use. The manufacturer tests batches of packaging material on receipt.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 5 years has been set, which is satisfactory. Storage conditions “Protect from light”, “Store in refrigerator (2-8°C)” and “Avoid freezing” have been included. The product can be kept at room temperature (up to 25°C) for up to a month after taking out of refrigeration.

Conclusion

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

PRECLINICAL ASSESSMENT

As this is a bibliographic application, no new preclinical data have been provided and none are required. A suitable preclinical expert report has been provided, which was written by an appropriately qualified person.

CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY

No pharmacological properties have been submitted for the SPC. Instead the reader is referred to the SPC of the product to be reconstituted. This is satisfactory for a product of this nature.

BIOEQUIVALENCE

No bioequivalence data have been provided and none are required for an application of this type.

CLINICAL EFFICACY

No clinical efficacy data have been provided for this application and none are required.

CLINICAL SAFETY

No clinical safety data have been provided for this application and none are required.

EXPERT REPORTS

Since the solvent (Water for Injections with 0.1% Polysorbate 80) is exclusively produced as diluent for the freeze-dried Factor VIII/von Willebrand factor concentrate Wilate, non-clinical and clinical assessment is available only in conjunction with the non-clinical and clinical assessment of the concentrate Wilate. For information, the non-clinical and clinical overviews of Wilate have been included in the dossier.

PRODUCT LITERATURE

The Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and packaging are satisfactory for this type of product and in compliance with current regulations.

OVERALL CONCLUSION

The grant of a marketing authorisation is recommended.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of 0.1% w/w Polysorbate 80 in Water for Injection are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

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

EFFICACY

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk benefit is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1 The MHRA received the marketing authorisation application on 27th October 2005

2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 10th November 2005

3 Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 21st February 2006, 7th August 2006 and 24th July 2007. No further information was requested relating to the clinical dossier.

4 The applicant responded to the MHRA's requests, providing further information on 21st July 2006, 2nd November 2006 and 20th September 2007 for the quality sections.

5 The applications were determined on 21st September 2007

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

Summary of Product Characteristics (SPC)

1 NAME OF THE MEDICINAL PRODUCT

0.1% w/w polysorbate 80 in Water for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Water for Injections with 0.1% Polysorbate 80; 2.5 ml, 5 ml, 10 ml
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solvent for parental use

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Used for reconstitution of the freeze-dried human plasma preparation Wilate.

4.2 Posology and method of administration

For intravenous use.

As for the product to be reconstituted.

4.3 Contraindications

As for the product to be reconstituted.

4.4 Special warnings and precautions for use

The product should not be used if the solution is not clear or if the container is damaged.

As for the product to be reconstituted.

4.5 Interaction with other medicinal products and other forms of interaction

As for the product to be reconstituted.

4.6 Pregnancy and lactation

As for the product to be reconstituted.

4.7 Effects on ability to drive and use machines

As for the product to be reconstituted.

4.8 Undesirable effects

As for the product to be reconstituted.

4.9 Overdose

As for the product to be reconstituted.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

As for the product to be reconstituted.

5.2 Pharmacokinetic properties

As for the product to be reconstituted.

5.3 Preclinical safety data

As for the product to be reconstituted.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections
Polysorbate 80

6.2 Incompatibilities

As for the product to be reconstituted.

6.3 Shelf life

60 months

The product can be stored at room temperature (max. +25°C) for 1 month. In this case the shelf-life expires 1 month after the product has been taken out of the refrigerator for the first time. The new shelf-life has to be noted on the outer carton by the patient.

6.4 Special precautions for storage

Store in refrigerator (2°C to 8°C) protected from light. Do not freeze

6.5 Nature and contents of container

0.1% w/w polysorbate 80 in Water for Injection is supplied in colourless Type I glass vials 20 ml, closed with bromobutyl rubber stoppers and covered with flip off cap.

The carton contains:
1 vial with 0.1% w/w polysorbate 80 in Water for Injection
1 equipment pack with the administration devices (1 disposable syringe, 1 transfer set [1 double-ended needle and 1 filter needle], 1 infusion set)
2 alcohol swabs
and the package leaflet

0.1% w/w polysorbate 80 in Water for Injection is supplied in three pack sizes with the following filling volumes: 2.5 ml, 5 ml and 10 ml.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Octapharma Ltd.
6, Elm Court, Copse Drive
Coventry, CV5 9RG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 10673/0026

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/09/2007

10 DATE OF REVISION OF THE TEXT

21/09/2007

PACKAGE LEAFLET: INFORMATION FOR THE USER

0.1% w/w polysorbate 80 in Water for Injection – 2.5 ml, 5ml, 10 ml
Solvent for parental use

Read all of this leaflet carefully before you start using this 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 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 0.1% w/w polysorbate 80 in Water for Injection IS AND WHAT IT IS USED FOR

Water for Injections with 0.1% Polysorbate 80
Used for reconstitution of the freeze-dried human plasma preparation Wilate.

2. BEFORE YOU USE 0.1% w/w polysorbate 80 in Water for Injection

Do not use 0.1% w/w polysorbate 80 in Water for Injection

The product should not be used if the solution is not clear or if the container is damaged.

As for the product to be reconstituted.

Take special care with 0.1% w/w polysorbate 80 in Water for Injection

As for the product to be reconstituted.

Taking other medicines

As for the product to be reconstituted.

Using 0.1% w/w polysorbate 80 in Water for Injection with food and drink

As for the product to be reconstituted.

Pregnancy and breast-feeding

As for the product to be reconstituted.

Driving and using machines

As for the product to be reconstituted.

Important information about some of the ingredients of 0.1% w/w polysorbate 80 in Water for Injection

As for the product to be reconstituted.

3. HOW TO USE 0.1% w/w polysorbate 80 in Water for Injection

For intravenous use.

As for the product to be reconstituted.

If you use more 0.1% w/w polysorbate 80 in Water for Injection than you should

As for the product to be reconstituted.

If you forget to use 0.1% w/w polysorbate 80 in Water for Injection

As for the product to be reconstituted.

If you stop using 0.1% w/w polysorbate 80 in Water for Injection

As for the product to be reconstituted.

4. POSSIBLE SIDE EFFECTS

As for the product to be reconstituted.

5. HOW TO STORE 0.1% w/w polysorbate 80 in Water for Injection

Store in refrigerator (2°C to 8°C) protected from light. Do not freeze

Shelf-life: 60 months

The product can be stored at room temperature (max. +25°C) for 1 month. In this case the shelf-life expires 1 month after the product has been taken out of the refrigerator for the first time. The new shelf-life has to be noted on the outer carton by the patient.

6. FURTHER INFORMATION

What 0.1% w/w polysorbate 80 in Water for Injection contains

Water for Injections with 0.1% Polysorbate 80; 2.5 ml, 5 ml, 10 ml

What 0.1% w/w polysorbate 80 in Water for Injection looks like and contents of the pack

0.1% w/w polysorbate 80 in Water for Injection is supplied in colourless Type I glass vials 20 ml, closed with bromobutyl rubber stoppers and covered with flip off cap.

The carton contains:
1 vial with 0.1% w/w polysorbate 80 in Water for Injection
1 equipment pack with the administration devices (1 disposable syringe, 1 transfer set [1 double-ended needle and 1 filter needle], 1 infusion set)
2 alcohol swabs
and the package leaflet

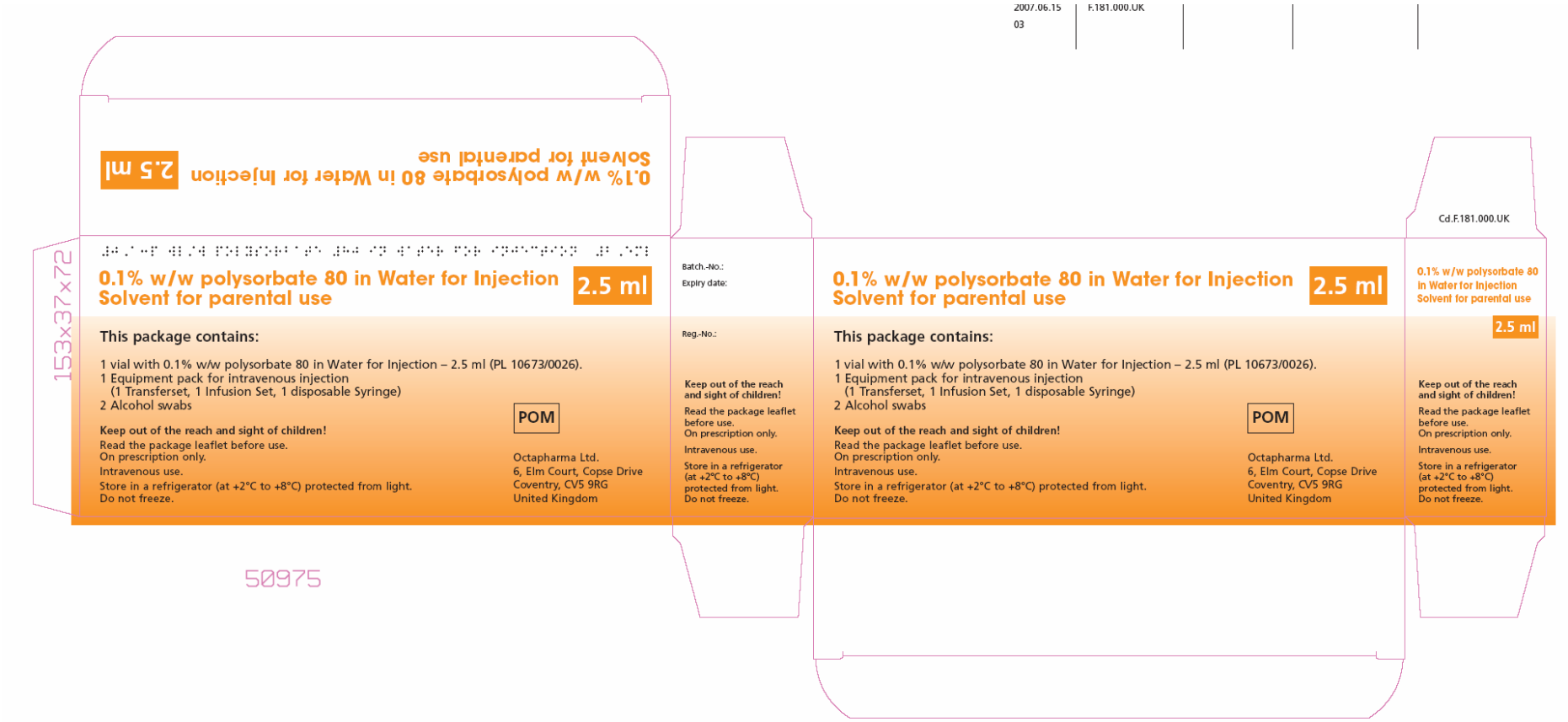
0.1% w/w polysorbate 80 in Water for Injection is supplied in three pack sizes with the following filling volumes: 2.5 ml, 5 ml and 10 ml.

Marketing Authorisation Holder and Manufacturer

Octapharma Ltd.
6, Elm Court, Copse Drive
Coventry, CV5 9RG
United Kingdom

This leaflet was last approved in 06/2007.

PL 10673/0026


2007.06.15
03
F.181.000.UK
0.1% w/w polysorbate 80 in Water for Injection
Solvent for parental use
2.5 ml
Cd.F.181.000.UK
153x37x72
0.1% w/w polysorbate 80 in Water for Injection
Solvent for parental use
2.5 ml
This package contains:
1 vial with 0.1% w/w polysorbate 80 in Water for Injection – 2.5 ml (PL 10673/0026).
1 Equipment pack for intravenous injection
(1 Transferset, 1 Infusion Set, 1 disposable Syringe)
2 Alcohol swabs
Keep out of the reach and sight of children!
Read the package leaflet before use.
On prescription only.
Intravenous use.
Store in a refrigerator (at +2°C to +8°C) protected from light.
Do not freeze.
POM
Octapharma Ltd.
6, Elm Court, Copse Drive
Coventry, CV5 9RG
United Kingdom
Batch.-No.:
Expiry date:
Reg.-No.:
Keep out of the reach and sight of children!
Read the package leaflet before use.
On prescription only.
Intravenous use.
Store in a refrigerator (at +2°C to +8°C) protected from light.
Do not freeze.
50975
0.1% w/w polysorbate 80 in Water for Injection
Solvent for parental use
2.5 ml
This package contains:
1 vial with 0.1% w/w polysorbate 80 in Water for Injection – 2.5 ml (PL 10673/0026).
1 Equipment pack for intravenous injection
(1 Transferset, 1 Infusion Set, 1 disposable Syringe)
2 Alcohol swabs
Keep out of the reach and sight of children!
Read the package leaflet before use.
On prescription only.
Intravenous use.
Store in a refrigerator (at +2°C to +8°C) protected from light.
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POM
Octapharma Ltd.
6, Elm Court, Copse Drive
Coventry, CV5 9RG
United Kingdom
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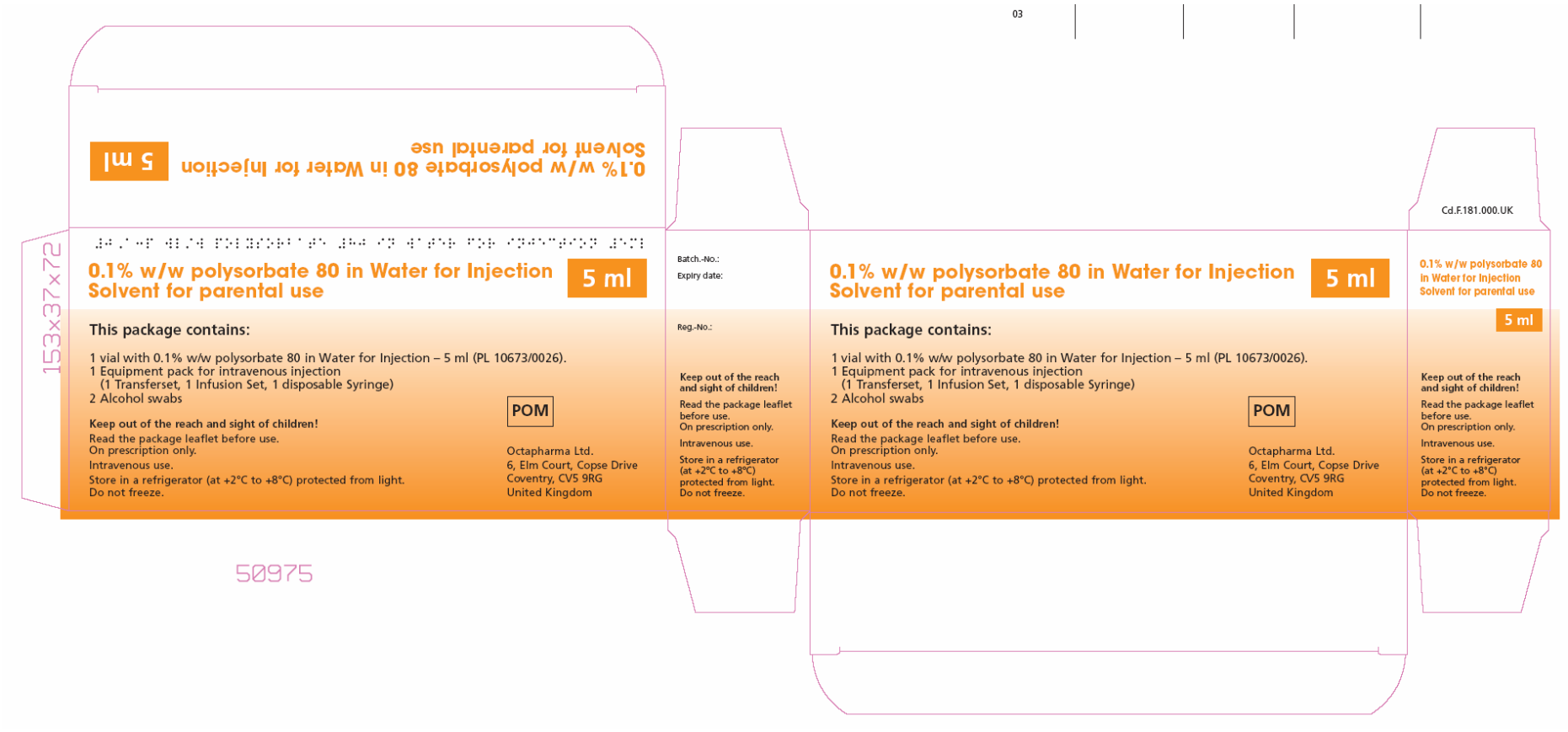
03
0.1% w/w polysorbate 80 in Water for Injection
Solvent for parental use
5 ml
153x37x72
0.1% w/w polysorbate 80 in Water for Injection
Solvent for parental use
5 ml
This package contains:
1 vial with 0.1% w/w polysorbate 80 in Water for Injection – 5 ml (PL 10673/0026).
1 Equipment pack for intravenous injection
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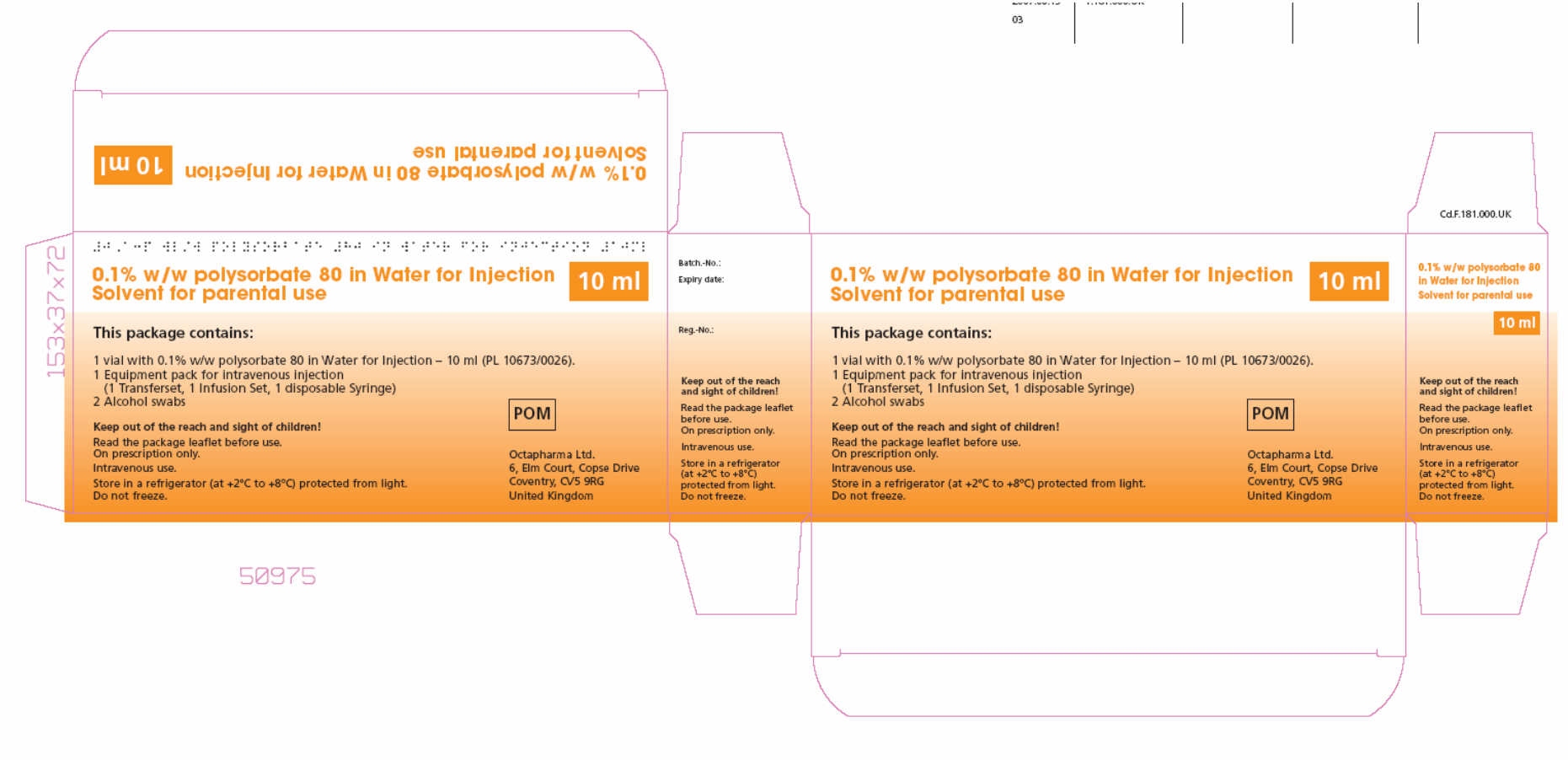
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