pancreatic exocrine insufficiency, immune-deficiency syndromes, small intestinal obstruction, diverticulitis, fistulae, surgical blind loop, previous ileo-caecal resections, post-radiation enteropathy, small intestinal pseudo-obstruction, small intestinal bacterial overgrowth syndrome, vaginal mycosis, intestinal mycosis, multiple system atrophy, food intolerance, intestinal infections, gallstones and hyperactivity of the immune system, wherein said at least one further disease ii) results in intestinal dysbiosis, and/or at least one further disease iii) selected from the group consisting of cirrhosis, hepatitis, appendicitis, pancreatitis, chronic kidney disease and cholecystitis, wherein said at least one further disease iii) increases the risk for peritonitis.

In the second object, the present invention is also concerned with a method of treating pain comprising administering an oral pharmaceutical dosage form comprising oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof to a patient suffering from i) pain and at least one further disease ii), wherein said at least one further disease ii) results in intestinal dysbiosis, or a method of treating pain comprising administering said oral pharmaceutical dosage form to a patient suffering from i) pain and at least one further disease iii), wherein said at least one further disease iii) increases the risk for intestinal bacterial translocation.

In another object, the present invention is also concerned with a use of oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof in the manufacture of an oral dosage form for treating pain in patients suffering from i) pain and at least one further disease ii), wherein said at least one further disease ii) results in intestinal dysbiosis, or for use in the treatment of pain in patients suffering from i) pain and at least one further disease iii), wherein said at least one further disease iii) increases the risk for intestinal bacterial translocation, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small

intestinal pseudo- obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections, intestinal mycosis, obesity, autism, metabolic syndrome, rheumatoid arthritis, allergy, diabetes mellitus including type 2 diabetes and sepsis, and/or wherein said at least one further disease iii) is selected from the group consisting of appendicitis, pancreatitis, cholangitis, burn injury, trauma and cholecystitis, and wherein i) pain is not a symptom of the at least one further disease ii) or the at least one further disease iii)

In another object, the present invention is also concerned with a method for treating pain in patients suffering from i) pain and at least one further disease ii), wherein said at least one further disease ii) results in intestinal dysbiosis, or for the treatment of pain in patients suffering from i) pain and at least one further disease iii), wherein said at least one further disease iii) increases the risk for intestinal bacterial translocation, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections, intestinal mycosis, obesity, autism, metabolic syndrome, rheumatoid arthritis, allergy, diabetes mellitus including type 2 diabetes and sepsis, and/or wherein said at least one further disease iii) is selected from the group consisting of appendicitis, pancreatitis, cholangitis, burn injury, trauma and cholecystitis, and wherein i) pain is not a symptom of the at least one further disease ii) or the at least one further disease iii), the method comprising the step of administering to said patient an oral dosage form comprising oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof and naloxone.

All embodiments mentioned above for the first object also apply for the second object of the present invention.

DESCRIPTION OF THE FIGURES

Figure 1 depicts a graphic of the study design of Example 1.

Figure 2 shows the outline of the group, dosing regimens and study designs used in Example 3.

CLAIMS

1. Use of oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof in the manufacture of an oral dosage form for treating pain in patients suffering from i) pain and at least one further disease ii), wherein said at least one further disease ii) results in intestinal dysbiosis, or for use in the treatment of pain in patients suffering from i) pain and at least one further disease iii), wherein said at least one further disease iii) increases the risk for intestinal bacterial translocation, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections, intestinal mycosis, obesity, autism, metabolic syndrome, rheumatoid arthritis, allergy, diabetes mellitus including type 2 diabetes and sepsis, and/or wherein said at least one further disease iii) is selected from the group consisting of appendicitis, pancreatitis, cholangitis, burn injury, trauma and cholecystitis, and wherein i) pain is not a symptom of the at least one further disease ii) or the at least one further disease iii).

2. Use according to claim 1, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation

enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections and intestinal mycosis.

3. Use according to claim 1 or 2, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections and intestinal mycosis.

4. Use according to any one of claims 1 to 3, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance and hyperactivity of the immune system.

5. Use according to claim 1, wherein said at least one further disease iii) is selected from the group consisting of pancreatitis, cholangitis, burn injury and cholecystitis.

6. Use according to any one of the preceding claims, wherein said intestinal dysbiosis and/or said increased risk for intestinal bacterial translocation is not induced by an opioid agonist but by said at least one further disease ii) or iii).

7. Use according to any one of the preceding claims, wherein said pain is moderate to severe pain.

8. Use according to any one of the preceding claims, wherein oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof are the only pharmaceutically active agents comprised in said dosage form.

9. Use according to any one of the preceding claims, wherein the pain treatment regimen excludes the co-administration of an active agent directed to the improvement of the intestinal dysbiosis and/or of an active agent decreasing the risk for intestinal bacterial translocation and/or of an active agent directed to the improvement of opioid-induced constipation and/or opioid-induced bowel dysfunction.

10. Use according to any one of the preceding claims, wherein the dosage form comprises oxycodone or a pharmaceutically acceptable salt thereof in an amount range of equivalent to about 1 mg to about 160 mg oxycodone HCl and naloxone or a pharmaceutically acceptable salt thereof in an amount range of equivalent to about 0.5 mg to about 80 mg naloxone HCl.

11. Use according to any one of the preceding claims, wherein the dosage form comprises oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof in a 2:1 ratio by weight.

12. Use according to any one of the preceding claims, wherein the dosage form is a prolonged release dosage form.

13. Use according to claim 12, wherein the dosage form comprises a prolonged release matrix.

14. Use according to claim 13, wherein the matrix comprises a fatty alcohol and/or a hydrophobic polymer.

15. Use according to claim 14, wherein the matrix comprises an alkylcellulose.

16. Use according to claim 15, wherein the alkylcellulose is ethylcellulose.

17. Use according to claim 12, wherein the dosage form comprises a prolonged release coating.

18. Use according to any one of claims 1 to 11, wherein the dosage form is an immediate release dosage form.

19. Use according to any one of the preceding claims, wherein the dosage form is a dosage form selected from the group consisting of a tablet, a capsule, a multi-particulate, a dragee, a granulate and a powder.

20. A method for treating pain in patients suffering from i) pain and at least one further disease ii), wherein said at least one further disease ii) results in intestinal dysbiosis, or for the treatment of pain in patients suffering from i) pain and at least one further disease iii), wherein said at least one further disease iii) increases the risk for intestinal bacterial translocation, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections, intestinal mycosis, obesity, autism, metabolic syndrome, rheumatoid arthritis, allergy, diabetes mellitus including type 2 diabetes and sepsis, and/or wherein said at least one further disease iii) is selected from the group consisting of appendicitis, pancreatitis, cholangitis, burn injury, trauma and cholecystitis, and wherein i) pain is not a symptom of the at least one further disease ii) or the at least one further disease iii), the method comprising the step of administering to said patient an oral dosage form comprising oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof and naloxone.

21. Method according to claim 20, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, colorectal cancer, ulcerative colitis, diverticulitis, fistulae, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections and intestinal mycosis.

22. Method according to claims 20 or 21, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance, hyperactivity of the immune system, previous ileo-caecal resection, post-radiation enteropathy, autonomic neuropathy including autonomic neuropathy in type 1 and 2 diabetes, intestinal infections and intestinal mycosis.

23. Method according to any one of claims 20 to 22, wherein said at least one further disease ii) is selected from the group consisting of achlorhydria, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth syndrome, small intestinal pseudo-obstruction, surgical blind loop, small intestinal obstruction, scleroderma, food intolerance and hyperactivity of the immune system.

24. Method according to claim 20, wherein said at least one further disease iii) is selected from the group consisting of pancreatitis, cholangitis, burn injury and cholecystitis.

25. Method according to any one the preceding claims, wherein said intestinal dysbiosis and/or said increased risk for intestinal bacterial translocation is not induced by an opioid agonist but by said at least one further disease ii) or iii).

26. Method according to any one of the preceding claims, wherein said pain is moderate to severe pain.

27. Method according to any one of the preceding claims, wherein oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof are the only pharmaceutically active agents comprised in said dosage form.

28. Method according to any one of the preceding claims, wherein the pain treatment regimen excludes the co-administration of an active agent directed to the improvement of the intestinal dysbiosis and/or of an active agent decreasing the risk for intestinal bacterial translocation and/or of an active agent directed to the improvement of opioid-induced constipation and/or opioid-induced bowel dysfunction.

29. Method according to any one of the preceding claims, wherein the dosage form comprises oxycodone or a pharmaceutically acceptable salt thereof in an amount range of equivalent to about 1 mg to about 160 mg oxycodone HCl and naloxone or a pharmaceutically acceptable salt thereof in an amount range of equivalent to about 0.5 mg to about 80 mg naloxone HCl.

30. Method according to any one of the preceding claims, wherein the dosage form comprises oxycodone or a pharmaceutically acceptable salt thereof and naloxone or a pharmaceutically acceptable salt thereof in a 2:1 ratio by weight.

31. Method according to any one of the preceding claims, wherein the dosage form is a prolonged release dosage form.

32. Method according to claim 31, wherein the dosage form comprises a prolonged release matrix.

33. Method according to claim 32, wherein the matrix comprises a fatty alcohol and/or a hydrophobic polymer.

34. Method according to claim 33, wherein the matrix comprises an alkylcellulose.

35. Method according to claim 34, wherein the alkylcellulose is ethylcellulose.

36.Method according to claim 31, wherein the dosage form comprises a prolonged release coating.

37. Method according to any one of claims 20 to 30, wherein the dosage form is an immediate release dosage form.

38. Method according to any one of the preceding claims, wherein the dosage form is a dosage form selected from the group consisting of a tablet, a capsule, a multi-particulate, a dragee, a granulate and a powder.