polyethylene glycol copolymer, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropylcellulose, or Arabic gum.

Preferably, the carrier is selected from calcium carbonate, calcium phosphate, dibasic calcium phosphate, tribasic calcium sulfate, calcium carboxymethylcellulose, cellulose, dextrin and its derivatives, dextrose, fructose, lactitol, lactose, starch and modified starches, magnesium carbonate, magnesium oxide, magnesium aluminum silicate, isomalt, mannitol, maltitol, maltodextrin, maltose, sorbitol, starch, sucrose, and xylitol, erythritol or a mixture thereof, or a sugar pellet. More preferably, the carrier is selected from lactose monohydate, magnesium aluminum silicate, microcrystalline cellulose, isomalt, mannitol, dibasic calcium phosphate, or a mixture thereof, or a sugar pellet.

In the fourth example, the present disclosure refers to unit dosage form comprising the pharmaceutical composition as disclosed herein.

The preferred unit dosage form is a tablet or a capsule. Other unit dosage forms have been discussed in previous studies.

In one aspect, the present disclosure refers to a method for manufacturing a pharmaceutical composition comprising brexpiprazole, with the following steps:

a) preparation of a solution consisting of a binder, brexpiprazole and optional surfactant in a solvent system; and

b) wet-granulation of a carrier with the solution obtained in a), wherein the wet-granulation is fluid-bed granulation.

In another aspect, the present disclosure refers to the use of a wet-granulation process with a solution of brexpiprazole as the granulation liquid in the preparation of the pharmaceutical composition comprising brexpiprazole, wherein the wet-granulation is fluid-bed granulation.

In the fifth example, the present disclosure refers to method for manufacturing a pharmaceutical composition comprising brexpiprazole, with the following steps:

a) Preparation of a solution of binder, brexpiprazole and optional surfactant in a solvent system.

b) Wet-granulation of a carrier with the solution obtained in a).

All preferable binders, solvent systems, carriers, optional surfactants are as described above for the pharmaceutical composition of the disclosure. Preferably, the wet-granulation method is fluid-bed granulation, and more preferably top spray fluid-bed granulation.

In the sixth example, the present disclosure refers to use of a wet-granulation process with a solution of brexpiprazole as the granulation liquid in preparation of the pharmaceutical composition comprising brexpiprazole. Such an approach allows for completely eliminating the influence of brexpiprazole particle size distribution on the dissolution profile of bexpiprazole. Control of the dissolution process of brexpiprazole can be achieved by varying the amount of carrier.

Patent claims

1. A method for manufacturing a pharmaceutical composition comprising brexpiprazole, with the following steps:

a) preparation of a solution consisting of a binder, brexpiprazole and optional surfactant in a solvent system; and

b) wet-granulation of a carrier with the solution obtained in a), wherein the wet-granulation is fluid-bed granulation.

2. The method of claim 1, wherein the solvent system consists of a mixture of acetone, ethanol, and water.

3. The method of claim 2, wherein acetone, ethanol, and water are used in a mass ratio 7.7:1:1.

4. The method of any one of claims 1 to 3, wherein the carrier is selected from the group consisting of lactose monohydate, magnesium aluminum silicate, microcrystalline cellulose, isomalt, mannitol, dibasic calcium phosphate, and mixtures thereof, or is a pellet.

5. The method of any one of claims 1 to 4, wherein the binder is selected from the group consisting of polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol copolymer, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropylcellulose, and Arabic gum.

6. The method of any one of claims 1 to 5, wherein the surfactant is selected from the group consisting of polysorbate 80, poloxamer 188, sorbitan monooleate, polysorbate 60, and polyethylene glycol.

7. Use of a wet-granulation process with a solution of brexpiprazole as the granulation liquid, in the preparation of a pharmaceutical composition comprising brexpiprazole, wherein the wet-granulation is fluid-bed granulation.