## 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**

| Component | Quantity (mg/capsule) | | | Function | Reference to Standard |
|---|---|---|---|---|---|
| AB1234 as Wonderdrug 5mg Tablets | 5 | 7.5 | 10 | Active | |
| Microcrystalline cellulose | | | | Back-filler | Ph. Eur. |
| Capsule, gelatin | 1 | 1 | 1 | Capsule Shell | Supplier's CoA |

### 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**
Wopnderdrug 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**

| Component | Quantity (% w/w) |
|---|---|
| Iron oxide | 1.1817 % |
| Titanium dioxide | 0.4916 % |
| Gelatin | qs 100% |

**Table 3 Specification for Swedish orange gelatin capsules**

| Test | Acceptance Criteria | Method |
|---|---|---|
| **Appearance** | 2-piece, Swedish orange opaque cap/body, unmarked hard gelatin capsule | Visual |
| **Identification of Gelatin**<br><br>Test A<br>Test B | <br><br>A yellow precipitate is formed.<br>Turbidity is produced | Methods provided by vendor (modified USNF Monograph for Gelatin) |
| **Capsule Weight** Weigh at least 30 capsules individually. | ±10% of target weight | Method provided by vendor |
| **Loss on Drying** | 13.0 – 16.0% of its weight | Method provided by the vendor (modified USP <731>) |
| **Microbial Limits Test**<br>Total aerobic microbial count<br>Total combined mold and yeast count<br>Absence of Staphylococcus aureus,<br>Pseudomonas aeruginosa, Escherichia<br>coli, and Salmonella species. | <br>Not more than 1000 CFU/g<br>Not more than 100 CFU/g<br><br><br>Absent | <br>USP <61> or<br>Ph. Eur. 2.6.12<br>& 2.6.13 |

### 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**

| Test | Acceptance Criteria |
|---|---|
| Description | Two (5mg), three (7.5mg) or four (10mg) half Wonderdrug 5mg Tablets with a white to off-white powder contained in a |

| | |
|---|---|
| | Size 0 hard gelatin capsule comprising a Swedish orange body and cap |
| **Identification of AB1234** | This is achieved by control of the input tablets and review of the batch records |
| **AB1234 content** | This is achieved by review of the batch records |

### 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.