Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedures

Sitagliptin/Metformin 50 mg/850 mg and 50 mg/1000 mg film-coated tablets

(sitagliptin hydrochloride and metformin hydrochloride)

Product Licence Numbers: PL 25258/0350-0351

Glenmark Pharmaceuticals Europe Limited

LAY SUMMARY

Sitagliptin/Metformin 50 mg/850 mg and 50 mg/1000 mg film-coated tablets (sitagliptin hydrochloride and metformin hydrochloride)

This is a summary of the Public Assessment Report (PAR) for Sitagliptin/Metformin 50 mg/850 mg and 50 mg/1000 mg film-coated tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Sitagliptin/Metformin in this lay summary for ease of reading.

For practical information about using Sitagliptin/Metformin, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Sitagliptin/Metformin and what is it used for?
These applications are for generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised in the European Union (EU) called Janumet 50 mg/850 mg and 50 mg/1000 mg film-coated tablets (Merck Sharp and Dohme B.V.).

Along with diet and exercise, this medicine helps lower the blood sugar. This medicine can be used alone or with certain other medicines for diabetes (insulin, sulphonylureas, or glitazones).

Type 2 diabetes is a condition in which the body does not make enough insulin, and the insulin that the body produces does not work as well as it should. The body can also make too much sugar. When this happens, sugar (glucose) builds up in the blood. This can lead to serious medical problems like heart disease, kidney disease, blindness, and amputation.

How does Sitagliptin/Metformin work?
Sitagliptin/Metformin contains two different medicines called sitagliptin and metformin. Sitagliptin belongs to a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors). Metformin belongs to a class of medicines called biguanides. These work together to control blood sugar levels in adult patients with a form of diabetes called ‘type 2 diabetes mellitus’. This medicine helps to increase the levels of insulin produced after a meal and lowers the amount of sugar made by the body.

How is Sitagliptin/Metformin used?
The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (by mouth).

The recommended dose is one tablet twice daily with meals to lower the chance of an upset stomach.

A doctor may need to increase the dose to control the blood sugar.

If patients have reduced kidney function, a doctor may prescribe a lower dose.
Patients should continue the diet recommended by a doctor during treatment with this medicine and take care that the carbohydrate intake is equally distributed over the day.

This medicine alone is unlikely to cause abnormally low blood sugar (hypoglycaemia). When this medicine is used with a sulphonylurea medicine or with insulin, low blood sugar can occur, and your doctor may reduce the dose of the sulphonylurea or insulin.

For further information on how Sitagliptin/Metformin is used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take Sitagliptin/Metformin exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Sitagliptin/Metformin have been shown in studies?
Because Sitagliptin/Metformin is a generic medicine, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Sitagliptin/Metformin?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of the patient by someone else who cares for them, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Sitagliptin/Metformin is a generic medicine and is bioequivalent to the reference medicines, their benefits and possible side effects are considered to be the same as the reference medicines.

Why was Sitagliptin/Metformin approved?
It was concluded that, Sitagliptin/Metformin has been shown to be bioequivalent to the reference medicines. Therefore, the MHRA decided that, as for the reference medicines, the benefits are greater than the risks and recommended that they can be approved for use.

What measures are being taken to ensure the safe and effective use of Sitagliptin/Metformin?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Sitagliptin/Metformin. The RMP details the important risks of Sitagliptin/Metformin, how these risks can be minimised, any uncertainties about Sitagliptin/Metformin (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Sitagliptin/Metformin:

The important identified risk is lactic acidosis.

The important potential risk is pancreatic cancer.

The missing information is use in pregnancy and during breast-feeding.

A (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Sitagliptin/Metformin
Marketing Authorisations for Sitagliptin/Metformin were granted in the United Kingdom (UK) on 23 December 2021.

The full PAR for Sitagliptin/Metformin follows this summary.

This summary was last updated in February 2022.

TABLE OF CONTENTS

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 applications for Sitagliptin/Metformin 50 mg/850 mg and 50 mg/1000 mg film-coated tablets (PL 25258/0350-0351) could be approved.

The products are approved for the following indications:

For adult patients with type 2 diabetes mellitus:

- as an adjunct to diet and exercise to improve glycaemic control in patients inadequately controlled on their maximal tolerated dose of metformin alone or those already being treated with the combination of sitagliptin and metformin.

- in combination with a sulphonylurea (i.e., triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.

- as triple combination therapy with a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e., a thiazolidinedione) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a PPARγ agonist.

- as add-on to insulin (i.e., triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in patients when stable dose of insulin and metformin alone do not provide adequate glycaemic control.

Sitagliptin is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for the treatment of type 2 diabetes. The DPP-4 inhibitors are a class of agents that act as incretin enhancers. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. When blood glucose levels are low, insulin release is not enhanced and glucagon secretion is not suppressed. Sitagliptin is a potent and highly selective inhibitor of the enzyme DPP-4 and does not inhibit the closely-related enzymes DPP-8 or DPP-9 at therapeutic concentrations. Sitagliptin differs in chemical structure and pharmacological action from GLP-1 analogues, insulin, sulphonylureas or meglitinides, biguanides, peroxisome proliferator-activated receptor gamma (PPAR) agonists, alpha-glucosidase inhibitors, and amylin analogues.

These applications were approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of a suitable originator medicinal products, Janumet 50 mg/850 mg and 50 mg/1000 mg film-coated tablets (Merck Sharp and Dohme B.V.), that have been licensed within the EU for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products.

With the exception of the bioequivalence studies, no new clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products. The bioequivalence studies were conducted in-line with current Good Clinical Practice (GCP).

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

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

National marketing authorisations were granted in the United Kingdom (UK) on 23 December 2021.

II QUALITY ASPECTS

II.1 Introduction

The products are consisted of film-coated tablets. Each film-coated tablet contains 50 mg of sitagliptin (as hydrochloride) and 850 mg or 1000 mg of metformin hydrochloride as active substances.

In addition to sitagliptin hydrochloride and metformin hydrochloride, these products also contain the excipients cellulose microcrystalline, povidone (K29/32), sodium laurilsulfate and sodium stearyl fumarate.

Film coating (50 mg/850 mg):
Lactose Monohydrate
Hypromellose
Titanium Dioxide
Triacetin
Iron Oxide Red

Film coating (50 mg/1000 mg):
Polyvinyl alcohol
Macrogol/polyethylene glycol
Talc
Titanium dioxide
Red iron oxide
Black iron oxide

The finished products are packaged either in:

- Blisters composed by polyvinylchloride (PVC)/ polyvinylidenechloride (PVdC) aluminium with pack sizes of 14, 28, 30, 56, 60, 98, 196 and 210 tablets.

Or

- White high-density polyethylene (HDPE) bottle with silicagel desiccant container in the polypropylene screw cap with a pack size of 100 tablets.

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 regulations concerning materials in contact with food.

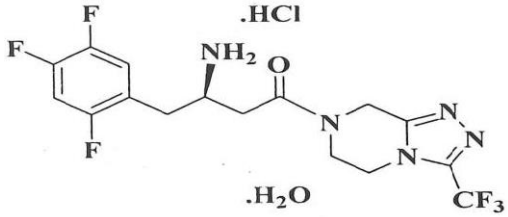
II.2 ACTIVE SUBSTANCES

rINN: Sitagliptin hydrochloride

Chemical Name: 1,2,4-Triazolo[4,3-a]pyrazine,7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, hydrochloride (1:1) monohydrate;
or
7-[(R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine hydrochloride monohydrate;
or

(3R)-3-Amino-1-[3-trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl-4-(2,4,5-trifluorophenyl)butan-1-one hydrochloride monohydrate

Molecular Formula: $C_{16}H_{16}ClF_6N_5O.H_2O$
Chemical Structure:



Molecular Weight: 461.79 g/mol
Appearance: White or almost white powder.
Solubility: Soluble in water, very slightly soluble in anhydrous ethanol, practically insoluble in heptane

Sitagliptin hydrochloride is not 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.

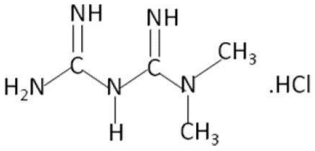
Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

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 regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

rINN: Metformin Hydrochloride
Chemical Name: 1,1-Dimethylbiguanide hydrochloride;
N,N-Dimethyl imido-dicarbonimidicdiamide hydrochloride;
N,N-Dimethyldiguanide hydrochloride;
N´-Dimethyl guanylguanidine hydrochloride
Molecular Formula: $C_4H_{12}ClN_5$
Chemical Structure:



Molecular Weight: 165.62 g/mol

Appearance: A white or almost white, crystalline.
Solubility: Freely soluble in water, slightly soluble in ethanol (96%); practically insoluble in acetone and in methylene chloride.

Metformin Hydrochloride is the subject of a European Pharmacopoeia monograph.

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

II.3 DRUG PRODUCTS

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution and impurity profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

With the exception of lactose monohydrate, no excipients of animal or human origin are used in the final products. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

These products do not contain or consist of genetically modified organisms (GMO).

Manufacture of the products

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

Satisfactory batch formulation data have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. 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 2 years, with the storage conditions “Do not store above 30°C” are approved.

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

The grant of marketing authorisations is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of sitagliptin hydrochloride and metformin hydrochloride 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.

III.2 Pharmacology

No new pharmacology data were provided, and none were required for these applications.

III.3 Pharmacokinetics

No new pharmacokinetic data were provided, and none were required for these applications.

III.4 Toxicology

No new toxicology data were provided, and none were required for these applications.

III.5 Ecotoxicity/Environmental Risk Assessment

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of already authorised products, an increase in environmental exposure is not anticipated following approval of the Marketing Authorisations for the proposed products.

III.6 Discussion on the non-clinical aspects

The grant of marketing authorisations is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of sitagliptin hydrochloride and metformin hydrochloride are well-known. With the exception of data from two bioequivalence studies, no new clinical data are provided or are required for this type of applications. An overview based on a literature review and a review of these studies are, thus, satisfactory.

IV. 2 Pharmacokinetics

In support of the applications, the applicant submitted the following bioequivalence studies:

Study 1

This study was an open label, balanced, randomized, two-treatment, two period, two-sequence, single oral dose, crossover, bioequivalence study of Sitagliptin and Metformin Hydrochloride 50 mg/850 mg tablets versus Janumet® (Sitagliptin and Metformin Hydrochloride 50 mg/850 mg tablets) of Merck Sharp & Dohme Ltd, in normal, healthy, adult, human subjects under fed conditions.

After an overnight fast of at least 10 hours, the subjects were served a high fat and high calorie breakfast, which they consumed completely within 30 minutes.

Blood samples were taken pre-dose and up to 72 hours post dose, with a washout period of 7 days between the treatment periods.

A summary of the pharmacokinetic results are presented below:

Sitagliptin

Parameter	Geometric Least Squares Means			90% Confidence Interval	Power(%)
	Test Product-T	Reference Product-R	Ratio (T/R)%		
InC_{max}	160.561	155.593	103.2	99.20-107.35	100.0
$InAUC_{0-t}$	2236.879	2275.465	98.3	96.57-100.07	100.0

Metformin

Parameter	Geometric Least Squares Means			90% Confidence Interval	Power(%)
	Test Product-T	Reference Product-R	Ratio (T/R)%		
InC_{max}	1680.174	1664.418	100.9	96.80-105.27	100.0
$InAUC_{0-t}$	15126.023	15074.120	100.3	97.07-103.73	100.0

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

Study 2

This study is an open label, balanced, randomized, two-treatment twoperiod, two-sequence, single oral dose, crossover, bioequivalence study of Sitagliptin and Metformin Hydrochloride 50 mg/1000 mg Tablets versus Janumet® (Sitagliptin and Metformin Hydrochloride 50 mg/1000 mg Tablets) of Merck Sharp & Dohme Ltd, in normal, healthy, adult, human subjects under fed conditions.

After an overnight fast of at least 10 hours, the subjects were served a high fat and high calorie breakfast, which they consumed completely within 30 minutes.

Blood samples were taken pre-dose and up to 72 hours post dose, with a washout period of 7 days between the treatment periods.

A summary of the pharmacokinetic results are presented below:

Sitagliptin

Parameter	Geometric Least Squares Means			90% Confidence Interval	Power(%)
	Test Product-T	Reference Product-R	Ratio (T/R)%		
InC_{max}	152.771	150.827	101.3	96.94-105.83	100.0
$InAUC_{0-t}$	2008.595	1957.067	102.6	100.69-104.62	100.0

Metformin

Parameter	Geometric Least Squares Means			90% Confidence Interval	Power(%)
	Test Product-T	Reference Product-R	Ratio (T/R)%		
InC_{max}	1801.810	1740.061	103.5	99.80-107.44	100.0
$InAUC_{0-t}$	15931.168	15374.713	103.6	100.80-106.52	100.0

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for these applications and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with these applications and none were required.

IV.5 Clinical safety

With the exception of the safety data submitted with the bioequivalence studies, no new safety data were submitted with these applications.

The safety data from the bioequivalence studies showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, 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 marketing authorisations is recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application in accordance with legal requirements.

The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Janumet 50 mg/850 mg and 50 mg/1000 mg film-coated tablets (Merck Sharp and Dohme B.V.). The bridging report submitted by the applicant is acceptable.

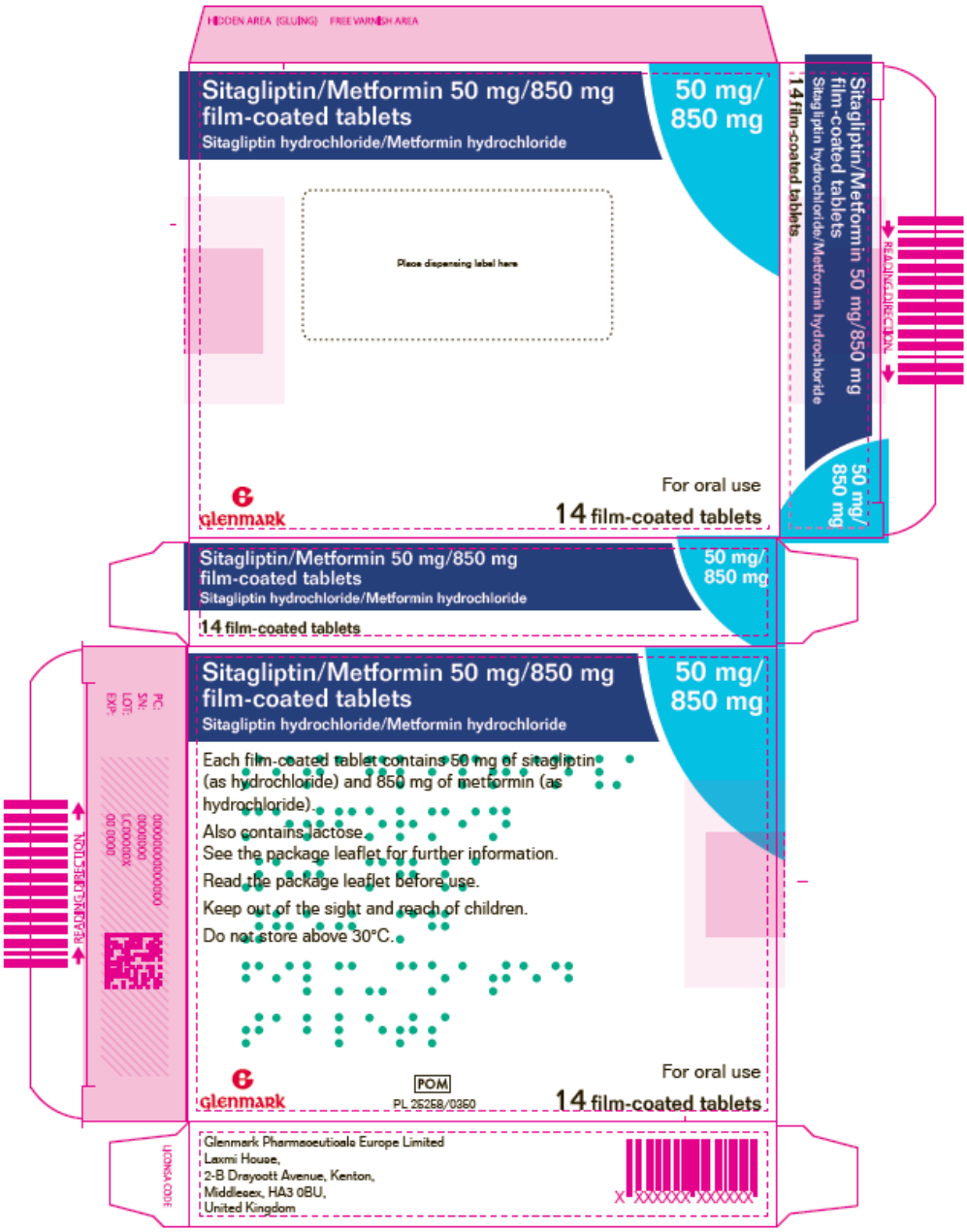
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

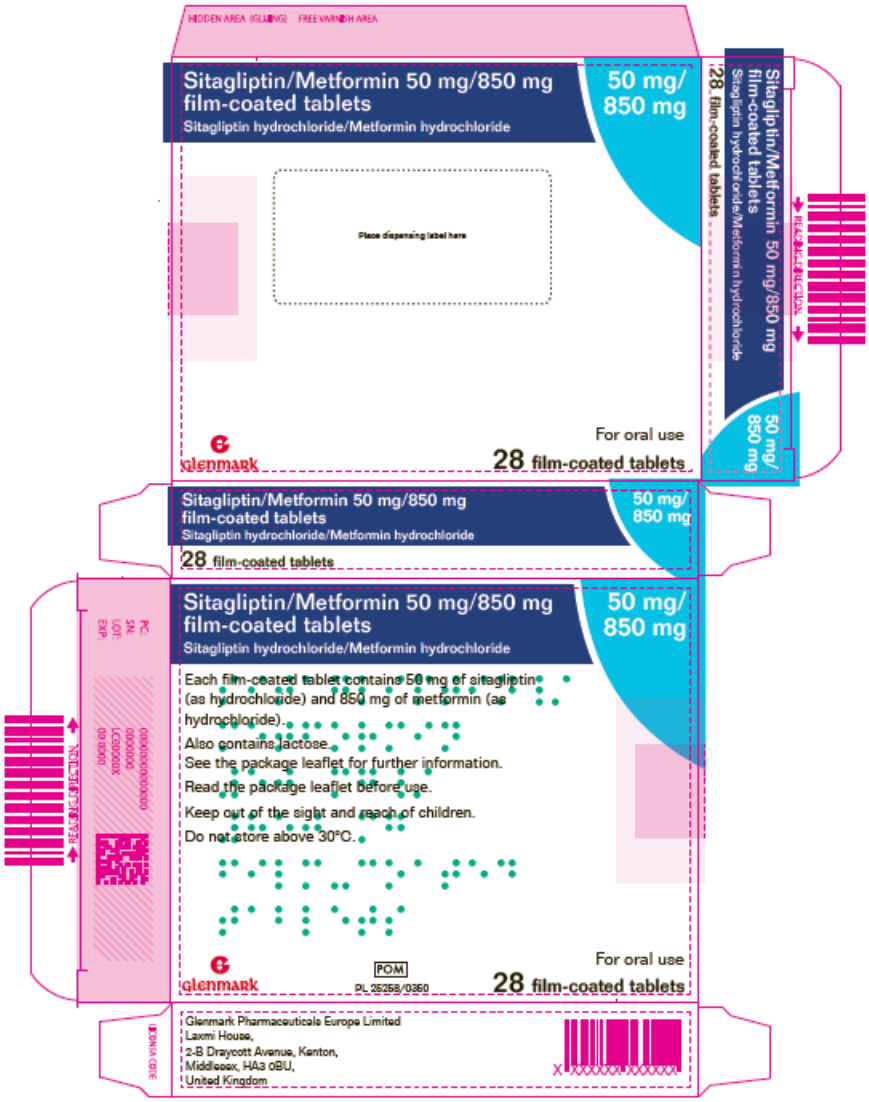
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with sitagliptin hydrochloride and metformin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is,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

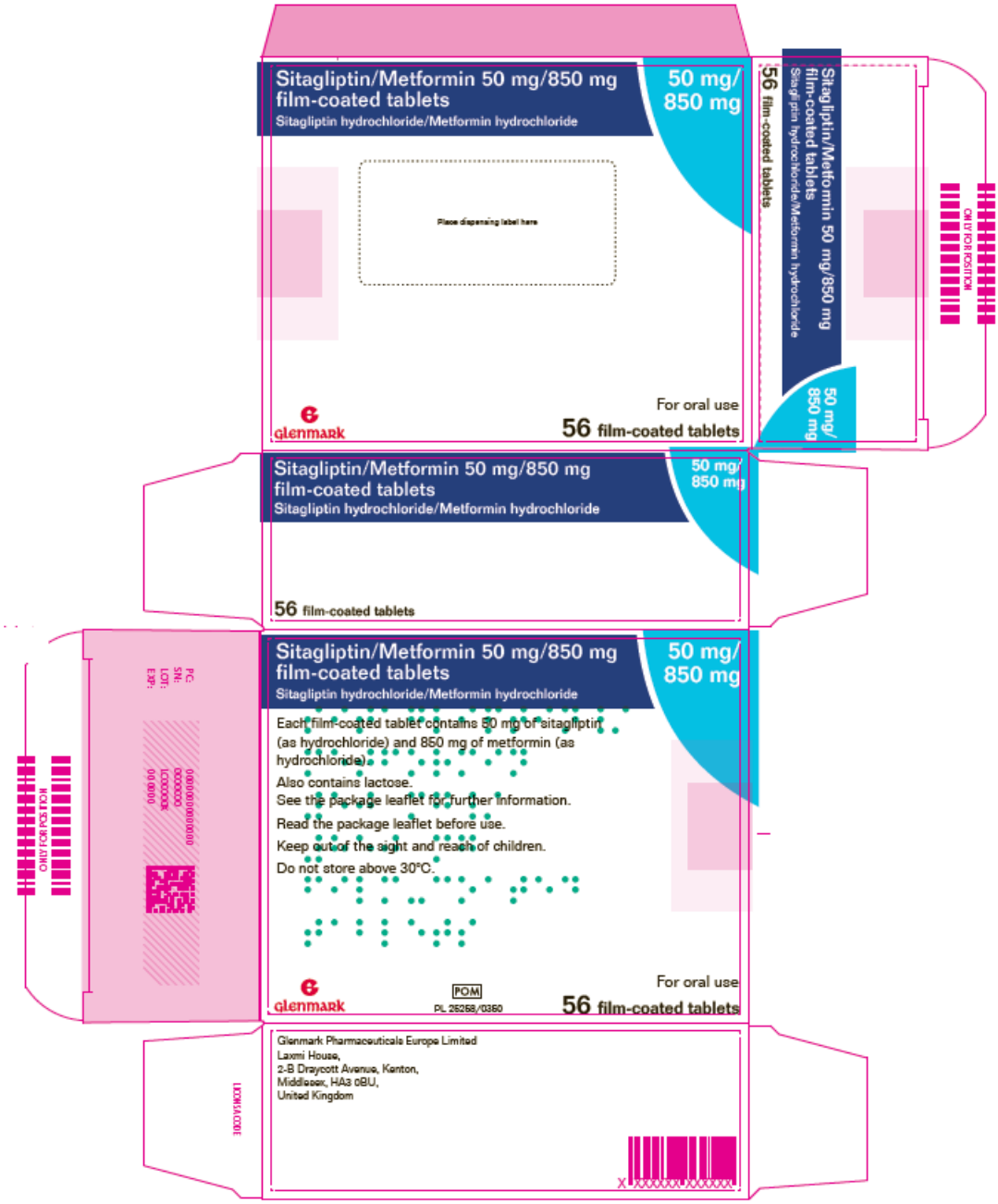
The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

Representative copies of the labels at the time of licensing are provided below.


HIDDEN AREA (GLUING) FREE VARNISH AREA
Sitagliptin/Metformin 50 mg/850 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/ 850 mg
Place dispensing label here
For oral use
14 film-coated tablets
glenmark
READING DIRECTION
POM
PL 25258/0350
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
UCONSA CODE


HIDDEN AREA (GLUING) FREE VARNISH AREA
Sitagliptin/Metformin 50 mg/850 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/ 850 mg
Place dispensing label here
For oral use
28 film-coated tablets
glenmark
Sitagliptin/Metformin 50 mg/850 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
28 film-coated tablets
50 mg/ 850 mg
Each film-coated tablet contains 50 mg of sitagliptin (as hydrochloride) and 850 mg of metformin (as hydrochloride).
Also contains lactose.
See the package leaflet for further information.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Do not store above 30°C.
POM
PL 25258/0360
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
REMOVE BEFORE USE
EXP
PC
SN
LOT


Sitagliptin/Metformin 50 mg/850 mg
film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/
850 mg
Place dispensing label here
For oral use
56 film-coated tablets
glenmark
56 film-coated tablets
Sitagliptin/Metformin 50 mg/850 mg
film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
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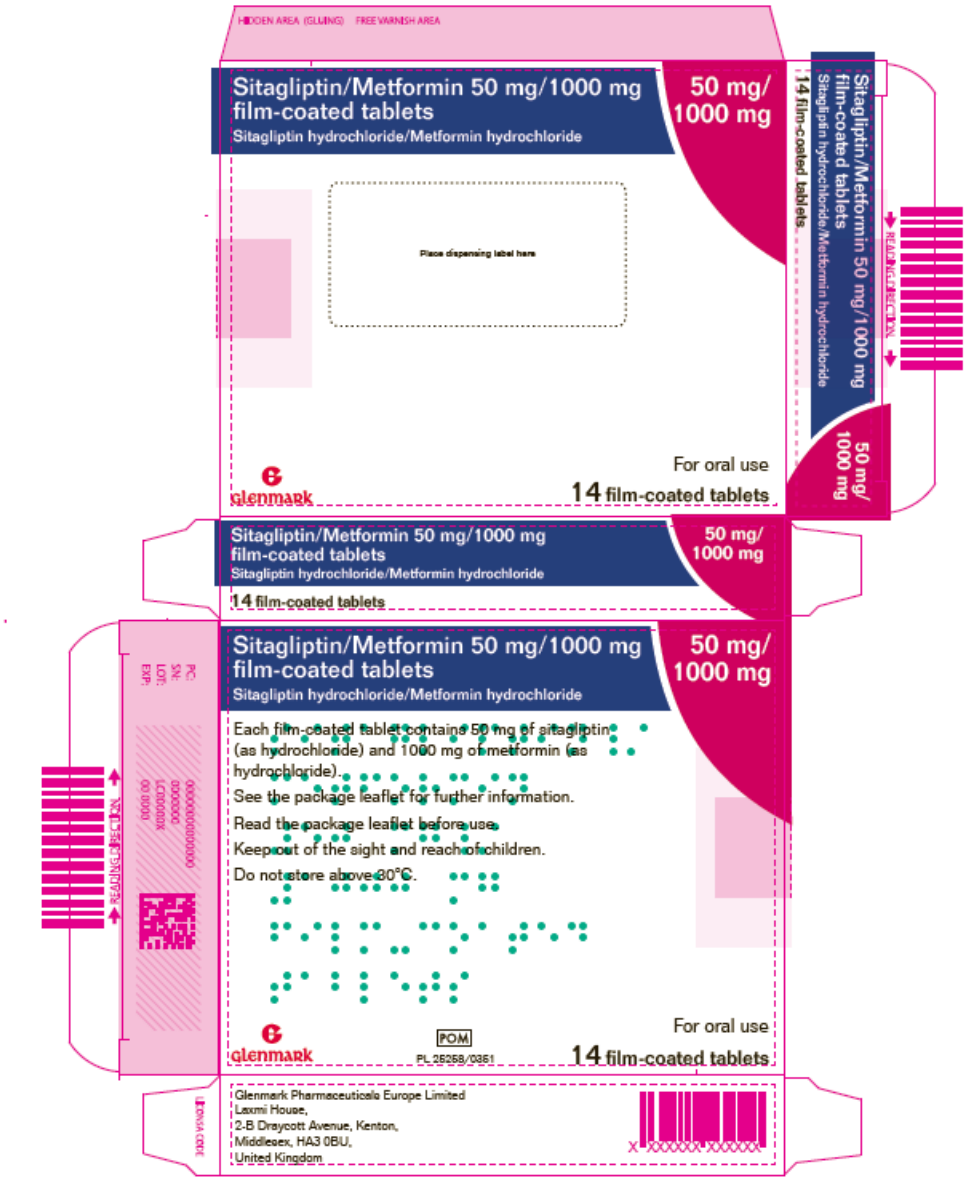
PL 25258/0350
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
PC:
SN:
LOT:
EXP:
ONLY FOR POSITION


HIDDEN AREA (GLUING) FREE VARNISH AREA
Sitagliptin/Metformin 50 mg/1000 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/ 1000 mg
Place dispensing label here
For oral use
glenmark
14 film-coated tablets
Sitagliptin/Metformin 50 mg/1000 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
14 film-coated tablets
READING DIRECTION
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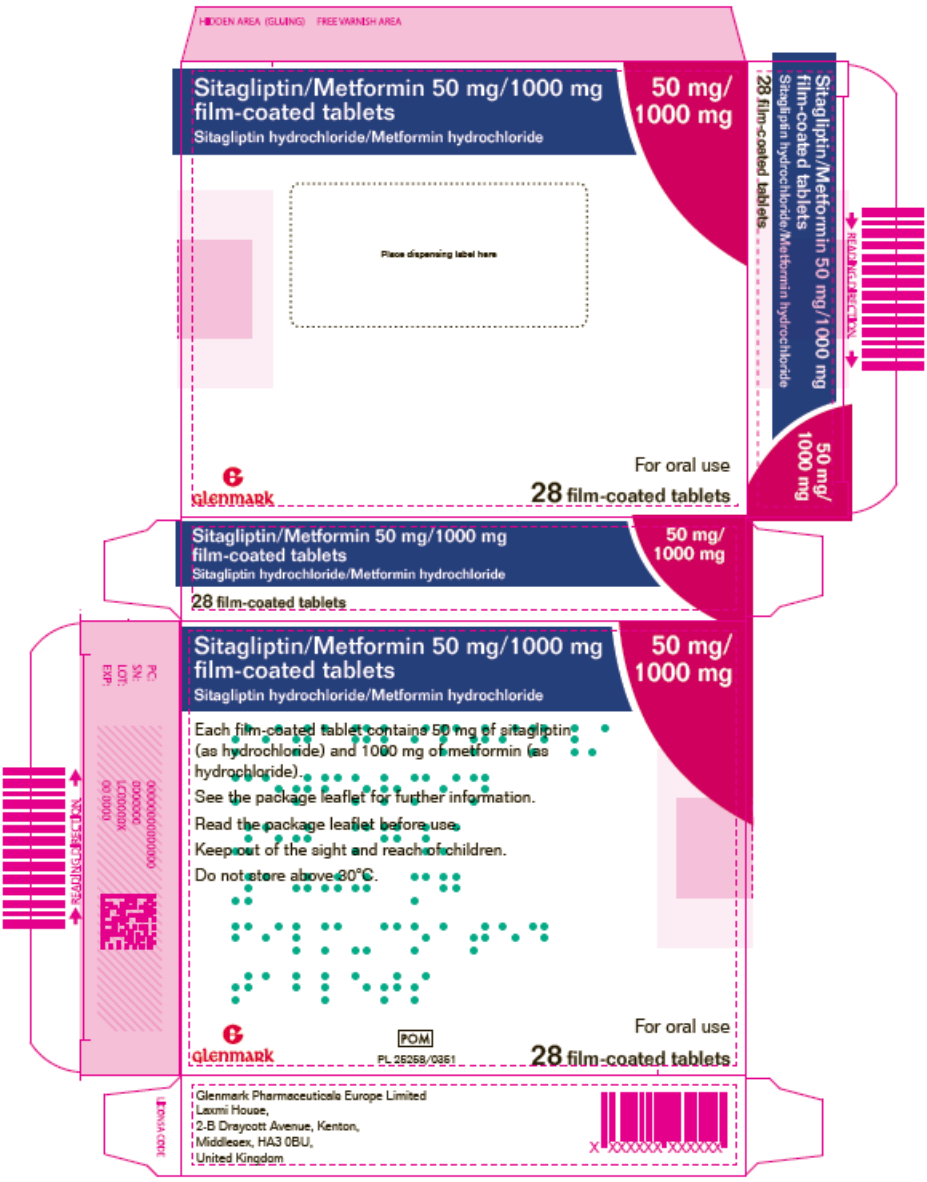
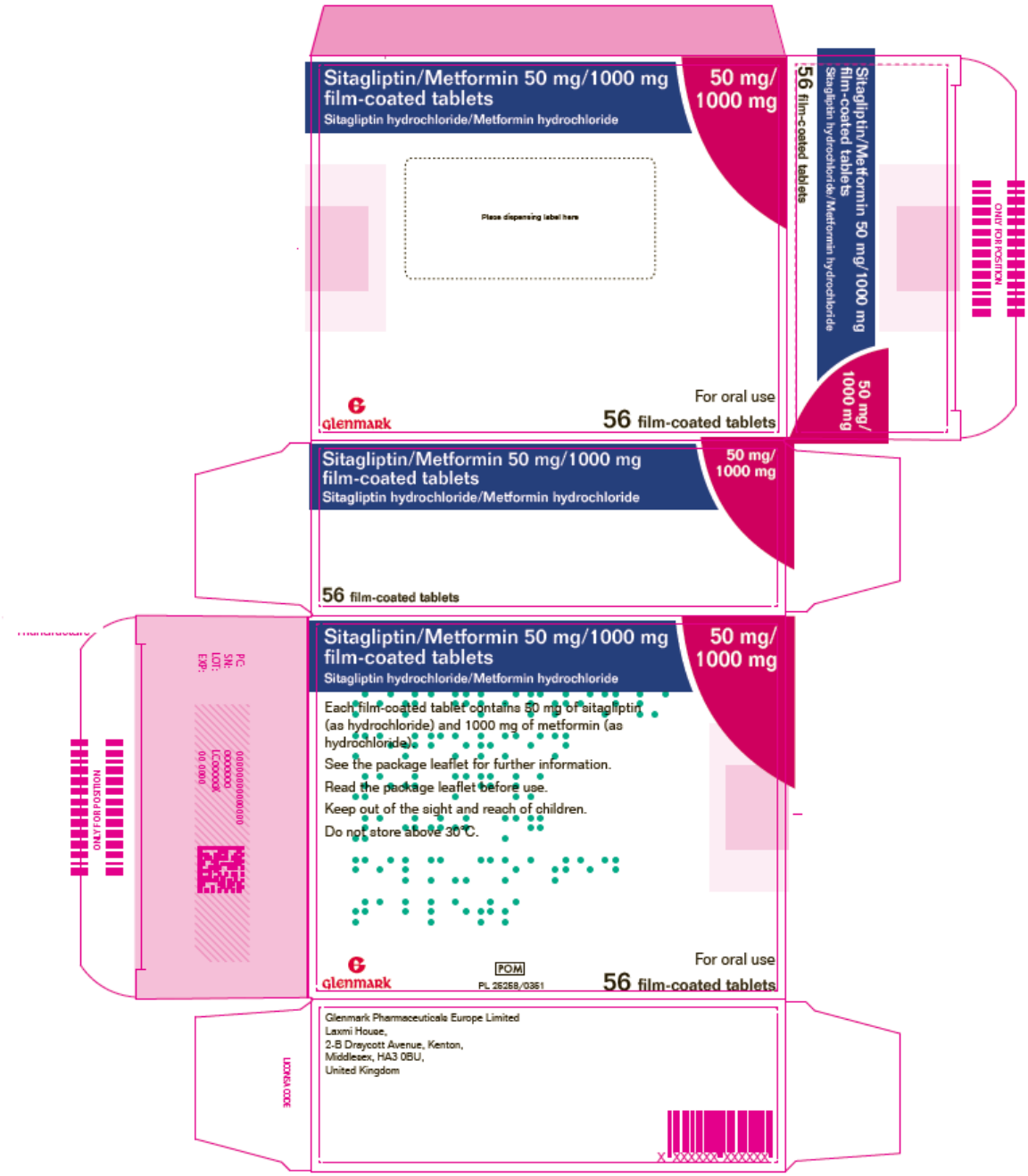
See the package leaflet for further information.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Do not store above 30°C.
POM
PL 25258/0351
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
PC:
SN:
LOT:
EXP:
LEAFLET CODE


HIDDEN AREA (GLUING) FREE VARNISH AREA
Sitagliptin/Metformin 50 mg/1000 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/ 1000 mg
Place dispensing label here
For oral use
28 film-coated tablets
glenmark
READING DIRECTION
PC:
SN:
LOT:
EXP:
Each film-coated tablet contains 50 mg of sitagliptin (as hydrochloride) and 1000 mg of metformin (as hydrochloride).
See the package leaflet for further information.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Do not store above 30°C.
POM
PL 25258/0351
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
EU/XXX/XXX


Sitagliptin/Metformin 50 mg/1000 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
50 mg/ 1000 mg
Please dispensing label here
For oral use
56 film-coated tablets
glenmark
56 film-coated tablets
Each film-coated tablet contains 50 mg of sitagliptin (as hydrochloride) and 1000 mg of metformin (as hydrochloride).
See the package leaflet for further information.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Do not store above 30°C.
POM
PL 25258/0351
Glenmark Pharmaceuticals Europe Limited
Laxmi House,
2-B Draycott Avenue, Kenton,
Middlesex, HA3 0BU,
United Kingdom
ONLY FOR POSITION
PC:
SN:
LOT:
EXP:


Sitagliptin/Metformin 50 mg/850 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
Glenmark Pharmaceuticals Europe Limited

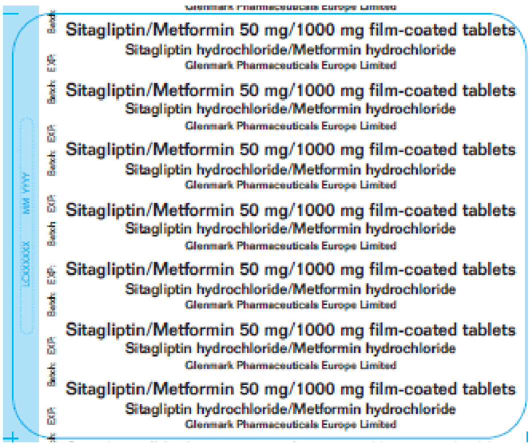

Sitagliptin/Metformin 50 mg/1000 mg film-coated tablets
Sitagliptin hydrochloride/Metformin hydrochloride
Glenmark Pharmaceuticals Europe Limited
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TABLE OF CONTENT OF THE PAR UPDATE

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 marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	Scope	Product information affected	Date of grant	Outcome	Assessment report attached Y/N