2.1.P.5.6 Justification of Specifications

1 Description

For the description of the Ivermectin 3 mg tablet the following characteristics have been selected:

- Colour: checked by visual examination.
- Shape: checked by visual examination.
- Size: checked by certified tools. The dimensions of the product were strictly controlled during manufacture and have not changed during storage.

2 Identification of the active substance

To identify the pharmaceutically active ingredient (ivermectin) in the product an HPLC-UV assay method was selected. It is able to discriminate between compounds that are present in the product. The specificity and the performance characteristics of the method have been verified by validation.

3 Uniformity of mass

The test is carried out as described in the European Pharmacopoeia [2.9.5. Uniformity of Single-Dose preparations] for tablets. The percentage of deviation requirement is determined by tablet mass, which is 60 mg.

4 Hardness

The test is carried out as described in the European Pharmacopoeia [2.9.8. Resistance to Crushing of Tablets] using a suitable instrument, able to measure the force in newton (N). The results are expressed as the mean, minimum and maximum values registered.

5 Disintegration

The test is carried out as described in the European Pharmacopoeia [2.9.1. Disintegration of Tablets and Capsules – Test A; Tablets and Capsules of Normal Size] using a suitable apparatus without disks. The apparatus is operated for the prescribed time (15 min) and the condition of the tablets in the tubes checked visually.

6 Friability

The test is carried out as described in the European Pharmacopoeia [2.9.7. Friability of Uncoated Tablets] using a suitable instrument. 6.5 g of tablet is tested. After 100 rotation of the drum, the condition of the tablets checked visually, and the weight loss is determined.

7 Uniformity of Dosage Units

The test is carried out as described in the European Pharmacopoeia [2.9.40. Uniformity of Dosage Units]. As the product contains less than 25 mg of the active substance which is also comprises less than 25 % of the total mass, the Content Uniformity Test of European Pharmacopoeia is applied [2.9.6. Uniformity of Content of Single-Dose Preparations]. The assay determination of individual contents of the active substance is carried out by an HPLC method with validated performance characteristics. The calculation of acceptance value (AV) and the acceptance criteria is applied as described in the Pharmacopoeia.

8 Dissolution

A selective dissolution method has been developed to determine the dissolved amount of ivermectin. The method has appropriate discriminatory power, and the dissolved active ingredient are detected by selective HPLC method. In the used medium the sink conditions were established and maintained during the test.
With the infinity time-point determination we demonstrated that with this method 100% of the API could be dissolved. The sample and standard solutions are stable in these conditions. The sampling is done manually, carried out as described US Pharmacopoeia. Prior to the HPLC measurements, the sample and standard solutions are filtered through a 0.45 µm CA filter. No significant absorbance of the API was observed. As our tablet is an immediate release dosage form a single-point measurement was accepted. Finally, the method had been validated.

9 Assay

For the fast and reliable determination of the ivermectin content an HPLC method have been developed. The selectivity of the method had been verified and the performance characteristics had been validated.

10 Microbiological Purity

The microbiological purity of the product is carried out as described in the current European Pharmacopoeia [2.6.12 Microbiological Examination of Non-Sterile Products: Microbiological Enumeration Tests and 2.6.13 Microbiological Examination of Non-Sterile Products: Test for Specified Micro-Organisms]. Acceptance criteria for total aerobic microbial count (TAMC), total combined yeast/mould count (TYMC) and growth of colonies of Escherichia coli has been established.

11 Related substances

A selective HPLC method had been developed to detect the related substances of the tablets. The method selectivity had been demonstrated by the baseline separation of known impurities. The sample and standard solutions are stable in test conditions. The method performance characteristics had been checked and verified during the validation process

12 Loss on drying

Determined by analyzing 2.0 g of powdered tablet in an automated moisture analyzer with halogen heating.