METFORMIN 100MG/ML ORAL SOLUTION

PL 20046/0255

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Focus Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Metformin 100mg/ml Oral Solution (PL 20046/0255) on 11 July 2013. This medicine is only available on prescription. Throughout this report the product may be referred to as Metformin.

Metformin 100mg/ml Oral Solution contains the active ingredient metformin (as metformin hydrochloride), a medicine to treat diabetes. It belongs to a group of medicines called biguanides.

Insulin is a hormone produced by the pancreas that makes the body take in glucose (sugar) from the blood. The body uses glucose to produce energy or stores it for future use. In patients with diabetes, the pancreas does not make enough insulin or the body is not able to use properly the insulin it produces. This leads to a high level of glucose in the blood. Metformin helps to lower the blood glucose to as normal a level as possible. In overweight adults, taking Metformin over a long period of time also helps to lower the risk of complications associated with diabetes. Metformin is associated with either a stable body weight or modest weight loss.

Metformin 100mg/ml Oral Solution is used to treat patients with type 2 diabetes (also called ‘non-insulin dependent diabetes’) when diet and exercise alone have not been enough to control your blood glucose levels. It is used particularly in overweight patients. Adults can take Metformin on its own or together with other medicines to treat diabetes (medicines taken by mouth or insulin). Children 10 years and over and adolescents can take Metformin on its own or together with insulin.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Metformin 100mg/ml Oral Solution outweigh the risks; hence a Marketing Authorisation has been granted.

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Focus Pharmaceuticals Limited a Marketing Authorisation for the medicinal product Metformin 100mg/ml Oral Solution (PL 20046/0255) on 11 July 2013. The product is a prescription-only medicine (POM). Metformin 100mg/ml Oral Solution is indicated for the following:

- treatment of type 2 diabetes mellitus, particularly in overweight patients, when dietary management and exercise alone does not result in adequate glycaemic control;
- in adults, may be used as monotherapy or in combination with other oral anti-diabetic agents or with insulin;
- in children from 10 years of age and adolescents, may be used as monotherapy or in combination with insulin.

A reduction of diabetic complications has been shown in overweight type 2 diabetic adult patients treated with metformin as first-line therapy after diet failure.

This application was submitted as an abridged application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Metformin 100 mg / ml Oral Solution (PL 35574/0012), which was a granted Marketing Authorisation to Alapis S.A. in April 2011, following completion (end of procedure date 09 March 2011) of Decentralised Procedure MT/H/0119/01/DC.

The active ingredient, metformin (as metformin hydrochloride), is a biguanide with antihyperglycaemic effects, lowering both basal and postprandial plasma glucose. Metformin does not stimulate insulin secretion and therefore does not produce hypoglycaemia. Metformin may act via 3 mechanisms:
1) reduction of hepatic glucose by inhibiting gluconeogenesis and glycogenolysis
2) by increasing insulin sensitivity in muscle, thus improving peripheral glucose uptake and utilisation
3) delay of intestinal glucose absorption.

Metformin stimulates intracellular glycogen synthesis by acting on glycogen synthase. Metformin increases the transport capacity of all types of membrane glucose transporters (GLUT).

In humans independently of its action on glycaemia, metformin has favourable effects on lipid metabolism. This has been shown at therapeutic doses in controlled, medium-term or long-term clinical studies: metformin reduces total cholesterol, LDL cholesterol and triglyceride levels.

No new data were submitted nor were they necessary for this simple application, as the data are identical to those of the previously granted cross-reference product.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 20046/0255
PROPRIETARY NAME(S): Metformin 100mg/ml Oral Solution
ACTIVE(S): Metformin hydrochloride
COMPANY NAME: Focus Pharmaceuticals Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS: POM

1. INTRODUCTION

This is an abridged application for Metformin 100mg/ml Oral Solution (PL 20046/0255) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Metformin 100 mg / ml Oral Solution (PL 35574/0012), which was authorised to Alapis S.A., Greece on 06 April 2011. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Metformin 100mg/ml Oral Solution. The product has been named in line with current requirements.

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

Each ml of Metformin 100mg/ml Oral Solution contains 100mg of metformin hydrochloride. Metformin 100mg/ml Oral Solution is supplied in 150ml amber (Type III) glass bottles, with tamper evident and child resistant screw-caps with PEBD seals. A 10ml oral syringe is also supplied.

The packaging, proposed shelf-life (18 months for the unopened product, 28 days for the opened product) and storage conditions ("Do not store above 25°C. Once opened, used within 28 days.") are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the product will be available as a prescription-only medicine (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company

Focus Pharmaceuticals Limited, Unit 5 Faraday Court, First Avenue, Centrum 100, Burton upon Trent Staffordshire, DE14 2WX, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (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
None of the excipients contain materials of animal or human origin.

2.11 Bioequivalence
No bioequivalence data are required to support this simple abridged application, as the proposed product is manufactured to the same formula and utilises the same processes as the reference product Metformin 100 mg / ml Oral Solution (PL 35574/0012).

3. EXPERT REPORT
The applicant cross-refers to the data for Metformin 100 mg / ml Oral Solution (PL 35574/0012) to which this application is claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed Summary of Product Characteristics is consistent with the details registered for the respective cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The Patient Information Leaflet has been prepared in line with the details registered for the cross-reference product.

User testing of the package leaflet for Metformin 100 mg / ml Oral Solution (PL 35574/0012) has previously been accepted, based on the results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended.

As the leaflet text for Metformin 100mg/ml Oral Solution (PL 20046/0255) and that for Metformin 100 mg / ml Oral Solution (PL 35574/0012) are considered the same, no further user testing of the leaflet for this product is considered necessary.

Carton and label
The proposed artwork is consistent with the artwork registered for the respective cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSION
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.

NON-CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the application is for an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

The grant of a Marketing Authorisation is recommended.

CLINICAL ASSESSMENT

As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

As the application is for an identical version of an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profile of the active ingredient is well-established.

The grant of a Marketing Authorisation is recommended.

OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application is consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for this type of application.

EFFICACY
This application is identical to the previously granted application for Metformin 100 mg / ml Oral Solution (PL 35574/0012).

SAFETY
No new safety data were supplied or required for this application. Metformin hydrochloride has a well-established safety profile. No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling text are satisfactory, and consistent with those for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with metformin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 20 March 2012.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 21 May 2012.

3 Following assessment of the application the MHRA requested further information relating to the dossier on 09 August 2012, 18 January 2013, 16 May 2013, 27 June 2013, 28 June 2013 and 08 July 2013.

4 The applicant responded to the MHRA's request, providing further information on the 12 November 2012, , 25 January 2013, 20 May 2013, 29 May 2013, 27 June 2013, 28 June 2013 and 08 July 2013.

4 The application was granted on 11 July 2013.

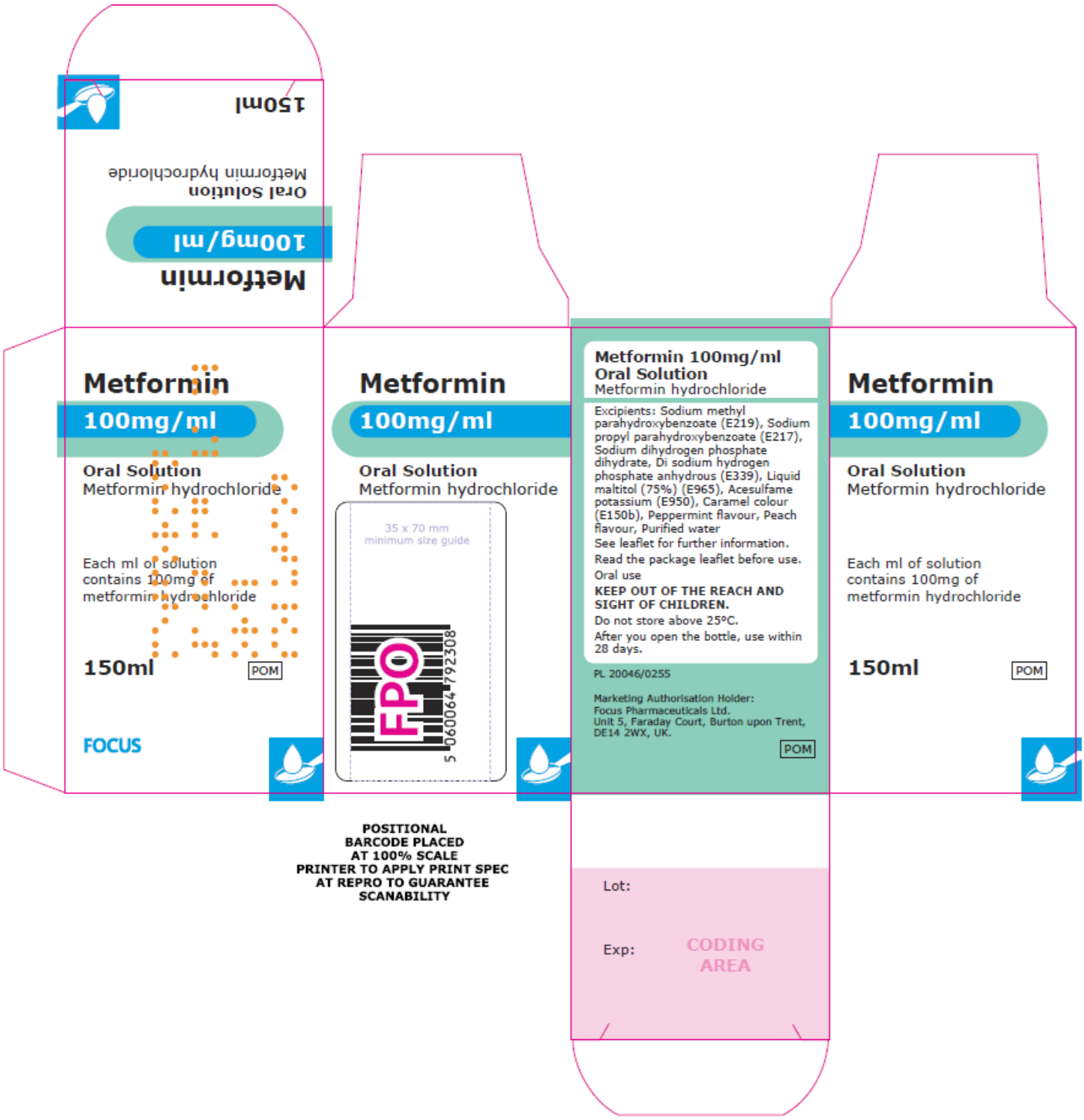
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

LABELLING


150ml
Metformin hydrochloride
Oral Solution
100mg/ml
Metformin
Metformin
100mg/ml
Oral Solution
Metformin hydrochloride
Each ml of solution contains 100mg of metformin hydrochloride
150ml
POM
FOCUS
Metformin
100mg/ml
Oral Solution
Metformin hydrochloride
35 x 70 mm
minimum size guide
FPO
5 060064 792308
Metformin 100mg/ml
Oral Solution
Metformin hydrochloride
Excipients: Sodium methyl parahydroxybenzoate (E219), Sodium propyl parahydroxybenzoate (E217), Sodium dihydrogen phosphate dihydrate, Di sodium hydrogen phosphate anhydrous (E339), Liquid maltitol (75%) (E965), Acesulfame potassium (E950), Caramel colour (E150b), Peppermint flavour, Peach flavour, Purified water
See leaflet for further information.
Read the package leaflet before use.
Oral use
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Do not store above 25°C.
After you open the bottle, use within 28 days.
PL 20046/0255
Marketing Authorisation Holder:
Focus Pharmaceuticals Ltd.
Unit 5, Faraday Court, Burton upon Trent, DE14 2WX, UK.
POM
Metformin
100mg/ml
Oral Solution
Metformin hydrochloride
Each ml of solution contains 100mg of metformin hydrochloride
150ml
POM
POSITIONAL BARCODE PLACED AT 100% SCALE PRINTER TO APPLY PRINT SPEC AT REPRO TO GUARANTEE SCANABILITY
Lot:
Exp:
CODING AREA
Metformin
100mg/ml
Oral Solution
Metformin hydrochloride
Each ml of solution contains 100mg of metformin hydrochloride.
150ml
FOCUS
Excipients: Sodium methyl parahydroxybenzoate (E219), Sodium propyl parahydroxybenzoate (E217), Sodium dihydrogen phosphate dihydrate, Di sodium hydrogen phosphate anhydrous (E339), Liquid maltitol (75%) (E965), Acesulfame potassium (E950), Caramel colour (E150b), Peppermint flavour, Peach flavour, Purified water
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