

This part outlines the scientific assessment and knowledge about this product at the time of prequalification. Updates to this information are included in parts 1 to 5 and 8 of this WHOPAR.

## SCIENTIFIC DISCUSSION

<b>Name of the Finished Pharmaceutical Product</b>	[HA500 trade name]*
<b>Manufacturer of Prequalified Product</b>	Hainan Poly Pharm Co Ltd No.1 Simalu Guilinyang Economic Development Area, Lingshan, Haikou City Hainan Province, China
<b>Active Pharmaceutical Ingredients (APIs)</b>	Ganciclovir
<b>Pharmaco-therapeutic group (ATC Code)</b>	Antivirals for systemic use (J05AB06)
<b>Therapeutic indication</b>	Ganciclovir indicated for the treatment of life-threatening or sight-threatening cytomegalovirus (CMV) infections in HIV-infected patients.

### 1. Introduction

[HA515 trade name] indicated for the treatment of life-threatening or sight-threatening cytomegalovirus (CMV) infections in HIV-infected patients.

### 2 Assessment of Quality

The assessment was done according to SOP 20 of the WHO Prequalification programme,

#### Active Pharmaceutical Ingredients (APIs)

Ganciclovir is described in the Ph. Eur and USP. The API used in the manufacture of the powder for injection is ganciclovir sodium, which is manufactured in several steps from a commercially available starting material. Compared to ganciclovir free acid, the sodium salt shows superior solubility in water.

The API specifications include tests for appearance, identification of the API and sodium, water content, pH, heavy metals, related substances (HPLC), assay (HPLC), residual solvents, bacterial endotoxins and microbial limits.

Stability testing was conducted according to the requirements of WHO. The proposed re-test period is justified based on the stability results when the API is stored in the original packing material.

#### Other ingredients

The powder for injection contains no excipient.

#### Finished pharmaceutical product (FPP)

##### *Pharmaceutical development and manufacture*

The multisource product is a sterile, white lyophilised powder for single use, containing 543 mg

\* Trade names are not prequalified by WHO. This is the national medicines regulatory authority's responsibility.

ganciclovir sodium equivalent to 500 mg ganciclovir. The powder is presented in clear borosilicate Type I glass vial with grey bromobutyl stopper and aluminium seal with a plastic flip-off top.

Similar to the comparator, Cytovene<sup>®</sup>, the multisource product contains no excipient. The powder for injection is manufactured following a standard aseptic process including the following steps: dissolving of the API in water for injections, sterile filtration and filling, freeze-drying and stoppering/sealing of the vials, followed by packaging. Care is taken to limit hydrolytic degradation of the API during the process. Key process parameters were optimised based on scientifically designed experiments involving the manufacture of multiple development batches. Satisfactory operating parameters and in-process controls have been defined at each stage of manufacture. Validation data have been provided for three consecutive production batches.

#### *Specifications*

The finished product specifications include tests for appearance, identification of the API (HPLC and UV), water, the reconstituted solution, pH, bacterial endotoxins, sterility, sub-visible particulate matter, visible particulate matter, related compounds (HPLC), dosage uniformity and assay (HPLC).

#### *Stability testing*

Stability studies have been performed at 25°C/60%RH and 30°C/65%RH as long-term storage conditions and for six months at accelerated conditions in the packaging intended for marketing of the product. The data showed little change with time and were well within the agreed specifications at both storage conditions. Based on the available stability data, the proposed shelf life and storage conditions of the unopened vials as stated in the SmPC are acceptable. The in-use storage times for the reconstituted solution and infusion solutions appearing in the SmPC are supported by in-use chemical and physical stability testing.

#### **Conclusion**

The quality part of the dossier is accepted.

### **3. Assessment of Bioequivalence**

The product is a powder for solution for injection. The formula contains ganciclovir as a freeze-dried powder and nitrogen to fill the container (inert). No other excipients are included in the formulation. It is acceptable not to perform a bioequivalence study based on the formulation (absence of excipients) and mode of administration (infusion).

### **4. Summary of Product Safety and Efficacy**

[HA515 trade name] has been shown to conform to the same relevant standards of quality, efficacy and safety as those required of the innovator product. According to the submitted data on quality [HA515 trade name] is pharmaceutically and therapeutically equivalent and thus interchangeable with the innovator product Cytovene<sup>®</sup> for which benefits have been proven in terms of clinical efficacy.

The clinical safety of this product is considered to be acceptable when guidance and restrictions as stated in the Summary of Product Characteristics (SmPC) are taken into account. Reference is made to the SmPC (WHOPAR part 4) for data on clinical safety.

### **5. Benefit risk assessment and overall conclusion**

#### **Quality**

The quality of this product is considered to be acceptable when used in accordance with the conditions defined in the SmPC. Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way.

### **Bioequivalence**

N/A

### **Efficacy and Safety**

Regarding clinical efficacy and safety, [HA515 trade name] are considered effective and safe to use when the guidance and restrictions presented in the Summary of Product Characteristics is taken into consideration.

### **Benefit Risk Assessment**

Based on the WHO assessment of data on quality, bioequivalence, safety and efficacy the team of assessors considered by consensus that the benefit–risk profile of [HA515 trade name] was acceptable for the following indication: **“for the treatment of life-threatening or sight-threatening cytomegalovirus (CMV) infections in HIV-infected patients”** and has advised inclusion of Ganciclovir 500 mg Powder for Infusion, manufactured at Hainan Poly Pharm Co Ltd, No.1 Simalu, Guilinyang Economic Development Area, Lingshan, Haikou City, Hainan Province, China in the list of prequalified medicinal products.