CHEMICAL PHARMACEUTICAL AND BIOLOGICAL DATA

Introduction
The product to be used is Wonderdrug 5mg Tablets which are blinded for use in the trial by encapsulation using a Swedish Orange capsule (body and cap) and back-filled with microcrystalline cellulose.

S DRUG SUBSTANCE
Not applicable

P DRUG PRODUCT

P.1 Description and Composition of the Drug Product

Description
The IMP is a hard gelatin capsule comprising a Swedish orange body and cap and containing 5, 7.5 or 10 mg of AB1234 present in the form of Wonderdrug 5mg Tablets.

Composition
The complete statement of the components and quantitative composition of ABC1234 Capsules is given below in Table 6.

Table 1 Composition of Wonderdrug 5/7.5/10mg Capsules

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity (mg/capsule)</th>
<th>Function</th>
<th>Reference to Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB1234 as Wonderdrug 5mg Tablets</td>
<td>5 7.5 10</td>
<td>Active</td>
<td></td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td></td>
<td>Back-filler</td>
<td>Ph. Eur.</td>
</tr>
<tr>
<td>Capsule, gelatin</td>
<td>1 1 1</td>
<td>Capsule Shell</td>
<td>Supplier’s CoA</td>
</tr>
</tbody>
</table>

P.2 Pharmaceutical Development
The drug product is a hard gelatin capsule. The microcrystalline cellulose is pharmacopoeial. The commercial tablets are uncoated immediate release tablets. These are blinded by encapsulation using gelatin capsules with a microcrystalline cellulose back-filler. To enable the 7.5mg dose to be provided, Wonderdrug 5mg Tablets are halved and each capsule is filled with half tablets (two, three or four) prior to back-filling.

No in vitro dissolution testing has been undertaken. This is justified on the following basis:
- the lack of film coating and any mechanism to prolong release of the active substance from the dose form,
- the aqueous solubility of the drug substance
- the rapid disintegration of the gelatin capsule (5 minutes, data not provided).
The microcrystalline cellulose used as a back-filler is present in the Wonderdrug formulation.

Since there is a minimal increase in surface area of the halved tablets, no stability testing has been undertaken.

The over-encapsulated tablets will be packaged in HDPE containers. This is the same container closure system as for the marketed product.

P.3 Manufacture

P.3.1 Manufacturer(s)
Manufacture, packaging and labelling of the over-encapsulated Wonderdrug 5mg Tablets is carried out by:

Hospital Manufacturing Limited
Hospital Way
Anytown
Anywhere
UK

A copy of the MA(IMP) has been included as part of this submission.

P.3.2 Batch Formula
It is expected that a batch of 250 capsules will be manufactured. (Given the simple composition a batch formula has not been included)

P.3.3 Description of Manufacturing Process and Process Controls
Wonderdrug 5mg Tablets are cut in half. The required number of half tablets (two, three or four) is placed inside a capsule shell by hand, back-filled with microcrystalline cellulose and closed. The capsules are visually inspected and packed into HDPE bottles.

P.3.4 Controls of Critical Steps and Intermediates
There are no intermediates.

P.3.5 Process Validation and/or Evaluation
In view of the simplicity of the manufacturing method, no process validation has been undertaken.

2.2.1.P.4 Control of Excipients

2.2.1.P.4.1 Specifications
P.4 Control of Excipients:
P.4.1 Specifications
The microcrystalline cellulose complies with the current edition of the Ph. Eur.
The gelatin capsule is non-compendial. This will be sourced from CapsuCompany and will meet the specification provided below:
Table 2  
Composition of Swedish orange gelatin capsules

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron oxide</td>
<td>1.1817 %</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>0.4916 %</td>
</tr>
<tr>
<td>Gelatin</td>
<td>qs 100%</td>
</tr>
</tbody>
</table>

Table 3  
Specification for Swedish orange gelatin capsules

<table>
<thead>
<tr>
<th>Test</th>
<th>Acceptance Criteria</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>2-piece, Swedish orange opaque cap/body, unmarked hard gelatin capsule</td>
<td>Visual</td>
</tr>
<tr>
<td>Identification of Gelatin</td>
<td>A yellow precipitate is formed. Turbidity is produced</td>
<td>Methods provided by vendor (modified USNF Monograph for Gelatin)</td>
</tr>
<tr>
<td>Test A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capsule Weight</td>
<td>Weigh at least 30 capsules individually.</td>
<td>±10% of target weight</td>
</tr>
<tr>
<td>Loss on Drying</td>
<td>13.0 – 16.0% of its weight</td>
<td>Method provided by vendor</td>
</tr>
<tr>
<td>Microbial Limits Test</td>
<td>Not more than 1000 CFU/g</td>
<td>USP &lt;61&gt; or Ph. Eur. 2.6.12 &amp; 2.6.13</td>
</tr>
<tr>
<td>Total aerobic microbial count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total combined mold and yeast count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and Salmonella species.</td>
<td>Absent</td>
<td></td>
</tr>
</tbody>
</table>

P.4.5  
Excipients of Human or Animal Origin
The gelatin in the capsules is of bovine origin. An EDQM Certificate of Suitability (RO-CEP 2000-xxx Rev 00 dated aa.bb.cccc) is available.

P.4.6  
Novel Excipients
None involved.

P.5  
Control of Drug Product

P.5.1  
Specification(s)
Clinical trial batches will meet the following specification at release.

Table 4  
Regulatory Specification for Wonderdrug Capsules 5, 7.5 and 10 mg

<table>
<thead>
<tr>
<th>Test</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Two (5mg), three (7.5mg) or four (10mg) half Wonderdrug 5mg Tablets with a white to off-white powder contained in a</td>
</tr>
</tbody>
</table>
P.5.2 Analytical Procedures
The methods used to control the drug substance are summarised below.

Description of ABC123 Capsules
The capsules are examined for conformance of colour and shape. The contents are tipped out and examined against a white background

Identification and Content of AB1234
The batch records are reviewed.

P.5.3 Validation of Analytical Procedures
Not applicable

P.5.4 Batch Analyses
Since there is no analytical testing undertaken, no batch analysis data have been provided.

P.5.5 Characterisation of Impurities
Not applicable

P.5.6 Justification of Specification(s)
Not applicable

P.6 Reference Standards or Materials
Not applicable

P.7 Container Closure System
The capsules are packaged into HDPE bottles, and closed with child-resistant plastic induction seal screw caps.

P.8 Stability
No stability studies are being conducted since the modification to the marketed product is minor and not expected to affect stability. A shelf life of 12 months will be applied to the capsules but will not exceed the expiry date of the input tablets.
2.1.A APPENDICES
2.A.1 Facilities and Equipment
Not Applicable.

2.1.A.2 Adventitious Agents Safety Evaluation
Gelatin used in the gelatin capsules has an EDQM Certificate of Suitability (RO-CEP 2000-xxx Rev 00 dated aa.bb.cccc).

2.1.A.3 Novel Excipients
None involved.

2.1.A.4 Solvents for Reconstitution and Diluents
None involved.