SUMMARY

In one aspect, there is provided a spraying device comprising a containment and a spray pump system, the containment filled with a buffered aqueous composition comprising budesonide solubilized therein, the buffered aqueous composition comprising

- a buffer adjusted to a pH of from 4 to 5, preferably adjusted to pH 4.3;
- propylene glycol at a concentration of from 5 to 15 %v/v, preferably of 10% v/v;
- escin, preferably alpha-escin, as a sole saponin component, at a concentration of from 0.1 - 1 mg/ml, preferably 0.3 mg/ml;
- EDTA at a concentration of from 0.5 - 2 mg/ml, preferably 1.0 mg/ml;
- optionally dexpanthenol at a concentration of from 5 - 50 mg/ml and
- solubilized budesonide at a nominal starting concentration of at least 100 µg/mL, preferably at least 200 µg/mL, typically from 200 to 400 µg/mL;

characterized in that the buffered aqueous composition is a mixture of ingredients prepared in a metal-free container and stored in the containment of the spraying device, which containment is made of metal-free material and capped and closed with a spray pump system suitable for nasal or buccal delivery of the aqueous buffered composition, wherein the capped and closed spraying device while being a primary packaging containment for the aqueous buffered composition is hermetically sealed into an oxygen-impermeable and oxygen-free secondary packaging containment, the latter preferably containing an oxygen absorbing agent and optionally also a moisture absorbing agent.

In another aspect, there is provided use of the spraying device as defined herein for the manufacture of a medicament, preferably for a medicament useful in the treatment of inflammatory diseases or conditions, said inflammatory diseases or conditions preferably selected from inflammations of the respiratory pathways, of the lungs, of the intestines, of mucosal tissues, and of the skin.

DESCRIPTION OF THE INVENTION

Solubilized budesonide formulations prepared in accordance with the teaching of WO2017009480A1 contain dexpanthenol typically in a concentration range of from 0.5 to 5% (w/v). Dexpanthenol is used in these formulations to maximize the solubilization capacity and to stabilize the solubilization of budesonide against precipitation during storage at room temperature, i.e. 20 - 25 °C. As indicated above, following the teaching of WO2017009480A1 it is possible to solubilize up to about 850 µg/ml of budesonide and keep it solubilized for long-term storage.

However, evaluating the stability of long-term storage of a hydrophic drug in an aqueous solvent system does not only cover the determination of unimpaired maintenance of drug concentration througout the storage period but shall also include checking for the chemical stability of the entire solubilization system over the envisaged storage period.

Chemical degradation or decomposition of one or more of the ingredients of an aqueous buffered pharmaceutical composition, including the active pharmaceutical ingredient (API), as well as possible reaction products emerging as the result of chemical interactions between two or more of the ingredients and/or decomposition compounds can be stability limiting. Such degradation, decomposition, and/or reaction products are generally considered undesired impurities and present an impediment to obtaining marketing authorization, potentially limiting the availablity of useful therapies.

It is therefore imperative to remove such impurities to the extent possible from aqueous formulations intended for use as pharmaceutical compositions and/or to find ways to avoid the development of such impurities in aqueous solutions comprising solubilized drugs.

In connection with the solubilized budesonide formulations prepared in accordance with the teaching of WO2017009480A1 and including dex-panthenol as part of the solubilization system it was found that the long-term storage stability of the formulations was substantially impaired by the gradual development of an initially unknown and unexpected contaminant, hereinafter designated impurity R", and in addition, by a second contaminant, hereinafter referred to as “impurity D”.