Public Assessment Report

Decentralised Procedure

Omeprazole 10mg Gastro-resistant Capsules, hard
Omeprazole 20mg Gastro-resistant Capsules, hard
Omeprazole 40mg Gastro-resistant Capsules, hard
(UK/H/4423/001-003/DC)
Omeprazole 20mg Gastro-resistant Capsules, hard
(UK/H/5144/001/DC)

PL 17780/0523
PL 17780/0524
PL 17780/0525
PL 17780/0583

Winthrop Pharmaceuticals UK Limited
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Winthrop Pharmaceuticals UK Limited (trading as Zentiva) Marketing Authorisations for the medicinal products Omeprazole 10mg Gastro-resistant Capsules, hard (product licence number: PL 17780/0523), Omeprazole 20mg Gastro-resistant Capsules, hard (PL 17780/0524), Omeprazole 40mg Gastro-resistant Capsules, hard (PL 17780/0525) and Omeprazole 20mg Gastro-resistant Capsules, hard (PL 17780/0583) on 7 May 2013. These medicines are available on prescription only.

Omeprazole Capsules belong to a group of medicines known as the proton pump inhibitors. They work by reducing the amount of acid that your stomach produces. Omeprazole Capsules are used to treat the following conditions:

In adults:

- Gastro-esophageal reflux disease (GERD). This is where acid from the stomach escapes into the gullet (the tube which connects your throat to your stomach) causing pain, inflammation and heartburn.
- Ulcers in the upper part of the intestine (duodenal ulcer) or stomach (gastric ulcer).
- Ulcers which are infected with bacteria called Helicobacter pylori. If you have this condition, your doctor may also prescribe antibiotics to treat the infection and allow the ulcer to heal.
- Ulcers caused by medicines called NSAIDs (non-steroidal anti-inflammatory drugs). Omeprazole capsules can also be used to stop ulcers from forming if you are taking NSAIDs.
- Too much acid in the stomach caused by a growth in the pancreas (Zollinger-Ellison syndrome).

In children:

**Children over 1 year of age and weighing 10 kg or more**

- Gastro-esophageal reflux disease (GERD). This is where acid from the stomach escapes into the gullet (the tube which connects your throat to your stomach) causing pain, inflammation and heartburn.
  In children, the symptoms of the condition can include the return of stomach contents into the mouth (regurgitation), being sick (vomiting) and poor weight gain.

**Children and adolescents over 4 years of age**

- Ulcers which are infected with bacteria called Helicobacter pylori. If your child has this condition, your doctor may also prescribe antibiotics to treat the infection and allow the ulcer to heal.

No new or unexpected safety concerns arose from these applications. It was judged that the benefits of taking Omeprazole Capsules outweigh the risks; hence Marketing Authorisations have been granted.
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## Module 1

### Information about Decentralised Procedure

| Names of the products in the Reference Member State | Omeprazole 10mg Gastro-resistant Capsules, hard  
Omeprazole 20mg Gastro-resistant Capsules, hard  
Omeprazole 40mg Gastro-resistant Capsules, hard  
Omeprazole 20mg Gastro-resistant Capsules, hard  
Omeprazole 20mg Gastro-resistant Capsules, hard |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of application</td>
<td>Article 10 (1), generic</td>
</tr>
<tr>
<td>Name of the drug substance</td>
<td>Omeprazole</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code) of the medicinal products</td>
<td>Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), proton pump inhibitors (A02BC01)</td>
</tr>
<tr>
<td>Pharmaceutical form and strengths of the medicinal products</td>
<td>Gastro-resistant capsule, hard; 10 mg, 20 mg and 40 mg</td>
</tr>
</tbody>
</table>
| Reference numbers for the Decentralised Procedure | UK/H/4423/001-003/DC  
UK/H/5144/001/DC |
| Reference Member State | United Kingdom |
| Member States concerned | UK/H/4423/001-003/DC: BG, CZ, DE, ES, FR, HU, IT, PL, PT, RO, SI, SK  
UK/H/5144/001/DC: DE |
| Start date of the Decentralised Procedure | 19 March 2012 |
| End date of the Decentralised Procedure | 14 March 2013 (day 210) |
| Marketing Authorisation numbers | PL 17780/0523  
PL 17780/0524  
PL 17780/0525  
PL 17780/0583 |
| Name and address of the authorisation holder | Winthrop Pharmaceuticals UK Limited (Trading as Zentiva)  
One Onslow Street  
Guildford  
Surrey GU1 4YS  
UK |
Module 2

Summary of Product Characteristics

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

Product Information Leaflet

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

Labelling

The following text is the approved label text for the products. No label mock-ups have been provided. In accordance with medicines legislation, the products shall not be marketed in the UK until approval of the label mock-ups has been obtained.
Omeprazole 10mg Gastro-resistant Capsules, hard (PL 17780/0523):

PARTICULARS TO APPEAR ON THE OUTER PACKAGING – PAPER FOLDING BOX

1. NAME OF THE MEDICINAL PRODUCT

Omeprazole 10mg Gastro-resistant Capsules, hard

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 10 mg omeprazole.

3. LIST OF EXCIPIENTS

Contains lactose anhydrous and sucrose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 gastro-resistant capsules, hard
14 gastro-resistant capsules, hard
15 gastro-resistant capsules, hard
28 gastro-resistant capsules, hard
30 gastro-resistant capsules, hard
50 gastro-resistant capsules, hard
60 gastro-resistant capsules, hard
90 gastro-resistant capsules, hard
100 gastro-resistant capsules, hard

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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:
After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. SPECIAL STORAGE CONDITIONS

Store below 25°C. Store in the original package in order to protect from moisture.
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Return unused medicinal product to the pharmacy.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 17780/0523

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omeprazole 10mg Gastro-resisant Capsules, hard
PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING – ETIQUETTE
(40 ml, 70 ml)

1. NAME OF THE MEDICINAL PRODUCT

Omeprazole 10mg Gastro-resistant Capsules, hard

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 10 mg omeprazole.

3. LIST OF EXCIPIENTS

Contains lactose anhydrous and sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

28 gastro-resistant capsules, hard
30 gastro-resistant capsules, hard
50 gastro-resistant capsules, hard
60 gastro-resistant capsules, hard
90 gastro-resistant capsules, hard
100 gastro-resistant capsules, hard

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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:
After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. SPECIAL STORAGE CONDITIONS

Store below 25°C. Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL
PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL
PRODUCTS, IF APPROPRIATE
<table>
<thead>
<tr>
<th></th>
<th>NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
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<tbody>
<tr>
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<td>Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK</td>
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<td>MARKETING AUTHORIZATION NUMBER(S)</td>
</tr>
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<td></td>
<td>Reg. No:</td>
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<td></td>
<td>BATCH NUMBER</td>
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<td></td>
<td>Batch:</td>
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<td></td>
<td>GENERAL CLASSIFICATION FOR SUPPLY</td>
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<tr>
<td></td>
<td>INSTRUCTIONS ON USE</td>
</tr>
<tr>
<td></td>
<td>INFORMATION IN BRAILLE</td>
</tr>
<tr>
<td>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS – BOTTLE LABEL (20 ml)</td>
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</tr>
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<td></td>
</tr>
<tr>
<td><strong>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</strong></td>
<td></td>
</tr>
<tr>
<td>Omeprazole 10mg Gastro-resistant Capsules, hard</td>
<td></td>
</tr>
<tr>
<td><strong>2. METHOD OF ADMINISTRATION</strong></td>
<td></td>
</tr>
<tr>
<td>Oral use.</td>
<td></td>
</tr>
<tr>
<td><strong>3. EXPIRY DATE</strong></td>
<td></td>
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<tr>
<td>EXP:</td>
<td></td>
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<tr>
<td><strong>4. BATCH NUMBER</strong></td>
<td></td>
</tr>
<tr>
<td>Batch:</td>
<td></td>
</tr>
<tr>
<td><strong>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</strong></td>
<td></td>
</tr>
<tr>
<td>7 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td>14 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td>15 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td>28 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td>30 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td>50 gastro-resistant capsules, hard</td>
<td></td>
</tr>
<tr>
<td><strong>6. OTHER</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Contains lactose anhydrous and sucrose. See leaflet for further information. Unopened store below 25°C. Store in the original package in order to protect from moisture. After first opening use the product within 3 months.
Omeprazole 20mg Gastro-resistant Capsules, hard (PL 17780/0524):

PARTICULARS TO APPEAR ON THE OUTER PACKAGING – PAPER FOLDING BOX

1. NAME OF THE MEDICINAL PRODUCT

Omeprazole 20mg Gastro-resistant Capsules, hard

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 20 mg omeprazole.

3. LIST OF EXCIPIENTS

Contains lactose anhydrous and sucrose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 gastro-resistant capsules, hard
14 gastro-resistant capsules, hard
15 gastro-resistant capsules, hard
28 gastro-resistant capsules, hard
30 gastro-resistant capsules, hard
50 gastro-resistant capsules, hard
60 gastro-resistant capsules, hard
90 gastro-resistant capsules, hard
100 gastro-resistant capsules, hard

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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:
After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. SPECIAL STORAGE CONDITIONS

Store below 25°C. Store in the original package in order to protect from moisture.
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Return unused medicinal product to the pharmacy.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 17780/0524

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omeprazole 20mg Gastro-resistant Capsules, hard
PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING – ETIQUETTE
(40 ml, 70 ml)

1. NAME OF THE MEDICINAL PRODUCT

Omeprazole 20mg Gastro-resistant Capsules, hard

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 20 mg omeprazole.

3. LIST OF EXCIPIENTS

Contains lactose anhydrous and sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

28 gastro-resistant capsules, hard
30 gastro-resistant capsules, hard
50 gastro-resistant capsules, hard
60 gastro-resistant capsules, hard
90 gastro-resistant capsules, hard
100 gastro-resistant capsules, hard

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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:
After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. SPECIAL STORAGE CONDITIONS

Store below 25°C. Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL
PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL
PRODUCTS, IF APPROPRIATE
11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Zenitiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

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

Reg. No:

13. **BATCH NUMBER**

Batch:

14. **GENERAL CLASSIFICATION FOR SUPPLY**

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS – BOTTLE LABEL (20 ml)</th>
</tr>
</thead>
</table>

1. **NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Omeprazole 20mg Gastro-resistant Capsules, hard

2. **METHOD OF ADMINISTRATION**

Oral use.

3. **EXPIRY DATE**

EXP:

4. **BATCH NUMBER**

Batch:

5. **CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

- 7 gastro-resistant capsules, hard
- 14 gastro-resistant capsules, hard
- 15 gastro-resistant capsules, hard
- 28 gastro-resistant capsules, hard
- 30 gastro-resistant capsules, hard

6. **OTHER**

Contains lactose anhydrous and sucrose. See leaflet for further information.
Unopened store below 25°C. Store in the original package in order to protect from moisture.
After first opening use the product within 3 months.

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

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

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

PL 17780/0524

9. **GENERAL CLASSIFICATION FOR SUPPLY**

POM
Omeprazole 40mg Gastro-resistant Capsules, hard ((PL 17780/0525):

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING – PAPER FOLDING BOX**

1. **NAME OF THE MEDICINAL PRODUCT**

   Omeprazole 40mg Gastro-resistant Capsules, hard

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

   Each gastro-resistant capsule contains 40 mg omeprazole.

3. **LIST OF EXCIPIENTS**

   Contains lactose anhydrous and sucrose. See leaflet for further information.

4. **PHARMACEUTICAL FORM AND CONTENTS**

   7 gastro-resistant capsules, hard
   14 gastro-resistant capsules, hard
   15 gastro-resistant capsules, hard
   28 gastro-resistant capsules, hard
   50 gastro-resistant capsules, hard
   50 gastro-resistant capsules, hard
   60 gastro-resistant capsules, hard
   90 gastro-resistant capsules, hard
   100 gastro-resistant capsules, hard

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 sight and reach of children.

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

8. **EXPIRY DATE**

   EXP:
   After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. **SPECIAL STORAGE CONDITIONS**

   Store below 25°C. Store in the original package in order to protect from moisture.
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Return unused medicinal product to the pharmacy.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 17780/0525

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omeprazole 40mg Gastro-resistant Capsules, hard
<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING – ETIQUETTE (40 ml, 70 ml, 100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. NAME OF THE MEDICINAL PRODUCT</td>
</tr>
<tr>
<td>Omeprazole 40mg Gastro-resistant Capsules, hard</td>
</tr>
<tr>
<td>2. STATEMENT OF ACTIVE SUBSTANCE(S)</td>
</tr>
<tr>
<td>Each gastro-resistant capsule contains 40 mg omeprazole.</td>
</tr>
<tr>
<td>3. LIST OF EXCIPIENTS</td>
</tr>
<tr>
<td>Contains lactose anhydrous and sucrose.</td>
</tr>
<tr>
<td>4. PHARMACEUTICAL FORM AND CONTENTS</td>
</tr>
<tr>
<td>28 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>30 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>50 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>60 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>90 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>100 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>5. METHOD AND ROUTE(S) OF ADMINISTRATION</td>
</tr>
<tr>
<td>Oral use.</td>
</tr>
<tr>
<td>Read the package leaflet before use.</td>
</tr>
<tr>
<td>6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN</td>
</tr>
<tr>
<td>Keep out of the sight and reach of children.</td>
</tr>
<tr>
<td>7. OTHER SPECIAL WARNING(S), IF NECESSARY</td>
</tr>
<tr>
<td>8. EXPIRY DATE</td>
</tr>
<tr>
<td>EXP:</td>
</tr>
<tr>
<td>After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.</td>
</tr>
<tr>
<td>9. SPECIAL STORAGE CONDITIONS</td>
</tr>
<tr>
<td>Store below 25°C. Store in the original package in order to protect from moisture.</td>
</tr>
<tr>
<td>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</td>
</tr>
</tbody>
</table>

MHRA PAR; OMEPRAZOLE 10MG, 20MG AND 40MG GASTRO-RESISTANT CAPSULES, HARD, PL 17780/0523-0525 AND 0583
### 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

### 12. MARKETING AUTHORISATION NUMBER(S)

Reg. No:

### 13. BATCH NUMBER

Batch:

### 14. GENERAL CLASSIFICATION FOR SUPPLY

### 15. INSTRUCTIONS ON USE

### 16. INFORMATION IN BRAILLE
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS – BOTTLE LABEL (20 ml)</th>
</tr>
</thead>
</table>

1. **NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Omeprazole 40mg Gastro-resistant Capsules, hard

2. **METHOD OF ADMINISTRATION**

Oral use.

3. **EXPIRY DATE**

EXP:

4. **BATCH NUMBER**

Batch:

5. **CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

7 gastro-resistant capsules, hard
14 gastro-resistant capsules, hard
15 gastro-resistant capsules, hard

6. **OTHER**

Contains lactose anhydrous and sucrose. See leaflet for further information. Unopened store below 25°C. Store in the original package in order to protect from moisture. After first opening use the product within 3 months.

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

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

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

PL 17780/0525

9. **GENERAL CLASSIFICATION FOR SUPPLY**

POM
Omeprazole 20mg Gastro-resistant Capsules, hard ((PL 17780/0583):

PARTICULARS TO APPEAR ON THE OUTER PACKAGING – PAPER FOLDING BOX

1. NAME OF THE MEDICINAL PRODUCT

Omeprazole 20mg Gastro-resistant Capsules, hard

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 20 mg omeprazole.

3. LIST OF EXCIPIENTS

Contains lactose anhydrous and sucrose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 gastro-resistant capsules, hard
14 gastro-resistant capsules, hard
15 gastro-resistant capsules, hard
28 gastro-resistant capsules, hard
30 gastro-resistant capsules, hard
50 gastro-resistant capsules, hard
60 gastro-resistant capsules, hard
90 gastro-resistant capsules, hard
100 gastro-resistant capsules, hard

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 sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:
After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. SPECIAL STORAGE CONDITIONS

Store below 25°C. Store in the original package in order to protect from moisture.
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Return unused medicinal product to the pharmacy.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK

12. MARKETING AUTHORISATION NUMBER(S)

PL 17780/0583

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omeprazole 20mg Gastro-resistant Capsules, hard
<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING – ETIQUETTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>(40 ml, 70 ml)</td>
</tr>
</tbody>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

Omeprazole 20mg Gastro-resistant Capsules, hard

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

Each gastro-resistant capsule contains 20 mg omeprazole.

3. **LIST OF EXCIPIENTS**

Contains lactose anhydrous and sucrose.

4. **PHARMACEUTICAL FORM AND CONTENTS**

- 28 gastro-resistant capsules, hard
- 30 gastro-resistant capsules, hard
- 50 gastro-resistant capsules, hard
- 60 gastro-resistant capsules, hard
- 90 gastro-resistant capsules, hard
- 100 gastro-resistant capsules, hard

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 sight and reach of children.

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

8. **EXPIRY DATE**

EXP: After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

9. **SPECIAL STORAGE CONDITIONS**

Store below 25°C. Store in the original package in order to protect from moisture.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**
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<tr>
<th></th>
<th>NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK</td>
</tr>
<tr>
<td></td>
<td>MARKETING AUTHORISATION NUMBER(S)</td>
</tr>
<tr>
<td></td>
<td>Reg. No:</td>
</tr>
<tr>
<td></td>
<td>BATCH NUMBER</td>
</tr>
<tr>
<td></td>
<td>Batch:</td>
</tr>
<tr>
<td></td>
<td>GENERAL CLASSIFICATION FOR SUPPLY</td>
</tr>
<tr>
<td></td>
<td>INSTRUCTIONS ON USE</td>
</tr>
<tr>
<td></td>
<td>INFORMATION IN BRAILLE</td>
</tr>
</tbody>
</table>
### MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS – BOTTLE LABEL (20 ml)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><strong>NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</strong></td>
</tr>
<tr>
<td></td>
<td>Omeprazole 20mg Gastro-resistant Capsules, hard</td>
</tr>
<tr>
<td>2.</td>
<td><strong>METHOD OF ADMINISTRATION</strong></td>
</tr>
<tr>
<td></td>
<td>Oral use.</td>
</tr>
<tr>
<td>3.</td>
<td><strong>EXPIRY DATE</strong></td>
</tr>
<tr>
<td></td>
<td>EXP:</td>
</tr>
<tr>
<td>4.</td>
<td><strong>BATCH NUMBER</strong></td>
</tr>
<tr>
<td></td>
<td>Batch:</td>
</tr>
<tr>
<td>5.</td>
<td><strong>CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</strong></td>
</tr>
<tr>
<td></td>
<td>7 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td></td>
<td>14 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td></td>
<td>15 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td></td>
<td>28 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td></td>
<td>30 gastro-resistant capsules, hard</td>
</tr>
<tr>
<td>6.</td>
<td><strong>OTHER</strong></td>
</tr>
<tr>
<td></td>
<td>Contains lactose anhydrous and sucrose. See leaflet for further information.</td>
</tr>
<tr>
<td></td>
<td>Unopened store below 25°C. Store in the original package in order to protect from moisture. After first opening use the product within 3 months.</td>
</tr>
<tr>
<td>7.</td>
<td><strong>NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</strong></td>
</tr>
<tr>
<td></td>
<td>Zentiva, One Onslow Street, Guildford, Surrey, GU1 4YS, UK</td>
</tr>
<tr>
<td>8.</td>
<td><strong>MARKETING AUTHORISATION NUMBER(S)</strong></td>
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<tr>
<td></td>
<td>PL 17780/0583</td>
</tr>
<tr>
<td>9.</td>
<td><strong>GENERAL CLASSIFICATION FOR SUPPLY</strong></td>
</tr>
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</table>
|   | POM
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 application for Omeprazole 10mg, 20mg and 40mg Gastro-resistant Capsules, hard could be approved. These prescription only medicines are used to treat the following conditions in adults:

- Treatment of duodenal ulcers
- Prevention of relapse of duodenal ulcers
- Treatment of gastric ulcers
- Prevention of relapse of gastric ulcers
- In combination with appropriate antibiotics, *Helicobacter pylori* (*H. pylori*) eradication in peptic ulcer disease
- Treatment of NSAID-associated gastric and duodenal ulcers
- Prevention of NSAID-associated gastric and duodenal ulcers in patients at risk
- Treatment of reflux esophagitis
- Long-term management of patients with healed reflux esophagitis
- Treatment of symptomatic gastro-esophageal reflux disease
- Treatment of Zollinger-Ellison syndrome

and the following conditions in children:

*Children over 1 year of age and ≥ 10 kg*

- Treatment of reflux esophagitis
- Symptomatic treatment of heartburn and acid regurgitation in gastro-esophageal reflux disease

*Children and adolescents over 4 years of age*

- In combination with antibiotics in treatment of duodenal ulcer caused by *H. pylori*

This Decentralised application was submitted under Article 10(1) of Directive 2001/83/EC, as amended, as a so-called generic application. The reference medicinal product for this application is Losec 20 mg Capsules, which was first authorised in the UK under Marketing Authorisation PL 00017/0238 to Astra Pharmaceuticals on 9 May 1989. Following a Change of Ownership on 14 May 2002, the Marketing Authorisation (PL 17901/0133) was transferred to AstraZeneca UK Ltd. The reference product has been authorised in the EEA for at least 10 years, therefore, the legal basis of this application is acceptable.

Omeprazole belongs to a class of antisecretory compounds that suppress gastric acid secretion by inhibiting the gastric H+, K+ ATPase at the secretory surface of the gastric parietal cell.
Two bioequivalence studies were submitted to support these applications comparing the 40mg test product with Losec 40 mg Capsules (AstraZeneca UK Ltd). The bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP) and the Declaration of Helsinki.

With the exception of the bioequivalence studies, no new non-clinical or clinical data were submitted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been in clinical use for over 10 years.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of these products. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

The RMS and CMS considered that the applications could be approved at Day 210 of the procedure on 14 March 2013. After a subsequent national phase, the Marketing Authorisations were granted in the UK on 7 May 2013.
### II. ABOUT THE PRODUCTS

| Names of the products in the Reference Member State | Omeprazole 10mg Gastro-resistant Capsules, hard  
| | Omeprazole 20mg Gastro-resistant Capsules, hard  
| | Omeprazole 40mg Gastro-resistant Capsules, hard  
| | Omeprazole 20mg Gastro-resistant Capsules, hard |

| Name of the drug substance | Omeprazole |

| Pharmacotherapeutic classification (ATC code) | Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), proton pump inhibitors (A02BC01) |

| Pharmaceutical form and strength | Gastro-resistant capsule, hard; 10 mg, 20 mg and 40 mg |

| Reference numbers for the Mutual Recognition Procedure | UK/H/4423/001-003/DC  
| | UK/H/5144/001/DC |

| Reference Member State | United Kingdom |

| Member States concerned | UK/H/4423/001-003/DC: BG, CZ, DE, ES, FR, HU, IT, PL, PT, RO, SI, SK  
| | UK/H/5144/001/DC: DE |

| Marketing Authorisation Numbers | PL 17780/0523  
| | PL 17780/0524  
| | PL 17780/0525  
| | PL 17780/0583 |

| Name and address of the authorisation holder | Winthrop Pharmaceuticals UK Limited (Trading as Zentiva)  
| | One Onslow Street  
| | Guildford  
| | Surrey GU1 4YS  
| | UK |
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

INN: Omeprazole

Chemical name: 5-Methoxy-2-[(RS)-[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfinyl]-1H-benzimidazole

CAS: 73590-58-6

Structure:

\[
\begin{align*}
H_2CO & \\
& \text{and enantiomer}
\end{align*}
\]

Molecular mass: 345.4

Formula: \(C_{17}H_{19}N_3O_3S\)

Appearance: White or almost white powder

Solubility: Very slightly soluble in water, soluble in methylene chloride, sparingly soluble in ethanol (96 per cent) and in methanol. It dissolves in dilute solutions of alkali hydroxides

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

DRUG PRODUCTS

Description and Composition

The drug products are presented as follows:

**Omeprazole 10mg Gastro-resistant Capsules, hard (PL 17780/0523):**

Gastro-resistant capsules, hard No.4 (length approximately 14.3mm) with light brown body and orange cap. The capsule contains off white to slightly yellowish-brown spherical pellets.

**Omeprazole 20mg Gastro-resistant Capsules, hard (PL 17780/0524 & 0583):**

Gastro-resistant capsules, hard No.3 (length approximately 15.9mm) with light brown body and red cap. The capsule contains off white to slightly yellowish-brown spherical pellets.

**Omeprazole 40mg Gastro-resistant Capsules, hard (PL 17780/0525):**

Gastro-resistant capsules, hard No.2 (length approximately 18.0mm) with light brown body and brown cap. The capsule contains off white to slightly yellowish-brown spherical pellets.
All capsule strengths contain sugar spheres (which contain sucrose and maize starch), lactose anhydrous, hypromellose 2910/6, hydroxypropylcellulose, sodium laurylsulfate, disodium phosphate dodecahydrate, methacrylic acid – ethylacrylate copolymer (1:1) dispersion 30 per cent, macrogol 6000 and talc (which make up the pellets) and black iron oxide (E 172), red iron oxide (E 172), yellow iron oxide (E 172), titanium dioxide (E 171) and gelatin (which make up the body of the capsule shell). The caps of the 10 mg and 20 mg capsule shells contain red iron oxide (E 172), yellow iron oxide (E172), titanium dioxide (E 171) and gelatin and the caps of the 40 mg capsule shells contain indigo carmine, red iron oxide (E 172), yellow iron oxide (E172), titanium dioxide (E 171) and gelatin.

Appropriate justifications for the inclusion of each excipient have been provided.

All excipients comply with their respective European Pharmacopoeia monograph. Satisfactory Certificates of Analysis are provided for each excipient, showing compliance with their respective monographs.

The lactose and gelatin used to make the capsules are materials of animal origin. A satisfactory statement is provided from the lactose supplier which confirms that the lactose is sourced from healthy animals under the same conditions as milk collected for human consumption and that the lactose is prepared without the use of ruminant materials other than milk and calf rennet. Certificates of Suitability from the gelatin suppliers have been provided and are current and acceptable.

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

**Pharmaceutical Development**

The objective of the development programme was to formulate safe, efficacious, stable products that could be considered generic medicinal products of Losec Capsules (AstraZeneca UK Ltd). Suitable pharmaceutical development data have been provided for these applications.

Comparative *in-vitro* dissolution and impurity profiles have been provided for batches of the test products and appropriate reference products. The dissolution and impurity profiles were satisfactory.

**Manufacture of the Drug Product**

Satisfactory batch formulae have been provided for the manufacture of all strengths of the product, along with an appropriate account of the manufacturing process. Process validation has been carried out and the results are satisfactory.

**Control of the Drug Product**

The finished product specifications are satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.
Container Closure System
The finished products are licensed for marketing in brown, glass bottles (in sizes of 20, 40, 70 and 100 ml) with a white HDPE screw closure with desiccant and folding paper box. The following pack sizes have been authorised (although not all pack sizes may be marketed):

**Omeprazole 10mg Gastro-resistant Capsules, hard (PL 17780/0523):**
- 7, 14, 15, 28, 30, 50 capsules in 20 ml bottle
- 28, 30, 50, 60 capsules in 40 ml bottle
- 90, 100 capsules in 70 ml bottle

**Omeprazole 20mg Gastro-resistant Capsules, hard (PL 17780/0524 and PL 17780/0583):**
- 7, 14, 15, 28, 30 capsules in 20 ml bottle
- 28, 30, 50 capsules in 40 ml bottle
- 60, 90, 100 capsules in 70 ml bottle

**Omeprazole 40mg Gastro-resistant Capsules, hard (PL 17780/0525):**
- 7, 14, 15 capsules in 20 ml bottle
- 28, 30 capsules in 40 ml bottle
- 50, 60, 90 capsules in 70 ml bottle
- 90, 100 capsules in 100 ml bottle

Satisfactory specifications and Certificates of Analysis for all packaging components used have been provided. All primary product packaging complies with EU legislation concerning materials in contact with food.

Stability of the Drug Product
Finished product stability studies have been conducted in accordance with current guidelines on batches of the finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years, which is acceptable when the storage precautions ‘Store below 25°C’ and ‘Store in the original package in order to protect from moisture’ are applied. After first opening the bottle, the product may be stored for a maximum of 3 months at 25°C.

Bioequivalence
Satisfactory Certificates of Analysis have been provided for batches of the test and reference products used in the bioequivalence studies. The bioequivalence studies are discussed in Section III.3, Clinical Aspects.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPCs and PILs and labelling text are satisfactory from a pharmaceutical perspective. No PIL or label mock-ups have been provided. In accordance with medicines legislation, the products shall not be marketed in the UK until approval of the PIL and label mock-ups has been obtained.

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) Forms**
All aspects of the MAA forms are satisfactory from a pharmaceutical perspective.

**Expert Report (Quality Overall Summary)**
The Quality Overall Summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
The grant of Marketing Authorisations is recommended.

### III.2 NON-CLINICAL ASPECTS

As the pharmacological, pharmacokinetic and toxicological properties of omeprazole are well known, no further non-clinical studies are required and none have been provided.

**Non-clinical Overview**
The non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

**Environmental Risk Assessment**
A suitable justification for the absence of a formal environmental risk assessment has been provided, based on the expectation that introduction of these generic products onto the market is unlikely to result in an increase in the combined sales of all omeprazole-containing products, which, in turn, is unlikely to increase exposure of the environment to omeprazole.

**Product Literature**
The product literature is acceptable from a non-clinical point of view.

**Conclusion**
The grant of Marketing Authorisations is recommended.

### III.3 CLINICAL ASPECTS

**Pharmacokinetics**
To support the applications, the applicant has conducted two bioequivalence studies:

1. **Single dose bioequivalence study under fasting conditions**

**Methods**

**Study design**
This was a randomised, open label, two-period, two-sequence, single dose, crossover bioequivalence study carried out to compare the pharmacokinetics of the test product,
Omeprazole 40 mg Gastro-resistant Capsules, with those of the reference product, Losec Capsules 40 mg, in 48 healthy, adult, male and female subjects under fasting conditions.

In each study period, subjects were confined to the research facility from 12 hours prior to drug administration until 12 hours post dose, and were fasted overnight for at least 10 hours prior to dosing. The wash-out period was 7 days. Blood samples were collected prior to study drug administration and at intervals up to 12 hours post-dose in each period.

**Test and reference products**
Omeprazole 40mg Gastro-resistant Capsules, hard were compared to the reference product, Losec 40 mg Capsules.

**Population studied**
48 subjects were randomised. One subject was withdrawn from the study during period 2 due to several gastrointestinal adverse events (AEs). 47 subjects were analysed and included in the PK analysis.

**Results**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$\text{AUC}_\tau$ ng/ml/h</th>
<th>$\text{C}_{\text{max}}$ ng/ml</th>
<th>$t_{\text{max}}$ h</th>
<th>$T_{1/2}$ h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>1915.44</td>
<td>1076.84</td>
<td>2.00</td>
<td>1.08</td>
</tr>
<tr>
<td>Reference</td>
<td>1919.37</td>
<td>1073.81</td>
<td>1.67</td>
<td>1.10</td>
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<tr>
<td><em>Ratio (90% CI)</em></td>
<td>99.79 (95.27-104.54)</td>
<td>100.28 (93.34-107.74)</td>
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<td></td>
</tr>
</tbody>
</table>

AUC$_\tau$ area under the plasma concentration-time curve from time zero to infinity
AUC$_0^\infty$ area under the plasma concentration-time curve from time zero to infinity
$\text{C}_{\text{max}}$ maximum plasma concentration
$T_{\text{max}}$ time for maximum concentration (median)
$T_{1/2}$ half-life

*ln-transformed values

**Adverse events**
Seven subjects (14.6%) reported 14 AEs after the single dose administration of the test product and 4 subjects (8.3%) reported 6 AEs after single dose administration of the reference product. The commonest AEs were headache and nausea.

**Conclusion**
The 90% geometric confidence intervals of the ratio (T/R) of least-squares means of the ln-transformed AUC$_{0-t}$ and $\text{C}_{\text{max}}$ are within 80.00% to 125.00%. Bioequivalence has been shown, under fasting conditions, in accordance with standard requirements.
2. Single dose bioequivalence study under fed conditions

Methods

Study design
This was a randomised, open label, four-period, two-sequence, replicate crossover bioequivalence study carried out to compare the pharmacokinetics of the test product, Omeprazole 40 mg Gastro-resistant Capsules, with those of the reference product, Losec Capsules 40 mg, in 44 healthy, adult, male and female subjects under fed conditions.

In each study period, following an overnight fast of at least 10 hours, subjects received a standardised high-fat (approximately 50% of total caloric content of the meal), high-calorie (approximately 800 to 1000 calories) meal 30 minutes before drug administration. A standardised lunch, a supper and a light snack were served afterwards, approximately 4.5, 9 and 12 hours after drug administration, respectively. Thirty minutes after the start of the breakfast, a single dose of the assigned formulation was administered orally. The wash-out period was 7 days. Blood samples were collected prior to study drug administration and at intervals up to 14 hours post-dose in each period.

Test and reference products
Omeprazole 40mg Gastro-resistant Capsules, hard were compared to the reference product, Losec 40 mg Capsules.

Population studied
44 subjects were randomised, analysed and included in the PK analysis.

Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC$_{\tau}$</th>
<th>C$_{\text{max}}$</th>
<th>t$_{\text{max}}$</th>
<th>T$_{1/2}$</th>
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</thead>
<tbody>
<tr>
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<td>352.28</td>
<td>6.00</td>
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<tr>
<td>Reference</td>
<td>1118.54</td>
<td>333.63</td>
<td>6.00</td>
<td>1.32</td>
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</table>

*Ratio (90% CI) = 97.38 (90.45-104.85) 105.59 (95.58-116.64)

<table>
<thead>
<tr>
<th>AUC$_{\infty}$</th>
<th>area under the plasma concentration-time curve from time zero to infinity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC$_{\tau}$</td>
<td>area under the plasma concentration-time curve from time zero to t hours</td>
</tr>
<tr>
<td>C$_{\text{max}}$</td>
<td>maximum plasma concentration</td>
</tr>
<tr>
<td>t$_{\text{max}}$</td>
<td>time for maximum concentration (median)</td>
</tr>
<tr>
<td>T$_{1/2}$</td>
<td>half-life</td>
</tr>
</tbody>
</table>

*ln-transformed values

Adverse events
Twenty-two subjects (50%) reported 38 AEs. 13 AEs were reported after the administration of the test product and 25 AEs were reported after the administration of the reference product. One severe AE (headache) was observed during the study. The
commonest AEs were somnolence, headache, nausea, abdominal pain, and runny nose.

Conclusion
The 90% geometric confidence intervals of the ratio (T/R) of least-squares means of the ln-transformed AUC$_{\text{b-t}}$ and C$_{\text{max}}$ are within 80.00% to 125.00%. Bioequivalence has been shown, under fed conditions, in accordance with standard requirements.

Overall Conclusion on Bioequivalence
Based on the submitted bioequivalence studies, Omeprazole 40mg Gastro-resistant Capsules, hard are considered bioequivalent to Losec 40 mg Capsules after single dose in both the fed and fasted state.

As the product range meets all the criteria specified in the Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1) for a biowaiver for the other strengths, the results and conclusions of the bioequivalence studies on Omeprazole 40mg Gastro-resistant Capsules, hard can be extrapolated to Omeprazole 10mg and 20mg Gastro-resistant Capsules, hard.

Clinical Efficacy
No new efficacy data are presented for this application and none are required.

Clinical Safety
With the exception of the data generated during the bioequivalence study, no new safety data are presented for this application and none are required. No new or unexpected safety issues arose during the bioequivalence studies.

Pharmacovigilance System
The RMS considers that the pharmacovigilance system fulfils the requirements. The applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the collection and notification of any adverse reaction suspected of occurring in the Community or in a third country.

Risk Management Plan
No safety concerns requiring additional risk minimisation activities have been identified. A detailed RMP is not considered necessary for these applications.

Clinical Overview
A Clinical Overview written by an appropriately qualified physician has been provided and is a satisfactory summary of the clinical aspects of the dossier.

Product Literature
All product literature (SmPC, PIL and labelling) are clinically acceptable. The SmPCs are consistent with those for the innovator products. The PILs are consistent with the details in the SmPCs and in line with the current guidelines. The labelling is in line with the current guidelines.

Conclusion
The grant of Marketing Authorisations is recommended.
IV. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Omeprazole Capsules 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.

CLINICAL
With the exception of the bioequivalence studies, no new clinical data were submitted and none are required for applications of this type. Bioequivalence has been demonstrated between the applicant’s products and the reference products.

SAFETY
With the exception of the bioequivalence studies, no new clinical data were submitted and none are required for applications of this type. No new or unexpected safety concerns arose from the bioequivalence studies.

PRODUCT LITERATURE
The SmPCs and PILs are satisfactory and consistent with those of the reference products. Satisfactory product labelling has also been submitted.

BENEFIT: RISK ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence studies support the claim that the applicant’s products and the reference products are interchangeable. Extensive clinical experience with omeprazole is considered to have demonstrated the therapeutic value of the compound. The benefit: risk balance is, therefore, considered 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>
</tr>
</thead>
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