Public Assessment Report

Mutual Recognition Procedure

FOSFOMYCIN 40 mg/ml powder for solution for infusion

(Fosfomycin)

Product Licence Number: PL 15011/0014

Procedure Number: UK/H/6206/001/MR

InfectoPharm Arzneimittel und Consilium GmbH
LAY SUMMARY

Fosfomycin 40 mg/ml powder for solution for infusion

(Fosfomycin)

This is a summary of the Public Assessment Report (PAR) for Fosfomycin 40 mg/ml powder for solution for infusion. It explains how Fosfomycin 40 mg/ml powder for solution for infusion was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Fosfomycin 40 mg/ml powder for solution for infusion.

This product will be referred to as Fosfomycin solution for infusion in this lay summary for ease of reading.

For practical information about using Fosfomycin solution for infusion, patients should read the package leaflet or contact their doctor or pharmacist.

What is Fosfomycin solution for infusion and what is it used for?

This application is for a generic medicine. This means that this medicine is the same as, and considered interchangeable with, reference medicine already authorised in the European Union (EU) called Infectofos, powder for solution for infusion (InfectoPharm Arzneimittel und Consilium GmbH).

Fosfomycin solution for infusion is used in adults and children to treat the following infections caused by bacteria.

- Infections of the lung
- Infections of the bones
- Infections of the kidney and bladder
- Infections of the brain (meningitis)

It is important that the patient receives effective treatment for this condition.

This medicine is used when other antibiotics cannot be used or have not worked. This medicine can be given alone or in combination with other antibiotics.

How does Fosfomycin solution for infusion work?

Fosfomycin solution for infusion belongs to a group of medicines called antibiotics. This medicine works by killing certain types of germs (bacteria) that cause serious infectious diseases.

How is Fosfomycin solution for infusion used?

The pharmaceutical form of this medicine is powder for solution for infusion and the route of administration is into a vein (a drip).

The infusion will normally take 15 to 60 minutes, depending on the dose. Usually this medicine is given 2, 3 or 4 times a day.

Dosage

The dose the patient will be given, and the frequency of the dose will depend on the type and severity of infection and the kidney function.
The dose in children depends on the child’s weight and the child’s age.

The general dosage guidelines for patients with normal kidney function are as follows:

<table>
<thead>
<tr>
<th>Age/weight</th>
<th>Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature neonates</td>
<td>100 mg/kg body weight in 2 divided doses</td>
</tr>
<tr>
<td>Neonates</td>
<td>200 mg/kg body weight in 3 divided doses</td>
</tr>
<tr>
<td>Infants 1-12 months (up to 10 kg body weight)</td>
<td>200-300 mg/kg body weight in 3 divided doses</td>
</tr>
<tr>
<td>Infants and children aged 1-12 years (10-40 kg body weight)</td>
<td>200-400 mg/kg body weight in 3-4 divided doses</td>
</tr>
<tr>
<td>Adolescents aged 12-18 years and adults (&gt; 40 kg body weight)</td>
<td>12-24 g in 2-4 divided doses</td>
</tr>
</tbody>
</table>

Individual doses must not exceed 8 g.

The patient’s doctor may need to reduce the dose for patients with kidney problems or require dialysis.

**Duration of treatment**

The patient’s doctor will decide how long the treatment should last depending on how fast the patient’s condition improves. When treating bacterial infections, it is important to complete the full course of treatment. Even after the fever has passed and the symptoms have abated, treatment should be continued for a few days more.

Certain infections, such as infections of the bones, may require an even longer treatment period after the symptoms have subsided.

For further information on how Fosfomycin solution for infusion is used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription. This medicine is given by a doctor or a nurse.

**What benefits of Fosfomycin solution for infusion have been shown in studies?**

Fosfomycin solution for infusion is a generic medicine that fulfils criteria meaning that no additional studies are required. Fosfomycin solution for infusion has been considered a generic medicine of the reference medicine based on a comparison of their physical and chemical characteristics. Further information is provided in the main body of the public assessment report (PAR).

**What are the possible side effects of Fosfomycin solution for infusion?**

Because Fosfomycin solution for infusion is a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

For the full list of all side effects reported with this medicine, see Section 4 of the package leaflet or the Summary of Product Characteristics (SmPC) available on the MHRA website.
Why was Fosfomycin solution for infusion approved?
It was concluded that, in accordance with EU requirements, Fosfomycin solution for infusion has been shown to be comparable to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, 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 Fosfomycin solution for infusion?
A Risk Management Plan (RMP) has been developed to ensure that Fosfomycin solution for infusion is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the package leaflet, 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 and reviewed continuously.

Other information about Fosfomycin solution for infusion
A National Marketing Authorisation was granted to DLRC Ltd (PL 33200/0003) in the UK on 19 June 2013. Following a change of ownership, this licence was transferred to the current Marketing Authorisation holder, InfectoPharm Arzneimittel und Consilium GmbH (PL 15011/0014), on 16 January 2014.

The name of the product was changed from Fomicyt 40 mg/ml powder for solution for infusion to Fosfomycin 40 mg/ml powder for solution for infusion on 12 June 2015.

A first-wave Mutual recognition procedure involving the Concerned Member State (CMS) Austria (UK/H/6206/001/MR) was concluded on 11 December 2018.

The full PAR for Fosfomycin solution for infusion follows this summary.

This summary was last updated in May 2019.
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I  INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Fosfomycin 40 mg/ml powder for solution for infusion (PL 15011/0014) could be approved.

The product is indicated for the treatment of the following infections in adults and children including neonates:
- Osteomyelitis
- Complicated urinary tract infections
- Nosocomial lower respiratory tract infections
- Bacterial meningitis
- Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above

Fosfomycin should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of the infections listed above, or when these alternative antibacterial agents have failed to demonstrate efficacy.

For information regarding the combination with other antibiotics see section 4.4 and 4.5 of the SmPC.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

A national licence was granted to DLRC Ltd (PL 33200/0003) in the UK on 19 June 2013. Following a change of ownership, this licence was transferred to the current Marketing Authorisation holder, InfectoPharm Arzneimittel und Consilium GmbH (PL 15011/0014), on 16 January 2014.

A first-wave Mutual recognition procedure (UK/H/6206/001/MR) was initiated on 20 October 2018. The Reference Member State (RMS) for this procedure was the UK and the Concerned Member State (CMS) was Austria.

The RMS and CMS considered that the application could be approved at the end of procedure (Day 60) on 11 December 2018.

Fosfomycin is exerts a bactericidal effect on proliferating pathogens by preventing the enzymatic synthesis of the bacterial cell wall. Fosfomycin inhibits the first stage of intracellular bacterial cell wall synthesis by blocking peptidoglycan synthesis. Fosfomycin is actively transported into the bacterial cell via two different transport systems (the sn-glycerol-3-phosphate and hexose-6 transport systems).

This application was submitted under Article 10(1) of Directive 2001/83/EC, as amended, as a generic medicine. The reference medicinal product is Infectofos, powder for solution for infusion. The reference product is manufactured in four strengths: 2g, 3g, 5g and 8g. The 2g, 3g and 5g strengths were first licensed on 08 May 1980 and the 8g strength was first licensed on 28 December 2010.

No new non-clinical studies were conducted, which is acceptable given that the application is based on being a generic medicinal product of a reference product that has been licensed for over 10 years.
A biowaiver was submitted with this application, which was accepted. No bioequivalence study was required and no new clinical studies were provided with this application.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

The applicant has not conducted any clinical studies with the medicinal product. In support of this application, the applicant submitted a large body of data from the literature including more than 60 clinical studies as well as in pharmacokinetic and pharmacodynamic data compiled by the company’s clinical expert. During the first round of assessment, several points were raised, particularly concerning the indications and posology of Fosfomycin.

The application was discussed at the Commission on Human Medicines (CHM) meeting in June 2011. The Committee provisionally concluded that further information on efficacy and safety should be requested before the product could be approved. The applicant provided responses to the points raised. Based on the assessment of these responses, the applicant was requested to provide written representation in support of the posology in adults and children as well as in patients with renal failure. Additional data were generated using a physiology-based pharmacokinetics model (PBPK) and revised dose proposals were submitted in September 2012. The data generally supported the previously submitted data derived from PK modelling and the dose proposals fell within the range of the posology recommended in other EU member states, where Fosfomycin has been licensed for decades.

This application was also referred to the Chemistry, Pharmacy and Standards Expert Advisory Group (CPSEAG) on 14th June 2011 and 11th September 2012, respectively. All outstanding quality issues have been satisfactorily resolved.

The name of the product was changed from Fomicyt 40 mg/ml powder for solution for infusion to Fosfomycin 40 mg/ml powder for solution for infusion on 12 June 2015.
II QUALITY ASPECTS

II.1 Introduction

This product consists of white to cream-coloured powder.

In addition to fosfomycin, this product also contains the excipient succinic acid.

The finished product is packaged in a clear type-II glass bottles with a rubber stopper (bromobutyl rubber) and pull-off cap containing 2 g (in 100 ml bottle), 4 g (in 100 ml bottle) or 8 g (in 250 ml bottle) of fosfomycin, respectively, in packs of 10 bottles each.

Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE

rINN: Fosfomycin sodium

Chemical Name: Disodium (2R, 3S)-(3-methyloxiran-2-yl) phosphonate

Molecular Formula: \( \text{C}_3\text{H}_5\text{Na}_2\text{O}_4\text{P} \)

Molecular Structure:

![Molecular Structure](image)

Molecular Weight: 182.02 g/mol

Appearance: A white or almost white, very hygroscopic powder.

Solubility: Fosfomycin sodium is very soluble in water, sparingly soluble in methanol and practically insoluble in ethanol and methylene chloride.

Fosfomycin sodium is the subject of a European Pharmacopoeia monograph.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current European regulations concerning materials in contact with food.
Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCT
Pharmaceutical development
A satisfactory account of the pharmaceutical development has been provided.

The excipient succinic acid complies with its respective national monograph. Satisfactory Certificate of Analysis has been provided for this excipient.

No excipients of animal or human origin are used in the final product.

This product does not contain or consist of genetically modified organisms (GMO).

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

A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specification
The finished product specification is satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 4 years, with no special storage conditions.

Chemical and physical in-use stability of the reconstituted solution that has been produced under aseptic conditions has been demonstrated for 24 hours at 25 °C if protected from light.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of fosfomycin sodium is well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for this application.
III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for this application.

III.4 Toxicology
No new toxicology data were provided, and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment
An Environmental Risk Assessment (ERA) has been provided. The results of the ERA show that there is no risk of increased environmental exposure with the use of this product.

The calculated predicted environmental concentration (PEC_{Surface water}) for fosfomycin is below the action limit of 0.01 μg/L. The Log P is not greater than 4.5. There is, therefore, screening the active substance in a step-wise procedure for persistence, bioaccumulation and toxicity is not necessary.

Fosfomycin 40 mg/ml powder for solution for infusion is unlikely to represent a risk for the environment following prescribed usage in patients. The performance of a Phase II environmental risk assessment is not required.

Moreover, since fosfomycin is intended for generic substitution, this will not lead to an increased exposure to the environment. Further discussion of the environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of fosfomycin sodium is well-known. According to the regulatory requirements, the applicant has provided a suitable bioequivalence and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

IV.2 Pharmacokinetics
No new pharmacokinetic data have been submitted for this application and none were required.

IV.3 Pharmacodynamics
No new pharmacodynamic data have been submitted for this application and none were required.

IV.4 Clinical efficacy
No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety
No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as Infectofos, powder for solution for infusion.

IV.6 Risk Management Plan (RMP)
The Applicant has submitted a RMP, in accordance with the requirements of Directive 2001/83/EC, as amended. The Applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects
The grant of a marketing authorisation is recommended for this application.

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 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 product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with fosfomycin sodium is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

The following text is the currently approved label text. No label mock-ups have been provided for this product. In accordance with medicines legislation, this product shall not be marketed in the UK until approval of the label mock-ups has been obtained.
PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND IMMEDIATE PACKAGING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

FOSFOMYCIN 40 mg/ml Powder for solution for infusion
Fosfomycin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

2 g in 50 ml after reconstitution
4 g in 100 ml after reconstitution
8 g in 200 ml after reconstitution

One bottle with 2.69 g of powder contains 2.64 g disodium fosfomycin, corresponding to 2 g fosfomycin and 0.64 g (28 mmol) sodium, for the reconstitution in 50 ml of solvent.
One bottle with 5.38 g of powder contains 5.28 g disodium fosfomycin, corresponding to 4 g fosfomycin and 1.28 g (56 mmol) sodium, for the reconstitution in 100 ml of solvent.
One bottle with 10.76 g of powder contains 10.56 g disodium fosfomycin, corresponding to 8 g fosfomycin and 2.56 g (111 mmol) sodium, for the reconstitution in 200 ml of solvent.

One ml of reconstituted solution contains 40 mg fosfomycin.

3. LIST OF EXCIPIENTS

Excipient: Succinic acid.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for infusion
10 bottles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF SIGHT AND THE REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear solutions.

8. EXPIRY DATE

EXP
9. SPECIAL STORAGE CONDITIONS

Use reconstituted solutions immediately or store in a refrigerator (at 2-8°C) protected from light for up to 24 hours.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any remaining solution should be discarded.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

INFECTOPHARM Arzneimittel und Consilium GmbH
Von-Humboldt-Str. 1, 64646 Heppenheim
Germany

Distributor:
Nordic Pharma Ltd
Unit 3, Commerce Park
Brunel Road
Theale, Reading
RG7 4AB, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 15011/0014

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<Justification for not including Braille accepted>

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC: <to be completed nationally>
SN: <to be completed nationally>
NN: <to be completed nationally>
PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND IMMEDIATE PACKAGING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

FOSFOMYCIN 40 mg/ml Powder for solution for infusion
Fosfomycin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

2 g in 50 ml after reconstitution
4 g in 100 ml after reconstitution
8 g in 200 ml after reconstitution

One bottle with 2.69 g of powder contains 2.64 g disodium fosfomycin, corresponding to 2 g fosfomycin and 0.64 g (28 mmol) sodium, for the reconstitution in 50 ml of solvent.
One bottle with 5.38 g of powder contains 5.28 g disodium fosfomycin, corresponding to 4 g fosfomycin and 1.28 g (56 mmol) sodium, for the reconstitution in 100 ml of solvent.
One bottle with 10.76 g of powder contains 10.56 g disodium fosfomycin, corresponding to 8 g fosfomycin and 2.56 g (112 mmol) sodium, for the reconstitution in 200 ml of solvent.

One ml of reconstituted solution contains 40 mg fosfomycin.

3. LIST OF EXCIPIENTS

Excipient: Succinic acid.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for infusion.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only clear solutions.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS
Use reconstituted solutions immediately or store in a refrigerator (at 2-8°C) protected from light for up to 24 hours.

| 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE |

Any remaining solution should be discarded.

| 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER |
| INFECTOPHARM Arzneimittel und Consilium GmbH |
| Von-Humboldt-Str. 1, 64646 Heppenheim |
| Germany |
| Distributor: Nordic Pharma |

| 12. MARKETING AUTHORISATION NUMBER(S) |
| PL 15011/0014 |

| 13. BATCH NUMBER |
| Batch |

| 14. GENERAL CLASSIFICATION FOR SUPPLY |
| POM |

| 15. INSTRUCTIONS ON USE |
TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European medicines Agency (EMA) website. Minor changes to the product licence are recorded in the current SmPC and/or PIL available on the MHRA website.

<table>
<thead>
<tr>
<th>Application type</th>
<th>Scope</th>
<th>Date of start of procedure</th>
<th>Date of end of procedure</th>
<th>Outcome</th>
<th>Assessment report attached Y/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type IB</td>
<td>To update section 4.2 (posology and method of administration) of the Summary of Product Characteristics (SmPC), from ‘The first dose should be increased by 100% (loading dose)’ to ‘the first dose should be increased by 100% (loading dose), but must not exceed 8g’. This is a minor editorial change to make the dosing recommendation more clear.</td>
<td>SmPC</td>
<td>11/08/2014</td>
<td>01/09/2014</td>
<td>Approved</td>
</tr>
</tbody>
</table>
Annex 1

Reference: PL 15011/0014 - 0010

Product: Fosfomycin 40 mg/ml powder for solution for infusion

Type of Procedure: National

Submission category: Type IB Variation

Reason
To update section 4.2 (posology and method of administration) of the Summary of Product Characteristics (SmPC), from ‘The first dose should be increased by 100% (loading dose)’ to/the first dose should be increased by 100% (loading dose), but must not exceed 8g’. This is a minor editorial change to make the dosing recommendation more clear

Supporting evidence
The Company has submitted updated sections of the SmPC.

Evaluation
The updated document is satisfactory.

Conclusion
The proposed changes are acceptable.

In accordance with Directive 2010/84/EU, the SmPCs and PIL for products granted Marketing Authorisations at a national level are available on the MHRA website.

Decision: Grant

Date: 01 September 2014.