Claims

1. A multiple unit oral dosage form comprising a capsule shell, a first plurality of modified release units of doxylamine or a pharmaceutically acceptable salt thereof and a second plurality of modified release units of pyridoxine or a pharmaceutically acceptable salt thereof, characterized in that said capsule shell does not contain TiO_2.

2. The oral dosage form according to claim 1, characterized in that said capsule shell comprises at least one pharmaceutically acceptable capsule shell material.

3. The oral dosage form according to anyone of claims 1 or 2, characterized in that said capsule shell comprises at least one pharmaceutically acceptable capsule shell material and at least one pharmaceutically acceptable organic colourant.

4.The oral dosage form according to anyone of the preceding claims, characterized in that said capsule shell consists of at least one pharmaceutically acceptable capsule shell material, at least one pharmaceutically acceptable organic colourant, water and, optionally, at least a pharmaceutically acceptable gelling agent, at least one pharmaceutically acceptable co-gelling agent, at least one pharmaceutically acceptable plasticizer and/or at least one pharmaceutically acceptable inorganic colourant other than TiO_2.

5. The oral dosage form according to anyone of claims 2 to 4, characterized in that said capsule shell material is selected from gelatine, hydroxypropylmethylcellulose, pullulan, alginate, carrageenan, cellulose and/or starch.

6. The oral dosage form according to anyone of the preceding claims, characterized in that said capsule shell consists of gelatine, water, at least one pharmaceutically acceptable organic colourant and, optionally, at least one plasticizer and/or at least one pharmaceutically acceptable inorganic colourant other than TiO_2.

7. The oral dosage form according to anyone of the preceding claims, characterized

in that said capsule shell consists of HPMC, water, at least one pharmaceutically acceptable gelling agent, at least one pharmaceutically acceptable co-gelling agent, at least one pharmaceutically acceptable organic colourant and, optionally, at least one pharmaceutically acceptable plasticizer and/or at least one pharmaceutically acceptable inorganic colourant other than TiO_2.

8. The oral dosage form according to anyone of claims 3 to 7, characterized in that said at least one pharmaceutically acceptable organic colourant is selected from the group consisting of Curcumin (E100), Riboflavin (E101), Riboflavin-5'-phospate (E101a), Tartrazine (E102 or FD&C Yellow 5), Quinoline yellow (E104), Sunset Yellow FCF (E110 or Orange Yellow S, FD&C Yellow 6), Carminic acid/Carmine (E120 or Natural Red 4), Carmoisine (E122 or Azorubine), Amaranth (E123 or FD&C Red 2), Ponceau 4R (E124 or Brilliant Scarlet 4R), Erythrosine (E127 or FD&C Red 3), Allura Red AC (E129 or FD&C 40), Patent Blue V (E131), Indigo carmine (E132 or FD&C Blue 2), Brilliant blue FCF (E133 or FD&C Blue 1), Chlorophylls and Chlorophyllins (E140), copper complexes of Chlorophylls and Chlorophyllins (E141), Green S (E142), Fast Green FCF (E143 or FD&C Green 3), Plain caramel (E150a), Caustic sulfite caramel (E150b), Ammonia caramel (E150c), Sulfite ammonia caramel (E150d), Black PN (E151 or Brilliant Black BN), Vegetable carbon (E153), Brown HT (E155), Alpha-carotene, Beta-carotene, Gamma-carotene (E160a), Annatto, Bixin, Norbixin (E160b), Paprika oleoresin: capsanthin, capsorubin (E160c), Lycopene (E160d), Beta-apo-8'carotenal (E160e), Lutein (E161b), Canthaxanthin (E161g), Beetroot Red, Betanin (E162), Anthocyanins (E163), Saffron (E164) and mixtures thereof, preferably said organic colourant is selected from the group consisting of Indigo carmine, Patent Blue V, Brilliant blue, Erythrosine, Allura Red AC, Quinoline yellow and mixtures thereof.

9. The oral dosage form according to anyone of claims 3 to 8, characterized in that

said at least one pharmaceutically acceptable organic colourant is selected from the group consisting of Brilliant blue; Patent Blue V; Indigo carmine; Patent Blue V and erythrosine; Indigo carmine and quinoline yellow; Indigo carmine and Allura Red AC.

10. The oral dosage form according to claim 9, further containing an inorganic colourant other than TiO_2, preferably yellow iron oxide.

11. The oral dosage form according to anyone of the preceding claims, characterized in that the modified released units of doxylamine or a pharmaceutically acceptable salt thereof and the modified released units of pyridoxine or a pharmaceutically acceptable salt thereof are contained within the capsule shell, preferably within a hard capsule shell constituted by a body and a cap.

12. The oral dosage form according to any of the preceding claims, characterized in that the modified release units of doxylamine or a pharmaceutically acceptable salt thereof are small particles, preferably pellets, and the modified release units of pyridoxine or a pharmaceutically acceptable salt thereof are small particles, preferably pellets and in that neither of them contain TiO_2.

13. The oral dosage form according to anyone of the preceding claims, characterized in that each modified release unit of doxylamine or a pharmaceutically acceptable salt thereof comprises:

- a pharmaceutically acceptable inert nucleus;
- an inner active coating layer comprising a therapeutically effective amount of doxylamine or a pharmaceutically acceptable salt thereof, one or more coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients;
- optionally an intermediate enteric release coating layer comprising one or more enteric coating agents, one or more anticaking agents, optionally one or more pore-

forming agent; and optionally one or more pharmaceutically acceptable excipients, and

- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, one or more anticaking agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients; and/or

each modified release unit of pyridoxine or a pharmaceutically acceptable salt thereof comprises:

- a pharmaceutically acceptable inert nucleus;

- an inner active coating layer comprising a therapeutically effective amount of pyridoxine or a pharmaceutically acceptable salt thereof, one or more coating agents, and optionally one or more pharmaceutically acceptable excipients;

- optionally an intermediate enteric release coating layer comprising one or more enteric coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients, and

- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients;

wherein the nucleus and any of the pharmaceutically acceptable excipient, preferably any of the coating agents, are free of TiO_2.

14. The oral dosage form according to anyone of the preceding claims, characterized in that each modified release unit of doxylamine or a pharmaceutically acceptable salt thereof comprises:

- a pharmaceutically acceptable inert nucleus;

- an inner active coating layer comprising a therapeutically effective amount of doxylamine or a pharmaceutically acceptable salt thereof, one or more coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients;
- an intermediate enteric release coating layer comprising one or more enteric coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients, and
- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, one or more anticaking agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients; and/or

each modified release unit of pyridoxine or a pharmaceutically acceptable salt thereof comprises:

- a pharmaceutically acceptable inert nucleus;
- an inner active coating layer comprising a therapeutically effective amount of pyridoxine or a pharmaceutically acceptable salt thereof, one or more coating agents, and optionally one or more pharmaceutically acceptable excipients; and
- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients;

wherein said nucleus and any of the pharmaceutically acceptable excipients, preferably any of the coating agents, are free of titanium dioxide.

15. The oral dosage form according to anyone of the preceding claims, characterized in that each modified release unit of doxylamine or a pharmaceutically acceptable salt thereof comprises:

- a pharmaceutically acceptable active nucleus comprising a therapeutically effective amount of doxylamine or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable excipients;

- optionally an intermediate enteric release coating layer comprising one or more enteric coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients, and

- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, one or more anticaking agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients; and

each modified release unit of pyridoxine or a pharmaceutically acceptable salt thereof comprising:

- a pharmaceutically acceptable active nucleus comprising a therapeutically effective amount of pyridoxine or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable excipients; and

- optionally an intermediate enteric release coating layer comprising one or more enteric coating agents, one or more anticaking agents, optionally one or more pore-forming agent; and optionally one or more pharmaceutically acceptable excipients, and

- an external modified release coating layer comprising one or more enteric coating agents, one or more modified release coating agents, optionally one or more pore-forming agents, and optionally one or more pharmaceutically acceptable excipients,

wherein said nucleus and any of the pharmaceutically acceptable excipients, preferably any of the coating agents, are free of titanium dioxide.

16. The oral dosage form according to anyone of the preceding claims, comprising a pharmaceutically acceptable salt of doxylamine and a pharmaceutically acceptable salt of pyridoxine; preferably, it comprises doxylamine succinate and pyridoxine hydrochloride.

17. The oral dosage form according to anyone of the preceding claims, comprising from 5 mg to 50 mg per oral dosage form of doxylamine or a pharmaceutically acceptable salt thereof; and from 5 mg to 50 mg per oral dosage form of pyridoxine or a pharmaceutically acceptable salt thereof.

18. The oral dosage form according to anyone of the preceding claims characterized by not containing any opacifier.

19. A manufacturing process for the preparation of the oral dosage form according to anyone of the preceding claims, comprising:

a) preparing, separately, a first plurality of modified release modified release units of doxylamine or a pharmaceutically acceptable salt thereof and a second plurality of modified release units of pyridoxine or a pharmaceutically acceptable salt thereof,

b) optionally, mixing one or both pluralities of the modified release units prepared in step a) with additional excipients, or

c) alternatively, mixing the first and second plurality of modified release units prepared in step a) together and, optionally, mixing such mixture with additional excipients,

d) filling a capsule shell with:

- individually and separately, the first plurality of modified release units of doxylamine or a pharmaceutically acceptable salt thereof obtained in step a), optionally mixed with additional excipients, and the second plurality of modified release units of pyridoxine or a pharmaceutically acceptable salt thereof obtained in step a), optionally mixed with additional excipients, or

- alternatively, the mixture of the first and the second plurality of modified release units of doxylamine or a pharmaceutically acceptable salt and pyridoxine or a pharmaceutically acceptable salt thereof obtained in step c), optionally further mixed with additional excipients; and

e) optionally, packaging the capsules obtained in step d) in blisters or bottles.

20. The oral dosage form according to anyone of claims 1 to 18 for the manufacture of a medicament for preventing nausea and vomiting.