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LAY SUMMARY

Irbesartan 75 mg film-coated tablets
Irbesartan 150 mg film-coated tablets
Irbesartan 300 mg film-coated tablets
(irbesartan; film-coated tablet; 75 mg, 150 mg and 300 mg)

This is a summary of the Public Assessment Report (PAR) for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423). It explains how Irbesartan 75 mg, 150 mg and 300 mg film-coated 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 75 mg, 150 mg and 300 mg film-coated tablets.

For practical information about using Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets, patients should read the package leaflet(s) or contact their doctor or pharmacist.

Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets may be referred to as Irbesartan film-coated tablets in this report.

What are Irbesartan film-coated tablets and what are they used for?
Irbesartan film-coated tablets are medicines that contain the active substance irbesartan. Irbesartan film-coated tablets are used to:

- treat high blood pressure (essential hypertension);
- protect the kidney in patients with high blood pressure, type 2 diabetes and laboratory evidence of impaired kidney function.

These medicines are identical to Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004;FR/H/428/001-003/DC), which were authorised in the UK to Medipha Sante SN, France on 17 August 2010 following a Decentralised procedure with France as Reference Member State. Medipha Sante SN has agreed that the scientific data presented for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC can be used for the applications for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423).

How are Irbesartan film-coated tablets used?
Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets are taken by mouth. The tablets should be swallowed with a sufficient amount of fluid (e.g. one glass of water). The recommended dose is:

- **Patients with high blood pressure**
The usual dose is 150 mg once a day. The dose may later be increased to 300 mg once daily depending on blood pressure response.

- **Patients with high blood pressure and type 2 diabetes with kidney disease**
In patients with high blood pressure and type 2 diabetes; 300 mg once daily is the preferred maintenance dose for the treatment of associated kidney disease.

The doctor may advise a lower dose, especially when starting treatment in certain patients such as those on haemodialysis, or those over the age of 75 years.

The tablets can be taken with or without food. The tablets should be taken daily at about the same time each day. It is important that the tablets are taken until your doctor tells you otherwise.

Irbesartan should not be given to children under 18 years of age.
For further information on how Irbesartan film-coated tablets are used, refer to the Summary of Product Characteristics.

Irbesartan film-coated tablets can only be obtained on prescription.

**How do Irbesartan film-coated tablets work?**

The active ingredient, irbesartan, 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 slows the decrease of kidney function in patients with high blood pressure and type 2 diabetes.

**How have Irbesartan film-coated tablets been studied?**

These applications are identical to previously granted applications for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC).

The company (Bristol Laboratories Limited) referred to data provided by Medipha Sante SN for the grant of licences for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC), as a basis for the grant of identical licences for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423).

**What are the benefits and risks of Irbesartan film-coated tablets?**

As Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423) are considered identical to Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC), their benefits and risks are taken as being the same as those for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC).

**Why are Irbesartan film-coated 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 film-coated tablets outweigh their risks; and the grant of Marketing Authorisations was recommended.

**What measures are being taken to ensure the safe and effective use of Irbesartan film-coated tablets?**

A Risk Management Plan has been developed to ensure that Irbesartan film-coated tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Irbesartan film-coated tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

**Other information about Irbesartan film-coated tablets.**

Marketing Authorisations were granted in the UK on 06 December 2013.

For more information about treatment with Irbesartan film-coated tablets, read the package leaflet(s), or contact your doctor or pharmacist.

This summary was last updated in February 2014.

The full PAR for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets follows this summary.
SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Bristol Laboratories Limited Marketing Authorisations for the medicinal products Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423) on 06 December 2013. The products are prescription-only medicines (POM) and are indicated for the treatment of:

- essential hypertension;
- renal disease in patients with hypertension and type 2 diabetes mellitus as part of an antihypertensive medicinal product regimen.

The applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC), which were authorised in the UK to Medipha Sante SN, France on 17 August 2010 following a Decentralised procedure with France as Reference Member State.

The active ingredient, irbesartan, is an angiotensin II receptor antagonist. Angiotensin II receptor antagonists, also known as angiotensin receptor blockers (ARBs), AT₁-receptor antagonists or sartans, are a group of medicines which modulate the renin-angiotensin-aldosterone system. AT₁-receptor antagonists block the activation of angiotensin II AT₁-receptors. Blockade of AT₁-receptors directly causes vasodilatation, reduces secretion of vasopressin, reduces production and secretion of aldosterone, amongst other actions – the combined effect of which is reduction of blood pressure.

No new data were submitted nor were they necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 17907/0421-0423

PROPRIETARY NAME(S): Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets

ACTIVE(S): Irbesartan

COMPANY NAME: Bristol Laboratories Limited

E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended

LEGAL STATUS: POM

1. INTRODUCTION
These are abridged applications for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC), which were authorised in the UK to Medipha Sante SN, France on 17 August 2010 following a Decentralised procedure with France as Reference Member State. The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)
The proposed names of the products are Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each film-coated tablet for oral use contains 75 mg, 150 mg or 300 mg of irbesartan. The tablets are packaged in polyvinylchloride/polyvinylidene chloride/aluminium (PVC/PVDC/Al) blisters. The blisters are packed with the Patient Information Leaflet in cartons in pack sizes of 14, 28, 30, 56, 84, 90 and 98 film-coated tablets.

Not all pack sizes may be marketed.

The proposed shelf life is 30 months. There are no special storage instructions for the products.

The packaging, proposed shelf-life and absence of special storage conditions are consistent with the details registered for the cross-reference products.

2.3 Legal status
On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Bristol Laboratories Limited, Unit 3, Canalside, Northbridge Road, Berkhamsted, Herts HP4 1EG.

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 products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the cross-reference products.
2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specifications are in line with the details registered for the respective cross-reference products.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
With the exception of lactose monohydrate, none of the excipients contains material of animal or human origin. The suppliers of lactose monohydrate have confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the suppliers have confirmed that no ruminant material, other than calf rennet, is used during the production of lactose monohydrate. This is consistent with the respective cross-reference products.

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged applications, as the proposed products are manufactured to the same formula and utilise the same processes as the reference products Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC).

3. EXPERT REPORT
The applicant cross-refers to the data for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC), to which these applications are claimed to be identical. This is acceptable.

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

5. SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed Summaries of Product Characteristics are consistent with the details registered for the respective cross-reference products.

6. PATIENT INFORMATION LEAFLETS (PILs) AND LABELLING
PIL
The Patient Information Leaflets have been prepared in line with the details registered for the cross-reference products.

Medipha Sante SN has previously submitted results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive 2001/83/EC, for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC). The results indicate that the leaflet is well-structured and organised, easy to understand, and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

User-testing of the PIL for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423) has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC) as the ‘parent PIL’.

Carton and label
The proposed artwork is consistent with the artwork registered for the respective cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the names of the products 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 applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications 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 submitted an acceptable Environmental Risk Assessment, prepared in accordance with CHMP Guideline on Environmental Risk Assessment of Medicinal Products for Human Use (Ref: EMEA/CHMP/SWP/4447/00), which indicates that the products are unlikely to represent a risk to the environment following prescribed usage.

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications 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.

Suitable justification has been provided for non-submission of a Risk Management Plan (RMP). As these applications are identical versions of already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profile of the active ingredient is well-established. These applications were received prior to the date (July 2012) when the pharmacovigilance regulations in accordance with Directive 2010/84/EU came into force.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

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

EFFICACY
These applications are identical to previously granted applications for Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 34760/0002-0004; FR/H/428/001-003/DC).

SAFETY
No new safety data were supplied or required for these applications. Irbesartan has a well-established safety profile. No new or unexpected safety concerns arise from these applications.

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

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 products are identical to the cross-reference products. Extensive clinical experience with irbesartan is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Marketing Authorisation applications on 25 December 2011.

2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 24 April 2012.

3. Following assessment of the application the MHRA requested further information relating to the dossier on 19 July 2012, 19 July 2013, 07 October 2013 and 12 November 2013.

4. The applicant responded to the MHRA’s request, providing further information on the 17 May 2013, 05 September 2013, 05 November 2013 and 18 November 2013.

5. The applications were granted on 06 December 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.
MHRA PAR – Irbesartan 75 mg, 150 mg and 300 mg film-coated tablets (PL 17907/0421-0423)