UK Public Assessment Report

Irbesartan 75 mg film-coated tablets
Irbesartan 150 mg film-coated tablets
Irbesartan 300 mg film-coated tablets

PL 42930/0005-0007

Wilcare Pharma Limited
Lay Summary
Irbesartan 75 mg film-coated tablets
Irbesartan 150 mg film-coated tablets
Irbesartan 300 mg film-coated tablets
(irbesartan)

This is a summary of the Public Assessment Report (PAR) for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 42930/0005-0007). Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets will be referred to as Irbesartan tablets throughout this report, for ease of reading. It explains how Irbesartan tablets 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 Irbesartan tablets.

For practical information about using Irbesartan tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Irbesartan tablets and what are they used for?
These medicines are the same as Irbesartan 75 mg, 150 mg and 300 mg tablets, which are already authorised (PL 34771/0078-0080). The company that makes Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080), Macleods Pharma UK Limited, has agreed that its scientific data can be used as a basis for the grant of identical licences for Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 42930/0005-0007), respectively.

Irbesartan tablets are used in adult patients to treat high blood pressure (essential hypertension), and to protect the kidneys in patients with high blood pressure, type 2 diabetes and laboratory evidence of impaired kidney function.

How do Irbesartan tablets work?
Irbesartan tablets contain the active substance irbesartan, which belongs to a group of medicines known as angiotensin-II receptor antagonists. Angiotensin-II is a substance produced in the body which binds to receptors in blood vessels causing them to tighten. This results in an increase in blood pressure. Irbesartan prevents the binding of angiotensin-II to these receptors, causing the blood vessels to relax and the blood pressure to lower. Irbesartan tablets slow the decrease of kidney function in patients with high blood pressure and type 2 diabetes.

How are Irbesartan tablets used?
Irbesartan tablets should be swallowed with a glass of water. These tablets can be taken with or without food but the daily dose should be taken at about the same time each day. It is important that the patient continues to take the tablets unless the prescribing doctor advises otherwise.

Please read Section 3 of the package leaflet for further information.

The usual dose for patients with high blood pressure is 150 mg once a day (i.e. two Irbesartan 75 mg film-coated tablets or one Irbesartan 150 mg film-coated tablet). This may be increased to 300 mg at a later stage, depending on the blood pressure response.
The usual starting dose for patients with high blood pressure and type 2 diabetes with kidney disease is 300 mg once daily. The prescribing doctor may advise a lower dose when starting treatment on certain patients, such as those on haemodialysis, or those over the age of 75 years.

Irbesartan 75 mg, 150 mg and 300 mg tablets can only be obtained with a prescription.

**What benefits of Irbesartan tablets have been shown in studies?**
Irbesartan 75 mg, 150 mg and 300 mg tablets are considered identical to the previously granted marketing authorisation for Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080), with the same benefits and risks. No new studies have been provided for Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 42930/0005-0007) but reference is made to the studies for Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080).

**What are the possible side effects from Irbesartan tablets?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

For information about side effects that may occur with using Irbesartan 75 mg, 150 mg and 300 mg tablets, please refer to the package leaflet or the Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency website.

**Why are Irbesartan tablets approved?**
No new or unexpected safety concerns arose from these applications. It was, therefore, considered that the benefits of Irbesartan 75 mg, 150 mg and 300 mg tablets outweigh the risks, and the grant of these marketing authorisations was recommended.

**What measures are being taken to ensure the safe and effective use of Irbesartan tablets?**
A Risk Management Plan (RMP) has been developed to ensure that Irbesartan tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPCs and the package leaflet for Irbesartan tablets, 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 and healthcare professionals will be monitored and reviewed continuously as well.

**Other information about Irbesartan tablets**
These marketing authorisations were granted in the UK on 16 June 2015.

For more information about using Irbesartan tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in August 2015.

The full PAR for Irbesartan tablets follows this summary.
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I Introduction
Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations to Wilcare Pharma Limited for the medicinal products Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 42930/0005-0007) on 16 June 2015.

Irbesartan 75 mg, 150 mg and 300 mg tablets are prescription-only medicines (legal status POM) indicated for the:
- Treatment of essential hypertension
- Treatment of renal disease in patients with hypertension and type 2 diabetes mellitus as part of an antihypertensive medicinal product regimen.

These applications were submitted as abridged simple applications, so-called ‘informed consent’ marketing authorisation applications, according to Article 10c of Directive 2001/83/EC, as amended. These applications cross-refer, and claim to be identical, to Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080), respectively, which were granted to Macleods Pharma UK Limited on 08 May 2012 (PL 34771/0078-0080).

These medicinal products contain the active substance irbesartan.

No new data have been submitted and none are required for these ‘informed consent’ applications, as the data are identical to that of the previously granted, cross-referred products.
II Quality aspects

II.1 Introduction
These are simple, informed consent, marketing authorisation applications for Irbesartan 75 mg, 150 mg and 300 mg tablets submitted under Article 10c of Directive 2001/83/EC, as amended.

These applications cross-refer to Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080). The current applications are considered valid.

Irbesartan 75 mg tablets are formulated as white to off-white oval film coated tablets debossed with "ML 94" on one side and plain on other side (approximate size is 10.8 x 5.7 mm).

Irbesartan 150 mg tablets are formulated as white to off-white oval film coated tablets debossed with "ML 95" on one side and plain on other side (approximate size is 13.6 x 7.2 mm).

Irbesartan 300 mg tablets are formulated as white to off-white oval film coated tablets debossed with "ML 96" on one side and plain on other side (approximate size is 17.2 x 9.2 mm).

Irbesartan 75 mg, 150 mg and 300 mg tablets contain 75 mg, 150 mg and 300 mg of the active substance, irbesartan, respectively. The excipients present in the tablet core of each strength tablet are carmellose calcium, colloidal anhydrous silica, povidone, sodium starch glycolate type A, talc and magnesium stearate. The excipients present in the film coating of each strength tablet are: hypromellose (E464), lactose monohydrate, titanium dioxide (E171) and macrogol. The qualitative and quantitative compositions of these excipients in Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 42930/0005-0007) are identical to those of the respective cross-reference products (PL 34771/0078-0080).

Irbesartan 75 mg, 150 mg and 300 mg tablets are packed into polyvinylidene chloride (PVdC) coated clear polyvinyl chloride (PVC)/polyethylene (PE) film/aluminium foil blisters in pack sizes of 28 tablets. These blisters are further packed into cardboard cartons. This packaging is identical to that of the cross-reference products.

II.2 Drug Substance
Irbesartan
The drug substance specification is identical to that of the cross-reference products and is acceptable.

II.3 Medicinal Product
Pharmaceutical development
A statement from the MA Holder, Wilcare Pharma Limited, has been provided confirming that it has access to all of the data associated with PL 34771/0078-0080 supporting the informed consent application, and is in possession of the quality section of the dossier.
Manufacture of the product
The proposed manufacturing sites are consistent with those registered for the cross-reference products. Evidence of Good Manufacturing Practice (GMP) compliance has been provided, which is identical to that of the cross-reference products.

The proposed composition of each strength tablet is identical to that of the respective cross-reference product, and is acceptable.

The proposed manufacturing process for each strength tablet is identical to that of the respective cross-reference product and is acceptable.

None of the excipients contain materials of animal or human origin. It has been declared that the magnesium stearate is of vegetable origin.

Finished Product Specification
The proposed finished product specification of each strength tablet is identical to that of the respective cross-reference product and is acceptable.

Stability of the product
The proposed shelf-life for Irbesartan 75 mg, 150 mg and 300 mg tablets is 3 years. This shelf life is identical to that of the respective cross-reference products.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The quality data for these applications are consistent with those previously assessed for the marketing authorisations for Irbesartan 75 mg, 150 mg and 300 mg tablets (PL 34771/0078-0080) and, as such, have been judged to be satisfactory. The grant of marketing authorisations is recommended.

III Non-clinical aspects
As these are abridged ‘informed consent’ applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data has been supplied and none are required.

The grant of marketing authorisations is recommended.

IV Clinical aspects
As these are abridged ‘informed consent’ applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Irbesartan 75 mg, 150 mg and 300 mg tablets.
A summary of safety concerns, as approved in the RMP, are listed below:

**Summary table of safety concerns**

<table>
<thead>
<tr>
<th>Summary of safety concerns</th>
<th>Important identified risks</th>
<th>Important potential risks</th>
<th>Missing information</th>
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</thead>
<tbody>
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<td></td>
<td>Renal impairment</td>
<td>Use in 1st trimester of pregnancy</td>
<td>Use in children</td>
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<td>Symptomatic hypotension</td>
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<td>Use in patients who have undergone recent renal transplantation</td>
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<td>Hyperkalaemia</td>
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<td>Use in breast feeding</td>
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<td></td>
<td>Use in patients with primary aldosteronism</td>
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<td>Use in patients with severe hepatic impairment</td>
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</table>
Summary table of risk minimisation measures

<table>
<thead>
<tr>
<th>Safety concern</th>
<th>Routine risk minimisation measures</th>
<th>Additional risk minimisation measures</th>
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<tbody>
<tr>
<td>Renal impairment</td>
<td>The risks (1) associated with the use of the drug product in patients with renal impairment, (2) of renal impairment associated with the use of the drug product, and (3) of renal impairment associated with the concomitant use of the drug product with other medicinal products are described in the SPC Sections 4.2, 4.4, 4.5, 4.8, 4.9 and 5.2, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
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<tr>
<td>Symptomatic hypotension</td>
<td>The risks (1) of symptomatic hypotension associated with the use of the drug product (2) of hypotension associated with the concomitant use of the drug product with other medicinal products are described in the SPC Sections 4.4, 4.5 and 4.8, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
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<tr>
<td>Hyperkalaemia</td>
<td>The risks (1) of hyperkalaemia associated with the use of the drug product (2) associated with the use of the drug product in patients at risk of hyperkalaemia and (3) of hyperkalaemia associated with the concomitant use of the drug product with other medicinal products are described in the SPC Sections 4.4, 4.5 and 4.8, and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
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<tr>
<td>Safety concern</td>
<td>Routine risk minimisation measures</td>
<td>Additional risk minimisation measures</td>
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<tr>
<td>Use in patients with primary</td>
<td>The risk associated with the use of the drug product in patients with primary aldosteronism is described in the SPC Section 4.4, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
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<tr>
<td>aldosteronism</td>
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<td>Concomitant use of lithium</td>
<td>The risks associated with concomitant use of lithium with the drug product are described in the SPC Sections 4.4 and 4.5 and appropriate advice is provided to the prescriber to minimise these risk.</td>
<td>None</td>
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<tr>
<td>Hypersensitivity</td>
<td>The risk of hypersensitivity associated with the use of the drug product is described in the SPC Sections 4.3 and 4.8 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Use in 2nd and 3rd trimester of</td>
<td>The risk associated with use of the drug product in 2nd and 3rd trimester of pregnancy are described in the SPC Sections 4.3, 4.4 and 4.6 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
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<tr>
<td>pregnancy</td>
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### Important potential risks

| Use in 1st trimester of pregnancy    | The risks associated with use of the drug product in 1st trimester of pregnancy is described in the SPC Sections 4.4 and 4.6, and appropriate advice is provided to the prescriber to minimise these risk. | None                                 |

### Missing Information

| Use in children                      | The SPC Section 4.2, 4.4, 4.8, 5.1 and 5.2 state that safety of the drug product is not | None                                 |
The grant of marketing authorisations is recommended.

V  User consultation
The package leaflet text corresponds to the text within the package leaflet for the cross-reference products, and is acceptable. A package leaflet mock-up was not approved during the assessment process. The applicant has committed to submitting a bridging report, to support the user consultation of the package leaflet with target patient groups, once the licence has been granted. The applicant has confirmed that they will submit the bridging report for assessment prior to the commercial launch of the product, which is acceptable.

VI  Overall conclusion, benefit/risk assessment and recommendation
The quality of these products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the respective cross-reference products. The benefit-risk assessment is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), package leaflet text and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference products. In accordance with Directive 2012/84/EU, the current approved UK
versions of the SmPCs and package leaflet text for these products are available on the Medicines and Healthcare products Regulatory Agency website.

The currently approved labelling text is listed below:
Irbesartan 150 mg Film-coated Tablets

Each Film-coated tablet contains
Irbesartan 150 mg

Also contains lactose monohydrate
See leaflet for further information
UKPAR Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets

28 Film-coated tablets
Oral use

Irbesartan 300 mg Film-coated Tablets
Each Film-coated tablet contains
Irbesartan 300 mg
Also contains lactose monohydrate
See leaflet for further information
Annex - Table of content of the PAR update
Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

<table>
<thead>
<tr>
<th>Scope</th>
<th>Product information affected</th>
<th>Date of start of the procedure</th>
<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
<th>Assessment report attached Y/N (version)</th>
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