is controlled by using the capsule as a moisture buffer. According to one embodiment, the moisture content of the capsule ranges from about 0.1 wt % to about 16 wt %.

In another embodiment, a gelatin capsule with capsule shell water content from about 6 wt % to about 16 wt % is provided. The gelatin capsule may be a PEG based gelatin capsule with capsule shell water content from about 5 wt % to about 15 wt %. In another embodiment, the capsule may be a hydroxypropyl methyl cellulose (HPMC) capsule with capsule shell water content from about 0.1 wt % to about 10 wt %.

In one aspect of the present invention, there is provided the use of micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight in the manufacture of a medicament for the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form.

In one aspect of the present invention, there is provided a pharmaceutical dosage form suitable for use with a dry powder inhaler comprising

(a) micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, for use in the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form;

(b) a container for said micronized powder particles of colistimethate sodium.

In one aspect of the present invention, there is provided a pharmaceutical dosage form for use in the treatment of a pulmonary infection comprising

(a) micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, wherein the colistimethate sodium is not separated into component form;

(b) a container for said micronized powder particles of colistimethate sodium, wherein said pharmaceutical dosage form is suitable for use with a dry powder inhaler.

In one aspect of the present invention, there is provided a pharmaceutical capsule containing micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, for use in the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form.
In one aspect of the present invention, there is provided a blister pack comprising aluminium foil together with a plurality of pharmaceutical capsules as disclosed herein.

In one aspect of the present invention, there is provided the use of micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, wherein the colistimethate sodium is not separated into component form in the manufacture of a medicament for treatment of gram-negative infections of the respiratory tract wherein the medicament is to be administered to the respiratory tract of a patient.

As described herein in the following Detailed Description and drawings, the present disclosure results in improvements in storage stability, decreases moisture transfer and increases stability and operability of colistimethate sodium.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a particle size analysis of micronized colistin sulphomethate sodium.
Figure 2 shows the structure of colistin sulphomethate with accompanying sodium ions.
Figure 3 shows a neutralised colistin base, as described in U.S. Patent 5,767,068.
Figure 4 shows moisture content of colistimethate sodium as a function of time, relative humidity and storage conditions.
Figure 5 shows moisture content of gelatin capsule at various storage and relative humidity conditions.
Figure 6 shows the frequency of category 3 piercing of gelatin capsules as a function of time and storage conditions.
Figure 7 shows reductions in category 3 piercings of gelatin capsules.

CLAIMS

We Claim:

1. Use of micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight in the manufacture of a medicament for the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form.

2. The use according to Claim 1 wherein 10 % by volume of the particles have a particle size of less than 3 micrometres but not less than 1.5 micrometres.

3. A pharmaceutical dosage form for use in the treatment of a pulmonary infection comprising

(a) micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, wherein the colistimethate sodium is not separated into component form;

(b) a container for said micronized powder particles of colistimethate sodium, wherein said pharmaceutical dosage form is suitable for use with a dry powder inhaler.

4. The pharmaceutical dosage form according to Claim 3 wherein said container is a hard gelatin capsule.

5. A pharmaceutical capsule containing micronized powder particles of colistimethate sodium wherein at least 50% by volume of the micronized particles have a diameter of less than 7 micrometres but not less than 3 micrometres and the powder has a total moisture content of from 5 to 10 % by weight, for use in the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form.