Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Vildagliptin/Metformin hydrochloride Accord 50mg/850mg film-coated tablets
Vildagliptin/Metformin hydrochloride Accord 50mg/1000mg film-coated tablets

vildagliptin
and
metformin hydrochloride

PL 00142/1271-1272

Accord-UK Ltd

LAY SUMMARY

Vildagliptin/Metformin hydrochloride Accord 50mg/850mg and 50mg/1000mg film-coated tablets
vildagliptin and metformin hydrochloride

This is a summary of the Public Assessment Report (PAR) for Vildagliptin/Metformin hydrochloride Accord 50mg/850mg and 50mg/1000mg 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 Vildagliptin/Metformin hydrochloride in this lay summary for ease of reading.

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

What is Vildagliptin/Metformin hydrochloride and what is it used for?
These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Eucreas film coated tablets.

Vildagliptin/Metformin Tablets are used to treat adult patients with type 2 diabetes. This type of diabetes is also known as non- insulin-dependent diabetes mellitus. Vildagliptin/Metformin Tablets are used when diabetes cannot be controlled by diet and exercise alone or with other medicines used to treat diabetes (sulphonylureas).

How does Vildagliptin/Metformin hydrochloride work?
Type 2 diabetes develops if the body does not make enough insulin or if the insulin that the body makes does not work as well as it should. It can also develop if the body produces too much glucagon. Both insulin and glucagon are made in the pancreas. Insulin helps to lower the level of sugar in the blood, especially after meals. Glucagon triggers the liver to make sugar, causing the blood sugar level to rise.

Both active substances in Vildagliptin/Metformin Tablets, vildagliptin and metformin, help to control the level of sugar in the blood. The substance vildagliptin works by making the pancreas produce more insulin and less glucagon. The substance metformin works by helping the body to make better use of insulin. These medicines have been shown to reduce blood sugar, which may help to prevent complications from diabetes.

How are Vildagliptin/Metformin hydrochloride used?
The pharmaceutical form of these medicines is film-coated tablets and the route of administration is oral (by mouth).

The amount of Vildagliptin/Metformin Tablets that people have to take varies depending on their condition. The patient's doctor will tell them exactly the dose of Vildagliptin/Metformin Tablets to take.

The recommended dose is one film-coated tablet of either 50 mg/850 mg or 50 mg/1000 mg taken twice a day. The patient should swallow the Vildagliptin/Metformin Tablets whole with a glass of water, taking one tablet in the morning and the other in the evening with or

just after food. Taking the tablet just after food will lower the risk of an upset stomach.

If the patient has reduced kidney function, their doctor may prescribe a lower dose. If the patient is if taking an anti-diabetic medicine known as a sulphonylurea, their doctor may also prescribe a lower dose.

The patient's doctor may prescribe Vildagliptin/Metformin Tablets alone or with certain other medicines that lower the level of sugar in the patient's blood.

Patients taking Vildagliptin/Metformin Tablets should continue to follow any advice about diet that their doctor has given. In particular, if they are following a diabetic weight control diet, they should continue with this whilst taking Vildagliptin/Metformin Tablets.

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

These medicines can only be obtained with a prescription.

The patient should always take this medicine 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 Vildagliptin/Metformin hydrochloride have been shown in studies?
Because Vildagliptin/Metformin hydrochloride are generic medicines, 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 Vildagliptin/Metformin hydrochloride?
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 their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Vildagliptin/Metformin hydrochloride are generic medicines and are bioequivalent to the reference medicines, their benefits and possible side effects are considered to be the same as the reference medicines.

Why was Vildagliptin/Metformin hydrochloride approved?
It was concluded that, Vildagliptin/Metformin hydrochloride has been shown to be bioequivalent 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 Vildagliptin/Metformin hydrochloride?

As for all newly-authorised medicines, an Risk Management Plan (RMP) has been developed for Vildagliptin/Metformin hydrochloride. The RMP details the important risks of Vildagliptin/Metformin hydrochloride, how these risks can be minimised, any uncertainties about Vildagliptin/Metformin hydrochloride (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Vildagliptin/Metformin hydrochloride:

Important identified risk	• Drug induced liver injury (DILI) • Acute pancreatitis • Lactic acidosis
Important potential risk	• Muscle events/myopathy/rhabdomyolysis, in particular with current statin use (events of myalgia excluded)
Missing information	• None

The safety information in the proposed Product Information is aligned to the reference medicinal product.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Vildagliptin/Metformin hydrochloride are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

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

Other information about Vildagliptin/Metformin hydrochloride

Marketing Authorisations for Vildagliptin/Metformin hydrochloride were granted in the United Kingdom (UK) on 10 February 2023.

The full PAR for Vildagliptin/Metformin hydrochloride follows this summary.

This summary was last updated in August 2023.

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 Vildagliptin/Metformin hydrochloride Accord 50mg/850mg and 50mg/1000mg film-coated tablets (PL 00142/1271-1272) could be approved.

The products are approved for the following indications:

Vildagliptin/Metformin hydrochloride is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus:

- in patients who are inadequately controlled with metformin hydrochloride alone.
- in patients who are already being treated with the combination of vildagliptin and metformin hydrochloride, as separate tablets.
- in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control.

The names of the active substances in these tablets are vildagliptin and metformin hydrochloride. Vildagliptin/Metformin hydrochloride combines two antihyperglycaemic agents with complimentary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: vildagliptin, a member of the islet enhancer class, and metformin hydrochloride, a member of the biguanide class.

Vildagliptin, a member of the islet enhancer class, is a potent and selective dipeptidyl-peptidase-4 (DPP-4) inhibitor. Metformin acts primarily by decreasing endogenous hepatic glucose production.

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 suitable originator medicinal products, Eucreas film coated tablets that has been licensed for 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 a 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.

Marketing Authorisations for Vildagliptin/Metformin hydrochloride were granted in the United Kingdom (UK) on 10 February 2023.

II QUALITY ASPECTS

II.1 Introduction

What Vildagliptin/ Metformin hydrochloride contains

The active substances are vildagliptin and metformin hydrochloride.

Each Vildagliptin/ Metformin hydrochloride 50 mg/850 mg film-coated tablet contains 50 mg vildagliptin and 850 mg metformin hydrochloride (corresponding to 660 mg of metformin).

Each Vildagliptin/ Metformin hydrochloride 50 mg/1000 mg film-coated tablet contains 50 mg vildagliptin and 1000 mg metformin hydrochloride (corresponding to 780 mg of metformin).

Both strengths of *Vildagliptin/ Metformin hydrochloride* contain the following other ingredients:
Tablet core: Hydroxypropylcellulose, low-substituted hydroxypropylcellulose, microcrystalline cellulose, magnesium stearate.
Film-coating: Hypromellose, titanium dioxide (E171), iron oxide yellow (E172), macrogol 6000, talc.

Vildagliptin/ Metformin hydrochloride is available in blisters of 30 or 60 film-coated 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.

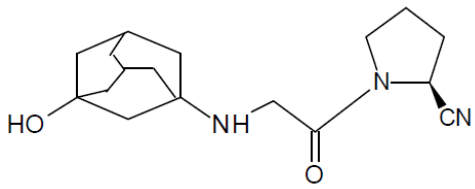
II.2 ACTIVE SUBSTANCES

rINN: Vildagliptin

Chemical Name: (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine
(S)-{[(3-hydroxyadamtan-1-yl)amino]acetyl}pyrrolidin-2-carbonitrile

Molecular Formula: $C_{17}H_{25}N_3O_2$

Chemical Structure:



Molecular Weight: 303.39
Appearance: White to off white powder
Solubility: Freely soluble in water, methanol, methylene dichloride and practically insoluble in ethyl acetate.

Vildagliptin 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.

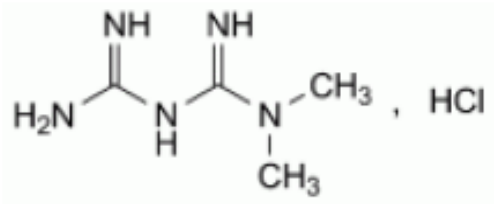
Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

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 suitable retest period when stored in the proposed packaging.

rINN: Metformin hydrochloride
Chemical Name: 1,1-Dimethylbiguanide hydrochloride
Molecular Formula: $C_4H_{12}ClN_5$
Chemical Structure:



Molecular Weight: 165.6
Appearance: White or almost white crystals
Solubility: Freely soluble in water, slightly soluble in ethanol (96 percent), practically insoluble in acetone and in methylene chloride

Metformin hydrochloride is the subject of a European Pharmacopoeia monograph.

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 suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCTS

Pharmaceutical development
A satisfactory account of the pharmaceutical development was provided.

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

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

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

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

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 year, without any special storage conditions, is acceptable.

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 was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of vildagliptin 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 was provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of an 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 was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of Vildagliptin and metformin hydrochloride are well-known. With the exception of data from two bioequivalence studies undertaken, no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of these studies is, thus, satisfactory.

IV. 2 Pharmacokinetics
In support of the application, the applicant submitted two bioequivalence studies; 0622-19 for the 50/850 mg product and 0622-19 0623-19 for the 50/1000 mg product, participants in both studies were under fed conditions.

Study Code : 0622-19
An open label, balanced, randomised, two-treatment, two period, two-sequence, crossover, single oral dose, bioequivalence study of Vildagliptin/Metformin hydrochloride Accord 50mg/850mg film-coated tablets (test product) versus Eucreas 50 mg/850mg film-coated tablets (reference product) in healthy, adult, human subjects under fed condition.

In each study period, after an overnight fast of at least 10 hours, subjects were served a high fat and high calorie vegetarian breakfast, after which a single oral dose of either the test product or the reference product containing was administered to the subjects. Blood samples were taken pre-dose and up to 36 hours post dose, with a washout period of 4 days between successive dosing days.

A summary of the pharmacokinetic results is presented below:

Relative Bioavailability Results for Vildagliptin (N = 54)

Parameters	Geometric Least Squares Means			90% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	172.690	172.609	100.0	93.12 - 107.48	22.5	100.0
$lnAUC_{0-t}$	1126.329	1082.723	104.0	99.14 - 109.16	15.0	100.0
$lnAUC_{0-\infty}$	1180.261	1129.630	104.5	99.53 - 109.68	15.2	100.0

Relative Bioavailability Results for Metformin (N = 54)

Parameters	Geometric Least Squares Means			90% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	1576.264	1572.037	100.3	95.53 - 105.24	15.1	100.0
$lnAUC_{0-t}$	16066.454	15428.256	104.1	100.37 - 108.05	11.5	100.0
$lnAUC_{0-\infty}$	16165.371	15519.846	104.2	100.39 - 108.07	11.5	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 Code : 0623-19
An open label, balanced, randomised, two-treatment, two period, two-sequence, crossover, single oral dose, bioequivalence study of Vildagliptin/Metformin hydrochloride Accord 50mg/1000mg film-coated tablets (test product) versus Eucreas 50mg/1000 mg film-coated tablets (reference product) in healthy, adult, human subjects under fed condition.

In each study period, after an overnight fast of at least 10 hours, subjects were served a high fat and high calorie vegetarian breakfast, after which a single oral dose of either the test product or the reference product containing was administered to the subjects. Blood samples were taken pre-dose and up to 36 hours post dose, with a washout period of 4 days between successive dosing days.

A summary of the pharmacokinetic results is presented below:

Relative Bioavailability Results for Vildagliptin (N = 54)

Parameters	Geometric Least Squares Means			90% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	148.260	140.771	105.3	98.62 - 112.47	20.6	100.0
$lnAUC_{0-t}$	1008.389	992.366	101.6	98.59 - 104.73	9.4	100.0
$lnAUC_{0-\infty}$^	1048.322	1043.453	100.5	97.13 - 103.92	10.3	100.0

^N=52; Note: Terminal rate constant (lambda_z) cannot be estimated based on obtained concentration data for subject nos. 1049 (Period-I, T) and 1051 (Period-I, R). Hence, $AUC_{0-\infty}$ and other elimination phase dependent parameters cannot be calculated. Hence, same was also excluded from the other treatment arm.

Relative Bioavailability Results for Metformin (N = 54)

Parameters	Geometric Least Squares Means			90% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	1535.932	1604.012	95.8	90.83 - 100.95	16.5	100.0
$lnAUC_{0-t}$	16917.812	17106.649	98.9	95.83 - 102.06	9.8	100.0
$lnAUC_{0-\infty}$	17022.503	17214.719	98.9	95.83 - 102.03	9.7	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 were 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 was recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was 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 Mycophenolic acid 180mg and 360mg gastro-resistant Tablets for design, layout and style of writing and the reference product Eucreas® film coated tablets for content and key messages. The bridging report submitted by the applicant is acceptable.

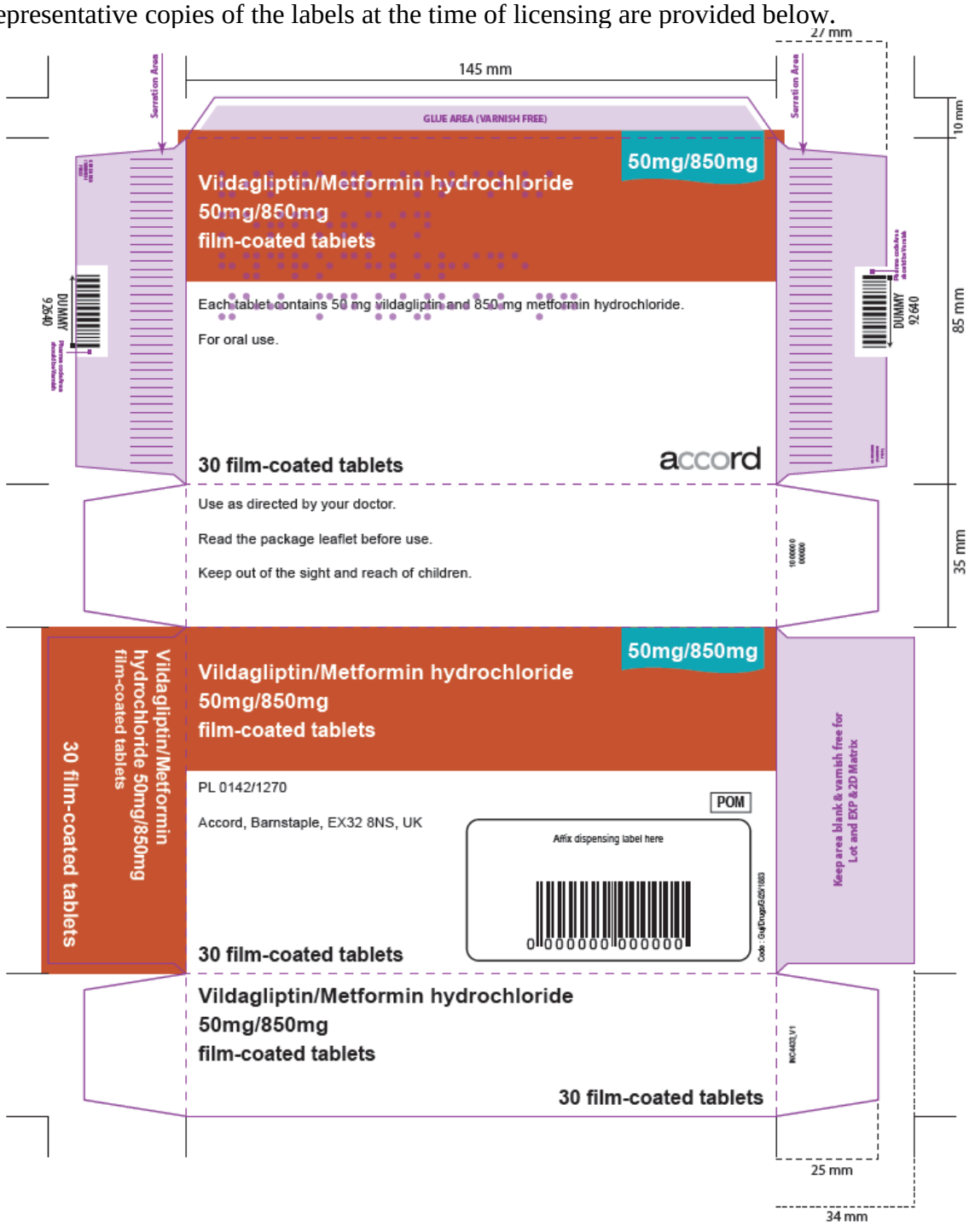
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

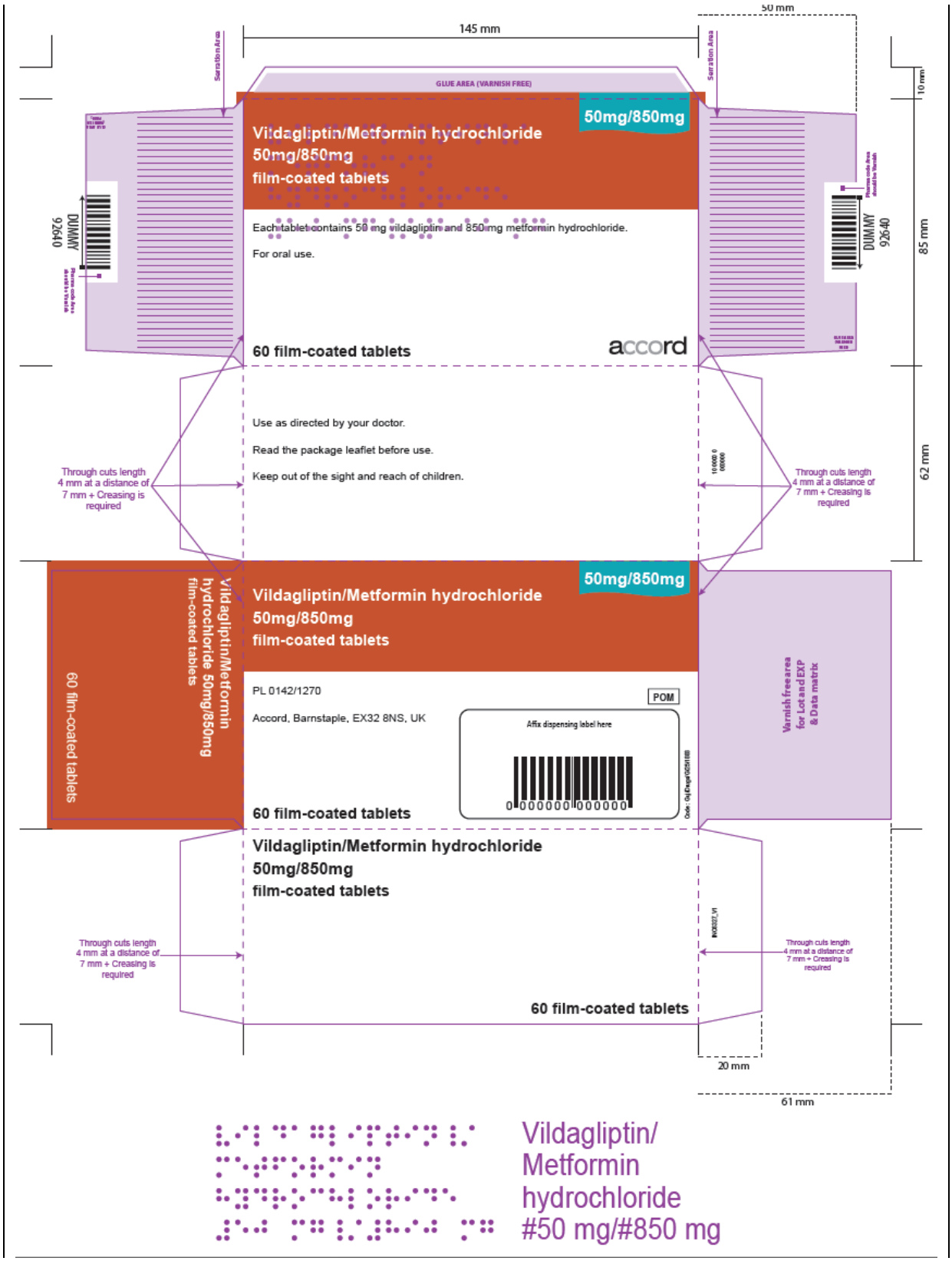
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with Vildagliptin and metformin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered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

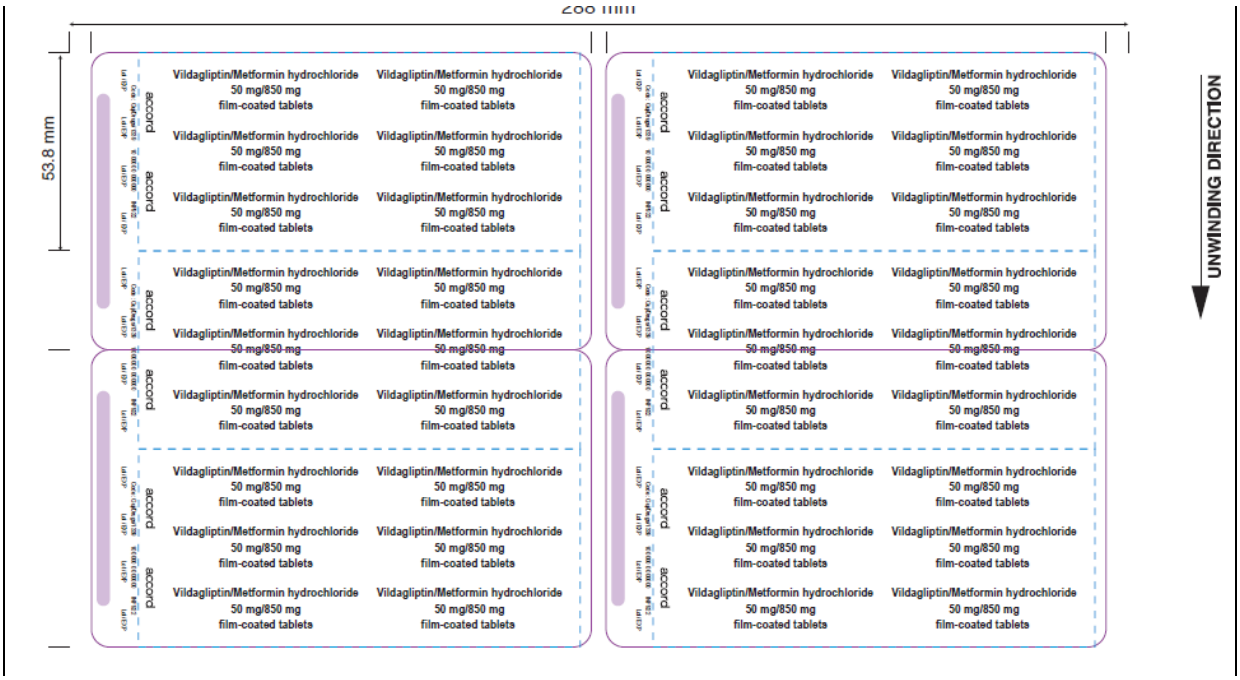
The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

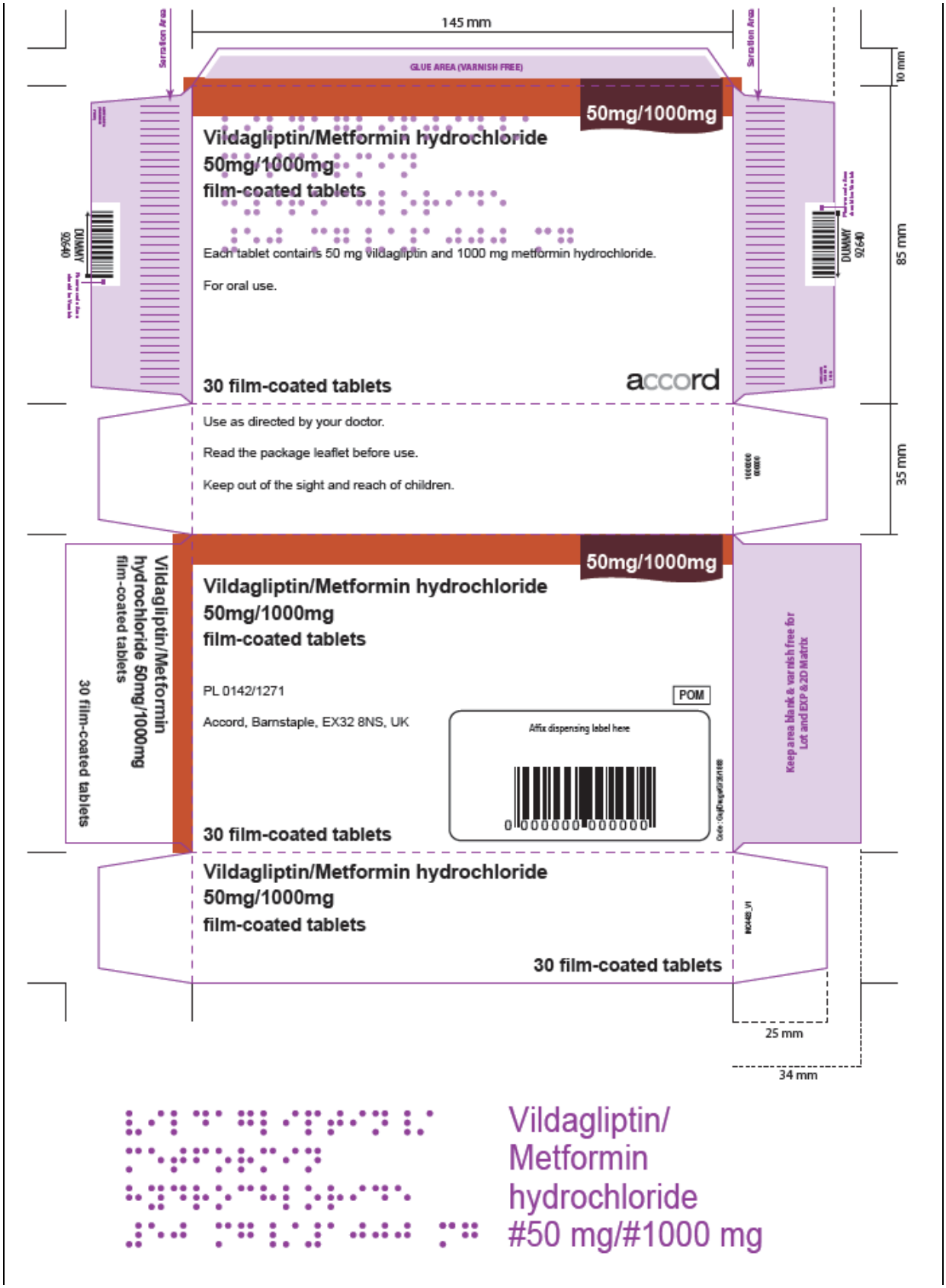
In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

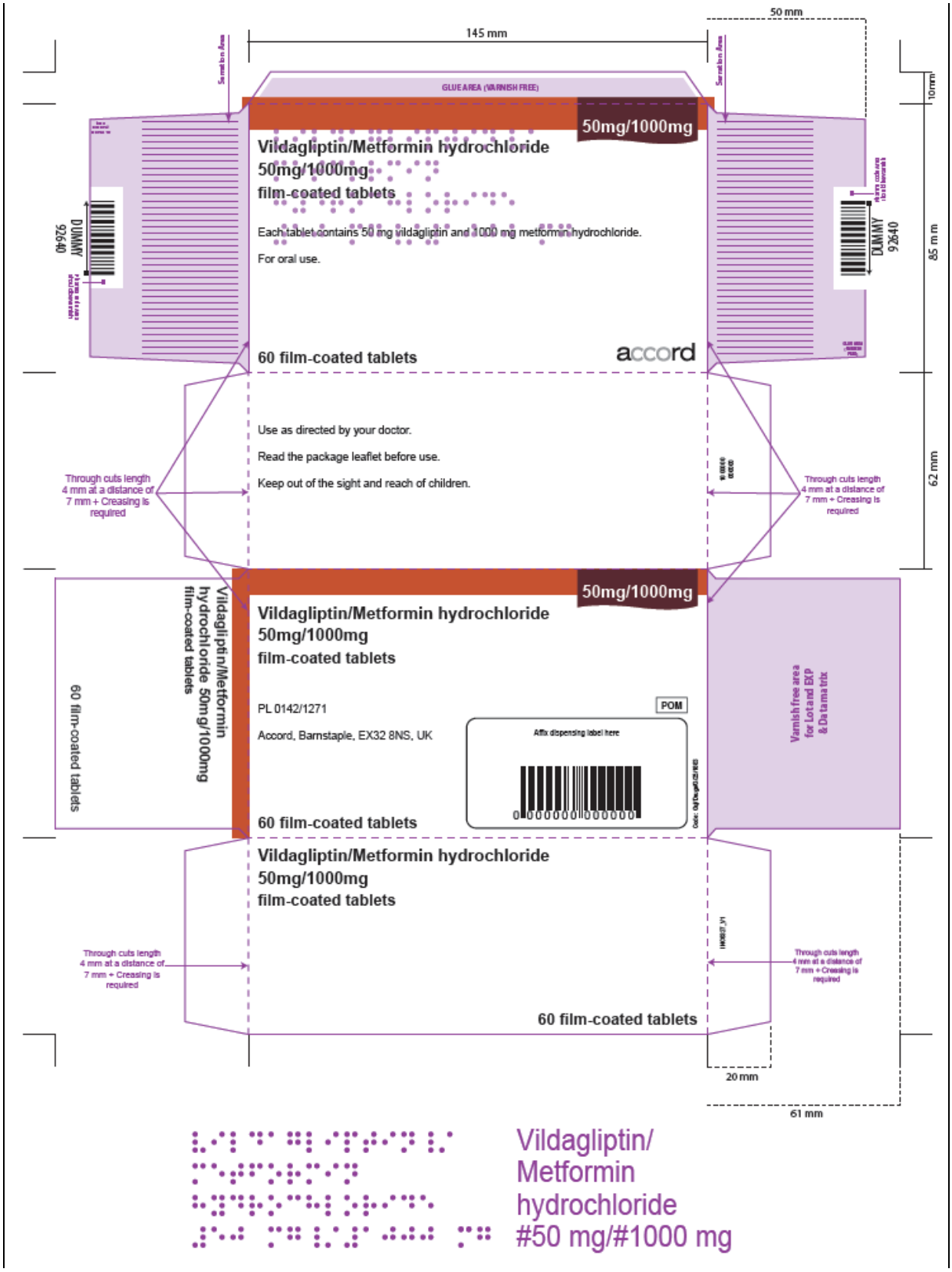
Representative copies of the labels at the time of licensing are provided below.




50 mm
145 mm
Serration Area
GLUE AREA (VARNISH FREE)
50mg/850mg
Vildagliptin/Metformin hydrochloride
50mg/850mg
film-coated tablets
Each tablet contains 50 mg vildagliptin and 850 mg metformin hydrochloride.
For oral use.
DUMMY
92640
10 mm
85 mm
62 mm
60 film-coated tablets
accord
Use as directed by your doctor.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Through cuts length 4 mm at a distance of 7 mm + Creasing is required
Through cuts length 4 mm at a distance of 7 mm + Creasing is required
Vildagliptin/Metformin hydrochloride 50mg/850mg film-coated tablets
60 film-coated tablets
PL 0142/1270
Accord, Barnstaple, EX32 8NS, UK
POM
Affix dispensing label here
Varnish free area for Lot and EXP & Data matrix
Through cuts length 4 mm at a distance of 7 mm + Creasing is required
Through cuts length 4 mm at a distance of 7 mm + Creasing is required
20 mm
61 mm
Vildagliptin/
Metformin
hydrochloride
#50 mg/#850 mg


200 mm
53.8 mm
UNWINDING DIRECTION
accord
Vildagliptin/Metformin hydrochloride
50 mg/850 mg
film-coated tablets


145 mm
Serration Area
GLUE AREA (VARNISH FREE)
50mg/1000mg
Vildagliptin/Metformin hydrochloride
50mg/1000mg
film-coated tablets
Each tablet contains 50 mg vildagliptin and 1000 mg metformin hydrochloride.
For oral use.
30 film-coated tablets
accord
Use as directed by your doctor.
Read the package leaflet before use.
Keep out of the sight and reach of children.
10 mm
85 mm
35 mm
Vildagliptin/Metformin hydrochloride 50mg/1000mg film-coated tablets
30 film-coated tablets
PL 0142/1271
Accord, Barnstaple, EX32 8NS, UK
POM
Affix dispensing label here
Keep area blank & varnish free for Lot and EXP & 2D Matrix
25 mm
34 mm
Vildagliptin/
Metformin
hydrochloride
#50 mg/#1000 mg


50 mm
145 mm
GLUE AREA (VARNISH FREE)
50mg/1000mg
Vildagliptin/Metformin hydrochloride
50mg/1000mg
film-coated tablets
Each tablet contains 50 mg vildagliptin and 1000 mg metformin hydrochloride.
For oral use.
DUMMY
92640
60 film-coated tablets
accord
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Read the package leaflet before use.
Keep out of the sight and reach of children.
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10mm
85 mm
62 mm
Vildagliptin/Metformin hydrochloride 50mg/1000mg film-coated tablets
60 film-coated tablets
PL 0142/1271
Accord, Barnstaple, EX32 8NS, UK
POM
Affix dispensing label here
Varnish free area for Lot and EXP & Datamatrix
20 mm
61 mm
Vildagliptin/
Metformin
hydrochloride
#50 mg/#1000 mg

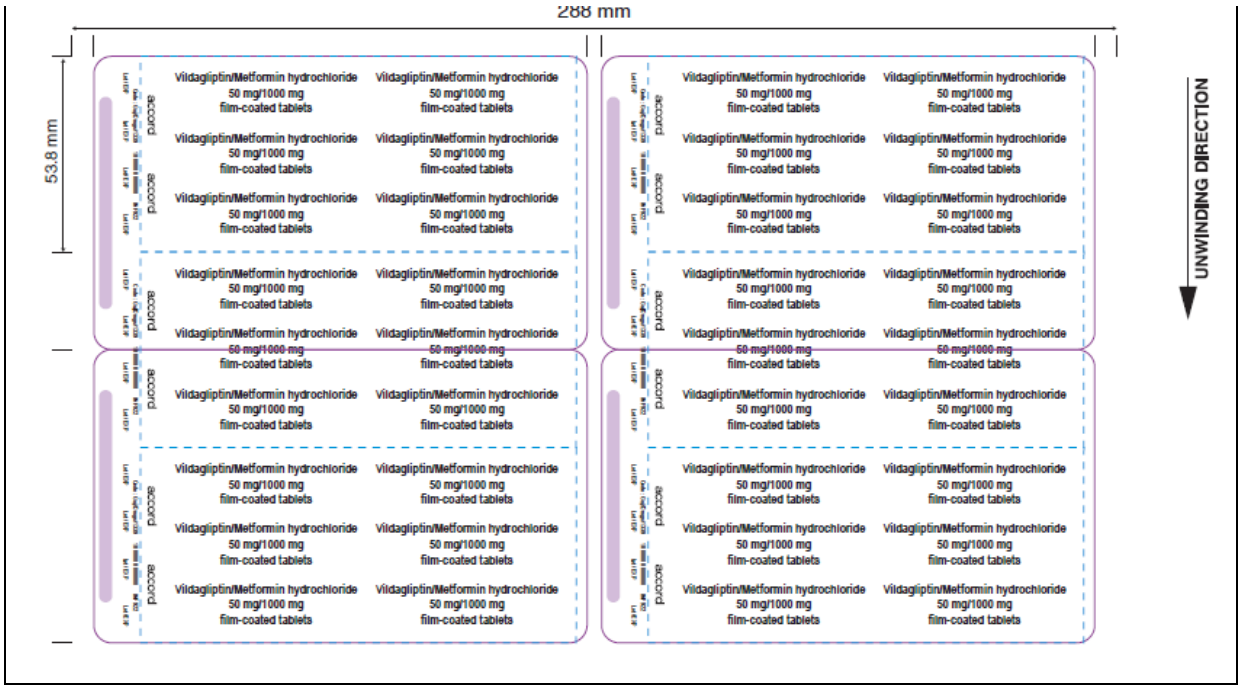
288 mm
53.8 mm
UNWINDING DIRECTION
Vildagliptin/Metformin hydrochloride
50 mg/1000 mg
film-coated tablets
accord

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