Public Assessment Report

Decentralised Procedure

VALSARTAN 40 MG FILM-COATED TABLETS
VALSARTAN 80 MG FILM-COATED TABLETS
VALSARTAN 160 MG FILM-COATED TABLETS
VALSARTAN 320 MG FILM-COATED TABLETS

(Valsartan)

Procedure No: UK/H/3444/001-4/DC

UK Licence No: PL 34771/0019-22

MACLEODS PHARMA UK LIMITED.
Lay Summary

On 24 August 2012, Germany, Spain, Italy and the UK agreed to grant Marketing Authorisations to Macleods Pharma UK Limited for the medicinal products Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets (PL 34771/0019-22; UK/H/3444/001-4/DC). The licences were granted via the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS). After a subsequent national phase, Marketing Authorisations were granted in the UK on 19 October 2012. These are Prescription-Only Medicines (POM).

Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets contain valsartan as the active ingredient. Valsartan belongs to a class of medicines known as angiotensin II receptor antagonists which help to control high blood pressure. Angiotensin II is a substance in the body that causes vessels to tighten, thus causing your blood pressure to increase. Valsartan works by blocking the effect of angiotensin II. As a result, blood vessels relax and blood pressure is lowered.

Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets are used to treat:
- High blood pressure in children and adolescents 6 to 18 years of age.

Valsartan 80 mg, 160 mg and 320 mg film-coated tablets are used to treat:
- High blood pressure in adults

Valsartan 40 mg, 80 mg, 160 mg film-coated tablets used to treat:
- Adult patients after a recent (between 12 hours and 10 days) heart attack (myocardial infarction).
- Symptomatic heart failure in adults.

No new or unexpected safety concerns arose from these applications and it was judged that the benefits of taking Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets outweigh the risks and therefore Marketing Authorisations were granted.
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## Module 1

| **Product Name** | Valsartan 40 mg film-coated tablets  
|                 | Valsartan 80 mg film-coated tablets  
|                 | Valsartan 160 mg film-coated tablets.  
|                 | Valsartan 320 mg film-coated tablets.  |
| **Type of Application** | Generic, Article 10.1 |
| **Active Substances** | Valsartan |
| **Form** | Film-coated tablets |
| **Strength** | 40 mg, 80 mg, 160 mg and 320 mg. |
| **MA Holder** | Macleods Pharma UK Limited  
|                | Golden Gate Lodge, Crewe Hall,  
|                | Crewe, Cheshire,  
|                | CW1 6UL,  
|                | UK |
| **Reference Member State (RMS)** | UK |
| **Concerned Member States (CMS)** | Germany, Spain and Italy |
| **Procedure Number** | UK/H/3444/001-4/DC |
| **Timetable** | Day 208–24 August 2012. |
Module 2
Summary of Product Characteristics

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 3
Patient Information Leaflet

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 4
Labelling

Carton:

Blister:

Space for embossing batch details & expiry
The following text is the approved labelling text as agreed during the decentralised procedure. No labelling mock-ups have been provided for the 160 mg and 320 mg strengths. In accordance with medicines legislation, the product shall not be marketed in the UK until approval of the labelling mock-ups has been obtained.

<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>{Blister made of PVdC coated clear PVC/PE film/ Aluminium}</td>
</tr>
</tbody>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

Valsartan 160 mg film-coated tablets

Valsartan

2. **NAME OF THE MARKETING AUTHORISATION HOLDER**

Macleods Pharma UK Limited

3. **EXPIRY DATE**

EXP

4. **BATCH NUMBER**

BN

5. **OTHER**

[To be completed nationally]
| PARTICULARS TO APPEAR ON THE <OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING> |
| {OUTER CARTON/ LABEL} |

1. **NAME OF THE MEDICINAL PRODUCT**

Valsartan 160 mg film-coated tablets

Valsartan

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

Each tablet contains valsartan 160 mg

3. **LIST OF EXCIPIENTS**

4. **PHARMACEUTICAL FORM AND CONTENTS**

Film-coated Tablets

28 tablets

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use

Read the package leaflet before use

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the reach and sight of children

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

None
8. **EXPIRY DATE**

EXP

9. **SPECIAL STORAGE CONDITIONS**

Store below 25°C in the original package. Protect from moisture.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

None

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Macleods Pharma UK Limited
Golden Gate Lodge, Crewe Hall,
Crewe, Cheshire,
CW1 6UL, United Kingdom

12. **MARKETING AUTHORISATION NUMBER(S)**

PL 34771/0021

13. **BATCH NUMBER**

BN

14. **GENERAL CLASSIFICATION FOR SUPPLY**

POM

15. **INSTRUCTIONS ON USE**

Not applicable as this product is for medical prescription only

16. **INFORMATION IN BRAILLE**

Valsartan 160 mg film-coated tablets
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
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<tr>
<td>{Blister made of PVdC coated clear PVC/PE film/ Aluminium}</td>
</tr>
</tbody>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

Valsartan 320 mg film-coated tablets

Valsartan

2. **NAME OF THE MARKETING AUTHORISATION HOLDER**

Macleods Pharma UK Limited

3. **EXPIRY DATE**

EXP

4. **BATCH NUMBER**

BN

5. **OTHER**

[to be completed nationally]
PARTICULARS TO APPEAR ON THE <OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING>

<OUTER CARTON/ LABEL>

1. **NAME OF THE MEDICINAL PRODUCT**

Valsartan 320 mg film-coated tablets

Valsartan

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

Each tablet contains valsartan 320 mg

3. **LIST OF EXCIPIENTS**

4. **PHARMACEUTICAL FORM AND CONTENTS**

Film-coated Tablets

28 tablets

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use

Read the package leaflet before use

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the reach and sight of children

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

None
8. **EXPIRY DATE**

   EXP

9. **SPECIAL STORAGE CONDITIONS**

   Store below 25°C in the original package. Protect from moisture.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

   None

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

   Macleods Pharma UK Limited
   Golden Gate Lodge, Crewe Hall,
   Crewe, Cheshire,
   CW1 6UL, United Kingdom

12. **MARKETING AUTHORISATION NUMBER(S)**

   PL 34771/0022

13. **BATCH NUMBER**

   BN

14. **GENERAL CLASSIFICATION FOR SUPPLY**

   POM

15. **INSTRUCTIONS ON USE**

   Not applicable as this product is for medical prescription only

16. **INFORMATION IN BRAILLE**

   Valsartan 320 mg film-coated tablets
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the Member States considered that the applications for Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets (PL 34771/0019-22; UK/H/3444/001-4/DC) could be approved. These applications were submitted via the decentralised procedure, with the UK as Reference Member State (RMS) and Germany, Spain and Italy as Concerned Member States (CMS). These products are prescription-only medicines (POM).

Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets are indicated for:
- Treatment of hypertension in children and adolescents 6 to 18 years of age.

Valsartan 80 mg, 160 mg and 320 mg film-coated tablets are indicated for:
- treatment of essential hypertension in adults

Valsartan 40 mg, 80 mg and 160 mg film-coated tablets are indicated for:
- Recent myocardial infarction
  Treatment of clinically stable adult patients with symptomatic heart failure or asymptomatic left ventricular systolic dysfunction after a recent (12 hours-10 days) myocardial infarction (see sections 4.4 and 5.1 of SmPC).

  - Heart failure
    Treatment of symptomatic heart failure in adult patients when Angiotensin Converting Enzyme (ACE) inhibitors cannot be used, or as add-on therapy to ACE inhibitors when beta blockers cannot be used.

These are abridged applications submitted under Article 10(1) of Directive 2001/83/EC as amended, cross-referring to Diovan 40 mg, 80 mg and 160 mg Capsules (Novartis Pharmaceuticals UK Limited, UK), which were first authorised in October 1997. The reference products have been registered in the EEA for more than 10 years, hence the period of data exclusivity has expired. The reference product used in the bioequivalence study was Diovan Forte 320 mg film-coated tablets (Novartis Pharma GmbH, Germany) taken from the german market. It has been confirmed that this product is identical to the equivalent product in the UK (Diovan 320 mg film-coated tablets).

Whilst reference is made to the capsule form of the originator, bioequivalence was established by comparison to the tablet form of Diovan. The Diovan tablets and capsules are considered part of the same “global marketing authorisation and the application is in accordance with Article 10(1) of Directive 2001/83/EC as amended.

Valsartan is an orally active, potent, and specific angiotensin II (Ang II) receptor antagonist. It acts selectively on the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. The increased plasma levels of Ang II following AT1 receptor blockade with valsartan may stimulate the unblocked AT2 receptor, which appears to counterbalance the effect of the AT1 receptor. Valsartan does not exhibit any partial agonist activity at the AT1 receptor and has much (about 20,000 fold) greater affinity for the AT1 receptor than for
the AT₂ receptor. Valsartan is not known to bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

No new non-clinical studies were conducted, which is acceptable given that the products are intended to be generic versions of the originator products that have been licensed for over 10 years.

One bioequivalence study (single dose) was submitted to support these applications, comparing the test product Valsartan 320 mg film-coated tablets (Macleods Pharma UK Limited) with the reference product Diovan Forte 320 mg film-coated tablets (Novartis Pharma GmbH, Germany).

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the applications were for products that are intended to be generic versions of the originator products that have been licensed for over 10 years. The bioequivalence study was carried out in accordance with Good Clinical Practice (GCP).

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

The RMS and CMS considered that the applications could be approved with the end of procedure (Day 208) on 24 August 2012. After the subsequent national phase, the licences were granted in the UK on 19 October 2012.
### II. ABOUT THE PRODUCT

| Name of the product in the Reference Member State | Valsartan 40 mg film-coated tablets  
patientartan 80 mg film-coated tablets  
Valsartan 160 mg film-coated tablets.  
Valsartan 320 mg film-coated tablets. |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Name(s) of the active substance(s) (INN)</td>
<td>Valsartan</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>Angiotensin-II antagonists, plain (C09CA03).</td>
</tr>
<tr>
<td>Pharmaceutical form and strength(s)</td>
<td>40 mg, 80 mg, 160 mg and 320 mg film-coated tablets</td>
</tr>
<tr>
<td>Reference numbers for the Mutual Recognition Procedure</td>
<td>UK/H/3444/001-4/DC</td>
</tr>
<tr>
<td>Reference Member State</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Concerned Member State</td>
<td>Germany, Spain and Italy</td>
</tr>
<tr>
<td>Marketing Authorisation Number(s)</td>
<td>PL 34771/0019-22</td>
</tr>
</tbody>
</table>
| Name and address of the authorisation holder   | Macleods Pharma UK Limited  
Golden Gate Lodge, Crewe Hall,  
Crewe, Cheshire,  
CW1 6UL, UK                                                                          |
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

S. Active substance

INN: Valsartan

Chemical names: L-Valine, N-(1-oxopentyl)-N-[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]

\[ N-[p-(o-1H-Tetrazol-5-ylphenyl)benzyl]-N-valeryl-L-valine \]

(2S)-3-Methyl-2-[pentanoyl][2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]amino]butanoic acid (IUPAC / Ph. Eur.)

Structure:

![Structure diagram]

Molecular formula: \( C_{24}H_{29}N_{5}O_{3} \)
Molecular mass: 435.5

Appearance: Valsartan is a white or almost white hygroscopic powder.
Solubility: Valsartan is practically insoluble in water, freely soluble in anhydrous ethanol and sparingly soluble in methylene chloride.

Valsartan is 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 specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised. Satisfactory Certificates of Analysis have been provided for all working standards. Batch analysis data are provided and comply with the proposed specification.
Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

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

P. Medicinal Product
Other Ingredients
Other ingredients consist of the pharmaceutical excipients microcrystalline cellulose, crospovidone (Type A), colloidal anhydrous silica, magnesium stearate, hypromellose (E464), titanium dioxide (E171), macrogol 8000 and talc. In addition:

- the 40 mg strength also contains iron oxide yellow (E172);
- the 80 mg strength also contains iron oxide yellow (E172) and iron oxide red (E172);
- the 160 mg strength also contains iron oxide yellow (E172), iron oxide red (E172) and iron oxide black (E172);
- the 320 mg strength also contains iron oxide red (E172) and iron oxide black (E172).

All excipients comply with their respective European Pharmacopoeia monographs with the exception of iron oxide, yellow, red and black which are controlled to National Formulary (NF) specifications. Satisfactory certificates of analysis have been provided for all excipients. Suitable batch analysis data have been provided for each excipient.

None of the excipients contain materials of animal or human origin.

No genetically modified organisms (GMO) have been used in the preparation of these products.

Pharmaceutical Development
The objective of the development programme was to formulate stable, robust, film-coated tablets containing 40 mg, 80 mg, 160 mg or 320 mg valsartan, which could be considered generic medicinal products of Diovan 40 mg, 80 mg, 160 mg and 320 mg tablets (Novartis Pharma GmbH, Germany).

A satisfactory account of the pharmaceutical development has been provided.

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

Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated at pilot scale and has shown satisfactory results. In addition the Marketing Authorisation Holder (MAH) has committed to perform process validation on commercial scale batches for all strengths.

Finished Product Specification
The proposed finished product specifications are acceptable. Test methods have been described and have been adequately validated. Batch data have been provided, which
comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

**Container-Closure System**
All strengths of the finished product are packaged in polyvinylidene chloride (PVdC) coated clear polyvinylchloride (PVC)/polyethylene (PE) film/aluminium foil blister strips in pack sizes of 28 film-coated tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

**Stability of the product**
Stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years with the storage conditions ‘Store below 25°C in the original package. Protect from moisture.’

**Bioequivalence/bioavailability**
Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence study.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels**
The SmPCs, PIL and labels are acceptable.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package 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.

**Marketing Authorisation Application (MAA) form**
The MAA forms are satisfactory.

**Quality Overall Summary**
The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

**Conclusion**
There are no objections to the approval of these products from a pharmaceutical view-point.

**III.2 NON-CLINICAL ASPECTS**
As the pharmacodynamic, pharmacokinetic and toxicological properties of valsartan are well-known, no new non-clinical studies are required and none have been provided.

The applicant’s non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant pharmacology and toxicology.
Since Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets are intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment (ERA) is therefore not deemed necessary.

There are no objections to the approval of these products from a non-clinical view-point.

### III.3 CLINICAL ASPECTS

#### Pharmacokinetics

In support of these applications, the marketing authorisation holder has submitted the following bioequivalence study:

**An open label, randomised, single-dose, two-period, two-sequence, two treatment, crossover study to compare the pharmacokinetics of the test product Valsartan 320 mg film-coated tablets (Macleods Pharma UK Limited) versus the reference product Diovan Forte 320 mg film-coated tablets (Novartis Pharma GmbH, Germany) in healthy adult volunteers under fasted conditions.**

All volunteers received a single oral dose of either the test or reference product as a 1 x 320 mg tablet administered with 240 ml of water after an overnight fast of at least 10 hours. Blood samples were taken for the measurement of pharmacokinetic parameters at pre- and up to 48 hours post dose. The washout period between treatment periods was at least 7 days.

The pharmacokinetic results for valsartan are presented below (log-transformed values; geometric least square mean and 90% confidence intervals):

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameters</th>
<th>90% Confidence Interval (%)</th>
<th>Ratio (T/R) (%)</th>
<th>Power (%)</th>
<th>Intra Subject C.V. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$</td>
<td>95.79 - 121.52</td>
<td>107.89</td>
<td>86.87</td>
<td>31.46</td>
</tr>
<tr>
<td>$AUC_{0-t}$</td>
<td>99.53 - 123.49</td>
<td>110.87</td>
<td>92.44</td>
<td>28.38</td>
</tr>
<tr>
<td>$AUC_{0-\text{inf}}$</td>
<td>99.30 - 122.18</td>
<td>110.15</td>
<td>94.15</td>
<td>27.25</td>
</tr>
</tbody>
</table>

The 90% confidence intervals for AUC and $C_{\text{max}}$ for test versus reference product for valsartan are within predefined acceptance criteria specified in "Guideline on the Investigation of Bioequivalence" (CPMP/EWP/QWP/1401/98 Rev 1/, Corr). Thus, the data support the claim that the test product is bioequivalent to the reference product.

As the 40 mg, 80 mg and 160 mg and 320 mg strengths of the product meet the criteria specified in “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev 1/, Corr), the results and conclusions of the bioequivalence study on the 320 mg strength can be extrapolated to the 40 mg, 80 mg and 160 mg strengths.
Pharmacodynamics
No new pharmacodynamic data were submitted and none were required for these applications.

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

Safety
With the exception of the data generated during the bioequivalence study, no new safety data were submitted and none were required for these applications. No new or unexpected safety issues were highlighted by the bioequivalence data.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPCs, PIL and labels are acceptable. The SmPCs are consistent with that for the originator products. The PIL is consistent with the SmPCs and in line with current guidelines. The labelling is in-line with current guidelines.

MAA Forms
The MAA forms are satisfactory.

Clinical Overview
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Pharmacovigilance System and Risk Management Plan
The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has 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 not submitting a Risk Management Plan for these products.

Conclusion
There are no objections to the approval of these products from a clinical view-point.
IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The quality characteristics of Valsartan 40 mg, 80 mg, 160 mg and 320 mg film-coated tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type. The pharmacodynamic, pharmacokinetic and toxicological properties of valsartan are well-known.

EFFICACY
With the exception of the bioequivalence study, no new data were submitted and none are required for applications of this type.

Bioequivalence has been demonstrated between the applicant’s Valsartan 320 mg film-coated tablets and its respective reference product Diovan Forte 320 mg film-coated tablet (Novartis Pharma GmbH, Germany). As the 40 mg, 80 mg, 160 mg and 320 mg strengths of the product meet the biowaiver criteria specified in “Guideline on the Investigation of Bioequivalence” (CPMP/EWP/QWP/1401/98 Rev 1/, Corr), the results and conclusions of the bioequivalence study on the 320 mg strength can be extrapolated to the 40 mg, 80 mg and 160 mg strengths.

SAFETY
With the exception of the bioequivalence study, no new data were submitted and none are required for applications of this type. As the safety profile of valsartan is well-known, no additional data were required. No new or unexpected safety concerns arose from the safety data from the bioequivalence study.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with that for the reference products, and in line with current guidelines.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s products and the originator products are interchangeable. Extensive clinical experience with valsartan is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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