Public assessment summary report

Name of the Finished Pharmaceutical Product	Verquvo 2.5 mg film-coated tablets Verquvo 5 mg film-coated tablets Verquvo 10 mg film-coated tablets
Manufacturer of Prequalified Product	Bayer Kaiser-Wilhelm- Allee, 51368 Leverkusen, Nordrhein-Westfalen, Germany
Active Pharmaceutical Ingredient	Vericiguat

1. Introduction

The finished product is presented as a film-coated tablet containing 2.5 mg, 5 mg or 10 mg of vericiguat as active substance. Verquvo is indicated for the treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy.

2. Assessment of quality

Active pharmaceutical Ingredient (API)

The active substance is a white to yellowish non-hygroscopic crystalline powder. It is practically insoluble between pH 3-7 and is very slightly soluble at more acidic pH. The active substance is micronized to improve solubility. Five polymorphic forms were identified during development, along with several solvated and hydrated forms and amorphous material. The chosen commercial polymorphic form (modification I) is routinely produced by the manufacturing process and is the most thermodynamically stable between -20 and 80°C. Vericiguat is achiral. Detailed description for each step, of the synthesis of vericiguat micronized drug substance was provided. The synthesis of vericiguat micronized drug substance involves 4 steps.

Batch results for three representative batches manufactured in commercial scale were provided. All batches were manufactured using the process described in the product dossier. And tested using the methods described in the dossier. All results comply with the specification and demonstrate consistent quality of the batches produced.

The vericiguat reference standard was obtained from a released batch without further purification. Identity and structure of the vericiguat reference standard were proven using IR, NMR and MS spectroscopy by comparison with the reference spectrum, which was presented in Structure elucidation.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture:

The aim of the development was to provide an oral immediate-release formulation containing vericiguat as active substance to meet the posology and patient requirements. The quality target product profile (QTPP) formed the basis of development. The critical quality attributes (CQAs) of the finished product were derived and defined as follows: identity, appearance, assay, uniformity of dosage units/content uniformity , dissolution, degradation products and microbiological quality.

Formulation development started with well-known standard excipients commonly used in immediate release tablet formulations. The manufacturing method of fluid-bed granulation has been applied from the beginning. Initially, a binder solution containing the micronized drug substance and a small amount of wetting agent (= suspension method) was sprayed on a premix consisting of tablet fillers and a disintegrant.

Manufacture of the product

Specifications:

The finished product release and shelf-life specifications for the 5 mg tablet include appropriate tests for this kind of dosage form including appearance (form, colour, markings), identity, uniformity of dosage units (Ph. Eur.), dissolution (Ph. Eur.), degradation products, assay and microbial purity (Ph. Eur.). The specifications for the 2.5 and 10 mg tablets are equivalent with the exception of their appearances.

Batch analysis results were provided for 3 pilot scale batches of each strength confirming the consistency of the manufacturing process and its ability to manufacture to the intended product specification. Compliant analysis data from batches used in phase III clinical trials was also provided. The finished product is released on the market based on release specifications, through traditional final product release testing.

Other ingredients:

Microcrystalline cellulose Croscarmellose sodium Hypromellose 2910 Lactose monohydrate Magnesium stearate Sodium laurilsulfate, Hypromellose 2910 Talc Titanium dioxide (E 171) Iron oxide red (E 172) (Verquvo 5 mg only) Iron oxide yellow (E 172) (Verquvo 10 mg only) were used.

In the formulation, the excipients magnesium stearate, sodium laurilsulfate and lactose monohydrate were identified as substances with possible bovine origin. The magnesium stearate used to manufacture the drug product is of vegetable origin and the sodium laurilsulfate is not of animal origin.

The manufacturer of lactose monohydrate certifies for the origin of the raw materials, that the milk is sourced from healthy animals in the same conditions as milk collected for human consumption, and no other ruminant materials, with the exception of calf rennet, are used in the preparation of such derivatives. Consequently, there is no risk of transmission of spongiform encephalopathy from pharmaceutical use of the drug product.

Stability testing:

Stability data from 3 batches of pilot scale batches of finished product stored for up to 24 months under long term conditions (25°C / 60% RH), for up to 24 months under intermediate conditions (30°C / 75% RH) and for up to 6 months under accelerated conditions (40°C / 75% RH) according to the ICH guidelines were provided. Supporting data were provided for batches stored refrigerated (up to 9 months) and frozen (up to 12 months). The batches are identical to those proposed for marketing and were packed in all 3 primary packaging formats (including 2 sizes of HDPE bottle) proposed for marketing. Samples were tested for appearance, degradation products, assay, dissolution and microbial purity. The analytical procedures used are stability indicating. No significant changes were observed under any of the tested conditions.

3. Clinical study Data

This section of the product dossier was not reviewed. Data with respect to the non-clinical and clinical section was verified from the competent stringent regulatory authority‘s website such as EMA.

4. Conclusion

Based on assessment of data on quality, safety and efficacy the assessors considered that the benefit–risk profile of Verquvo was acceptable for the following indication: Verquvo is indicated for the treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy.

PMR 88397312 (GFJBE/00/MU-202109845)
Pantone: 683, 178, Black, Varnish-free
Batch = Lot Manufact. Date = MFG Expiry date = EXP

001428

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Verquvo® 5 mg

Film Coated Tablets /
comprimés pelliculés
Vericiguat

Oral Use / Voie orale

1 x 14 Tablets / comprimés

MFG

Each film-coated tablet contains
5 mg vericiguat. Contains lactose.
Keep out of the reach and sight of children.
Do not store above 30°C.
Only on Prescription.

Chaque comprimé pelliculé contient
5 mg de vericiguat. Contient du lactose.
Médicament soumis à prescription médicale.
Conserver á une température ne dépassant pas 30°C.
Uniquement sur Ordonnance - Liste I

88397312
60x32x130

Verquvo® 5mg
Film Coated Tablets / comprimés pelliculés
Vericiguat

Verquvo® 5 mg

Film Coated Tablets /
comprimés pelliculés
Vericiguat

Oral Use / Voie orale

1 x 14 Tablets / comprimés

EXP

Lot

Verquvo® 5mg
Film Coated Tablets / comprimés pelliculés
Vericiguat

1 x 14 Tablets / comprimés

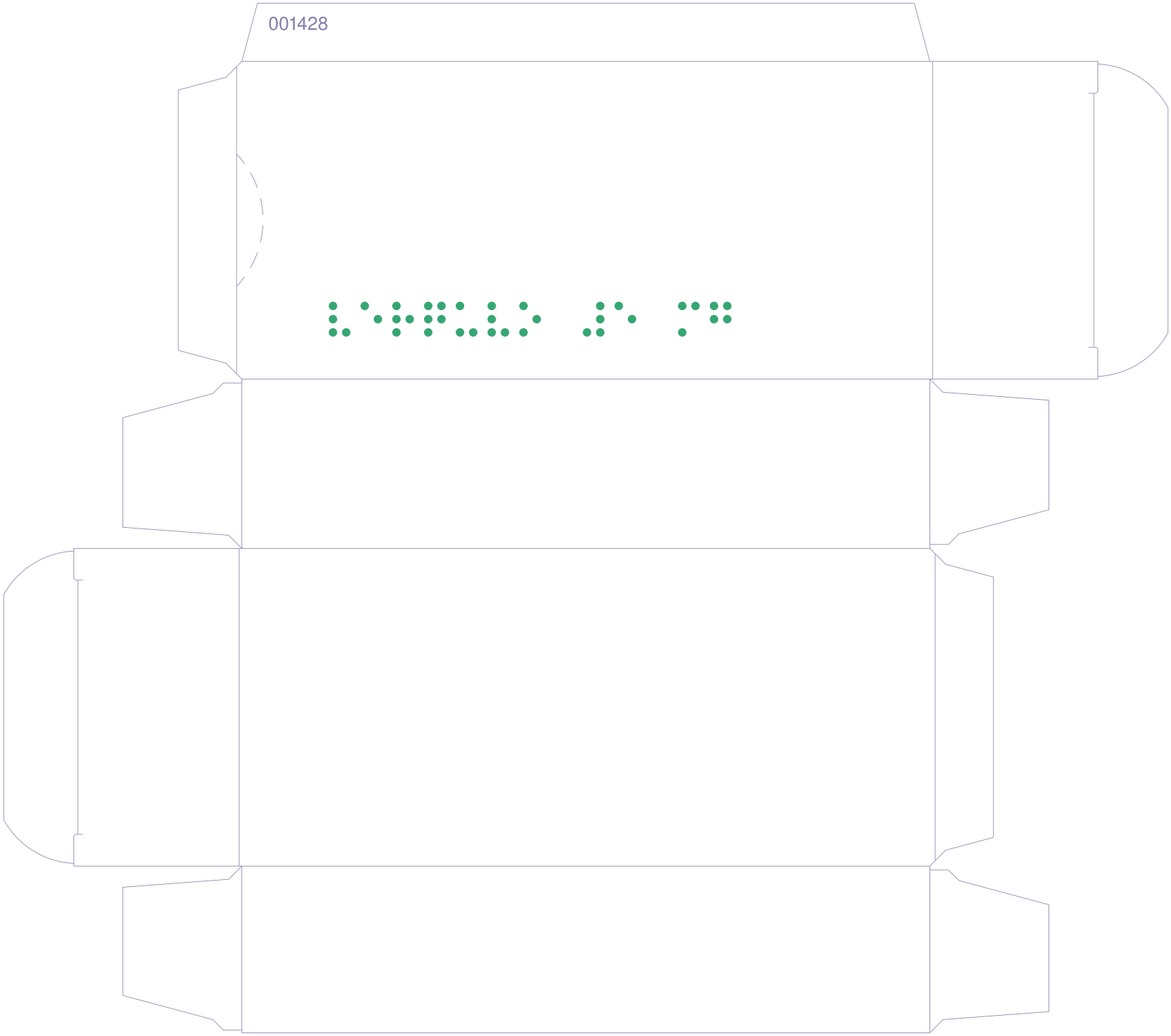
NAFDAC Reg. No:

Bayer AG
51368 Leverkusen
Germany / Allemagne

Bayer

PMR 88397312 **Embossing**

verquvo #5 mg



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