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 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~~ 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 ~~use in~~ the treatment of a pulmonary infection by powder inhalation, wherein the colistimethate sodium is not separated into component form.

2. ~~Micronized powder particles of colistimethate sodium~~ 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 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.

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.

6. The pharmaceutical capsule according to Claim 5 wherein said capsule is translucent.

7. The pharmaceutical capsule according to Claim 5 wherein said capsule additionally contains a micronized bronchodilatory drug.

8. The pharmaceutical capsule according to Claim 5 containing between 1,500,000 and 2,000,000 IU of colistimethate sodium.

~~8~~9. A blister pack comprising aluminium foil together with a plurality of pharmaceutical capsules according to Claim 5.

~~9~~10. ~~A method of therapeutic treatment of gram-negative infections of the respiratory tract which comprises administering to the respiratory tract of a patient~~ 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.

~~10~~11. The ~~method~~ use according to Claim ~~9~~ 10 wherein the patient having the gram-negative infections is a paediatric subject.

~~11~~12. The ~~method~~ use according to Claim ~~9~~ 10 wherein the gram-negative infections are caused by bacterial pathogens selected from the group consisting of *Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella* spp.