Claims

1. A coated tablet composition for administration once daily comprising a coating and a tablet core, wherein the coating comprises an immediate release part comprising one or more glucocorticoids and one or more pharmaceutically acceptable immediate release excipients or carriers adapted so that the one or more glucocorticoids are substantially immediately released; and wherein the tablet core comprises an extended release part comprising one or more glucocorticoids in an amount of 60-80% of the total hydrocortisone equivalents in the composition and one or more pharmaceutically acceptable extended release excipients or carriers adapted so that the one or more glucocorticoids are released over an extended period of time of at least about 8 hours,

wherein the amount of the one or more glucocorticoids in total corresponds to a daily dose of from about 1 to 80 mg hydrocortisone equivalents and wherein the amount of the one or more glucocorticoids of the immediate release part in the coating, expressed as hydrocortisone equivalents, being in a range of from about 20-40% of the total hydrocortisone equivalents in the composition and determined as the amount released 1 hour after start of testing of the composition in an in vitro dissolution test according to USP employing USP Dissolution Apparatus No. 2 (paddle), 50 rpm and simulated intestinal fluid without enzymes as dissolution medium,

and wherein the one or more pharmaceutically acceptable immediate release excipients or carriers in the coating are selected from the group consisting of methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, acrylic polymers, ethylcellulose, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinylalcohol, sodium carobxymethylcellulose, cellulose acetate, cellulose acetate phthalate, gelatin, methacrylic acid copolymer, polyethylene glycol, shellac, sucrose, titanium dioxide, carnauba wax, microcrystalline wax, glyceryl monostearate, talc or zein and any mixtures of combinations thereof;

and wherein the one or more pharmaceutically acceptable extended release excipients or carriers are selected from the group comprising:

a) one or more filler or binders selected from the group consisting of lactose, microcrystalline cellulose, L-hydroxypropylcellulose (low substituted), hydroxypropyl methylcellulose, methylcellulose polymers, sucrose, agarose, sorbitol, mannitol, dextrins,

maltodextrins, starches or modified starches, calcium phosphate, calcium sulphate, calcium carbonate, sodium alginate or collagen

b) one or more glidants and/or lubricants selected from the group consisting of stearic acid, magnesium stearate, calcium stearate or other metallic stearate, talc, waxes and glycerides, light mineral oil, PEG, glyceryl behenate, colloidal silica, hydrogenated vegetable oils, corn starch, sodium stearyl fumarate, polyethylene glycols, alkyl sulfates, sodium benzoate or sodium acetate.

2. A coated tablet composition according to anyone of the preceding claims, wherein the amount of one or more glucocorticoids of the first part, expressed as hydrocortisone equivalents, is in a range of from about 20 to about 40% such as, e.g. from about 25 to about 35% of the total hydrocortisone equivalents in the composition.

3. A coated tablet composition according to anyone of the preceding claims, wherein the second part of one or more glucocorticoids is released over an extended period of time of at least 10 hours.

4. A coated tablet composition according to claim 3, wherein the release is determined in the dissolution test as defined in claim 1.

5. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoids is selected from the group consisting of hydrocortisone, cortisone, prednisolone, prednisone, methylprednisone, triamcinolone, paramethasone, betamethasone, dexamethasone and fludrocortisones including pharmaceutically acceptable esters, salts and complexes thereof.

6. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoids of the first and the second part are the same glucocorticoid or a mixture of the same glucocorticoids.

7. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoids of the first and the second part are different glucocorticoids or a mixture of different glucocorticoids.

8. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoids of the first part is a synthetic glucocorticoid such as, e.g., hydrocortisone 21-succinate, prednisolone, prednisone, methylprednisone, triamcinolone, paramethasone, betamethasone, dexamethasone and fludrocortisone including pharmaceutically acceptable esters, salts and complexes thereof.

9. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoid of the first part is hydrocortisone or hydrocortisone 21-succinate or a pharmaceutically acceptable salt thereof.

10. A coated tablet composition according to anyone of the preceding claims, wherein the one or more glucocorticoid of the second part is hydrocortisone.

11. A coated tablet composition according to anyone of the preceding claims, wherein the total amount of hydrocortisone equivalents in the composition is from about 12 to about 75 mg.

12. A kit for once daily glucocorticoid administration comprising
(i) a first component comprising one or more glucocorticoids and one or more pharmaceutically acceptable immediate release excipients or carriers adapted so that, the first component effects substantially immediate release of the one or more glucocorticoids, and wherein the amount of the one or more glucocorticoids in the first component, expressed as hydrocortisone equivalents, is in the range of 20-40% of the total amount of glucocorticoids in the kit, and determined as the amount released after 1 hour after start of testing of the kit in an *in vitro* dissolution test employing USP Dissolution Apparatus No. 2 (paddle), 50 rpm and simulated intestinal fluid without enzymes as dissolution medium;

(ii) a second component comprising one or more glucocorticoids and one or more pharmaceutically acceptable extended release excipients or carriers adapted so that, the second component effects extended release of the one or more glucocorticoids over a period of time of at least about 8 hours, and wherein the amount of the one or more glucocorticoids in the second component, expressed as hydrocortisone equivalents, is in the range of 60-80% of the total amount of glucocorticoids in the kit;

wherein the amount of the one or more glucocorticoids in total corresponds to a daily dose of from about 1 to 80 mg hydrocortisone equivalents;

and wherein the one or more pharmaceutically acceptable immediate release excipients or carriers are selected from the group comprising one or more of methylcellulose, hydroxypropylmethylcelluose, hydroxypropylcellulose, acrylic polymers, ethylcellulose, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinylalcohol, sodium casrboxymethylcellulose, cellulose acetate, cellulose acetate phthalate, gelatin, methacrylic acid copolymer, polyethylene glycol, shellac, sucrose, titanium dioxide, carnauba wax, microcrystalline wax, glyceryl monostearate, talc or zein;

and wherein the one or more pharmaceutically acceptable extended release excipients or carriers are selected from the group comprising:

a) one or more filler or binders selected from the group consisting of lactose, microcrystalline cellulose, L-hydroxypropylcellulose (low substituted), hydroxypropyl methylcellulose, methylcellulose polymers, sucrose, agarose, sorbitol, mannitol, dextrins, maltodextrins, starches or modified starches, calcium phosphate, calcium sulphate, calcium carbonate, sodium alginate or collagen,

b) one or more glidants and/or lubricants selected from the group consisting of stearic acid, magnesium stearate, calcium stearate or other metallic stearate, talc, waxes and glycerides, light mineral oil, PEG, glyceryl behenate, colloidal silica, hydrogenated vegetable oils, corn starch, sodium stearyl fumarate, polyethylene glycols, alkyl sulfates, sodium benzoate or sodium acetate.

13. A kit according to anyone of claims 12, wherein the amount of one or more glucocorticoids of the first component, expressed as hydrocortisone equivalents, is in a

range of from about 15 to about 50% such as, e.g., from about 20 to about 40% or from about 25 to about 35% of the total hydrocortisone equivalents in the kit.

14. A kit according to anyone of claims 12-13, wherein the one or more glucocorticoids of the second component is released over an extended period of time of at least 10 hours.

15. A kit according to claim 14, wherein the release is determined in the dissolution test as defined in claim 12.

16. A kit according to anyone of claims 12-15, wherein the amount of one or more glucocorticoids of the second component, expressed as hydrocortisone equivalents, is in a range of from about 50 to about 90% of the total hydrocortisone equivalents in the kit.

17. A kit according to anyone of claims 12-16, wherein each of the first and the second component is in the form of a solid dosage form.

18. A kit according to claim 17, wherein the solid dosage form is selected from the group consisting of granules, beads, pellets and powders.

19. A kit according to anyone of claims 12-18, wherein each of the first and the second component is in the form of a unit dosage form.

20. A kit according to claim 19, wherein the unit dosage form is a tablet, capsule or a sachet.

21. A kit according to anyone of claims 12-20, wherein the first component is in the form of a dosage form that is adapted to administration to or via a mucosa.

22. A kit according to claim 21, wherein the mucosa is selected from the mucosa in the oral cavity, the nasal cavity, the rectum, the gastrointestinal mucosa, or pulmonary, bronchial or respiratory mucosa and epithelia.

23. A kit according to claim 22, wherein the mucosa is the mucosa in the oral cavity.

24. A kit according to anyone of claims 12-23, wherein the first component is in liquid, semi-solid or solid form.

25. A kit according to claim 19, wherein the first component is in the form of a tablet including a chewable tablet, a suckable tablet, an effervescent tablet, a sublingual tablet, a rapid-burst tablet, immediate release tablets, rapidly dissolvable tablets or the like.

26. A kit according to claim 24, wherein the first component is in the form of a spray, a wafer, a film, a hydrogel, a bioadhesive patch, an inhaler, a powder inhaler, a sachet, a suppository, a clysma, a solution or the like.

27. A kit according to anyone of claims 12-26, wherein the second component is in the form of a solid unit dosage form.

28. A kit according to anyone of claims 12-27, wherein the total amount of hydrocortisone equivalents in the kit is from about 1 to about 75 mg.

29. A kit according to anyone of claims 12-28, wherein the first and the second component are intended for substantially simultaneous administration.

30. A kit according to anyone of claims 12-28, wherein the first and the second component are intended for sequential administration.

31. A kit according to anyone of claims 12-30 further comprising a third component comprising one or more glucocorticoids designed for substantially immediate release of the one or more glucocorticoids.

32. Use of a first and a second amount of one or more glucocorticoids for the preparation of a coated tablet composition as defined in any of claims 1-11 for the

treatment of adrenocortical insufficiency, including Addison's disease by administration once daily of said coated tablet composition.

33. Use of a first and a second amount of one or more glucocorticoids for the preparation of a pharmaceutical kit as defined in any of claims 12-31 for the treatment of a glucocorticoid deficiency disorder by administration once daily of said kit.

34. Use according to claim 32 or 33, wherein the first amount of one or more glucocorticoids leads to a fast rise in the glucocorticoid serum level and the second amount of one or more glucocorticoids leads to an effective serum concentration of the one or more glucocorticoids during an extended period of time of at least 8 hours.

35. Use according to anyone of claims 32-34, wherein the first and the second effective amount of the one or more glucocorticoids are administered substantially simultaneously.

36. Use according to anyone of claims 32-34, wherein the first and the second effective amount of the one or more glucocorticoids are administered sequentially.

37. Use according to any of one claims 32-36, wherein the serum level obtained within 45 min after administration of the first effective amount of the one or more glucocorticoids is at least 200 nmol/l.

38. Use according to anyone of claims 32-37, wherein the serum level obtained 2 hours after administration of the first effective amount of the one or more glucocorticoids is in a range of from about 200 to about 1000 nmol/l.

39. Use according to anyone of claims 32-38, wherein the serum level obtained 6 hours after administration of the first effective amount of the one or more glucocorticoids is in a range of from about 200 to about 600 nmol/l.

40. Use according to anyone of claims 32-39, wherein the serum level obtained 10 hours after administration of the first effective amount of the one or more glucocorticoids is in a range of from about 50 to about 400 nmol.

41. Use according to anyone of claims 32-40, wherein the serum level obtained 14 hours after administration of the first effective amount of the one or more glucocorticoids is at the most 300 nmol/l.

42. Use according to anyone of claims 32-41, wherein the serum level obtained 18 hours after administration of the first effective amount of the one or more glucocorticoids is less than 100 nmol/l.

43. Use according to anyone of claims 32-42, wherein the first and the second effective amount of the one or more glucocorticoids are administered at wake-up in the morning between about 4am and noon.

44. Use according to claim 43, wherein the first and the second effective amount of the one or more glucocorticoids are administered to the subject in fasted state.

45. Use according to anyone of claims 32-44, wherein the serum level obtained in a time period corresponding to from about 0.5-1 to about 6.5-7 hours after administration of the first effective amount of the one or more glucocorticoids essentially mimics the serum level of cortisol of a healthy subject in the morning from 6am to noon.

46. Use according to anyone of claims 32-45, wherein a 3 hours substantially glucocorticoid-free serum level is obtained daily in a time period of from about 10pm to about 6am.

Claims

1. A coated tablet composition for administration once daily comprising a coating and a tablet core, wherein the coating comprises an immediate release part comprising one or more glucocorticoids and one or more pharmaceutically acceptable immediate release excipients or carriers adapted so that the one or more glucocorticoids are substantially immediately released; and wherein the tablet core comprises an extended release part comprising one or more glucocorticoids in an amount of 60-80% of the total hydrocortisone equivalents in the composition and one or more pharmaceutically acceptable extended release excipients or carriers adapted so that the one or more glucocorticoids are released over an extended period of time of at least about 8 hours,

wherein the amount of the one or more glucocorticoids in total corresponds to a daily dose of from about 1 to 80 mg hydrocortisone equivalents and wherein the amount of the one or more glucocorticoids of the immediate release part in the coating, expressed as hydrocortisone equivalents, being in a range of from about 20-40% of the total hydrocortisone equivalents in the composition and determined as the amount released 1 hour after start of testing of the composition in an *in vitro* dissolution test according to USP employing USP Dissolution Apparatus No. 2 (paddle), 50 rpm and simulated intestinal fluid without enzymes as dissolution medium,

and wherein the one or more pharmaceutically acceptable immediate release excipients or carriers in the coating are selected from the group consisting of methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, acrylic polymers, ethylcellulose, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinylalcohol, sodium carobxymethylcellulose, cellulose acetate, cellulose acetate phthalate, gelatin, methacrylic acid copolymer, polyethylene glycol, shellac, sucrose, titanium dioxide, camauba wax, microcrystalline wax, glyceryl monostearate, talc, zein and any mixtures of combinations thereof;

and further wherein the one or more pharmaceutically acceptable extended release excipients or carriers are selected from the group consisting of:

a) one or more fillers or binders selected from the group consisting of lactose, microcrystalline cellulose, low substituted L-hydroxypropylcellulose, hydroxypropyl methylcellulose, methylcellulose polymers, sucrose, agarose, sorbitol, mannitol, dextrins, maltodextrins, starches, modified starches, calcium

phosphate, calcium sulphate, calcium carbonate, sodium alginate and collagen; and

b) one or more glidants and/or lubricants selected from the group consisting of stearic acid, magnesium stearate, calcium stearate or other metallic stearate, talc, waxes and glycerides, light mineral oil, PEG, glyceryl behenate, colloidal silica, hydrogenated vegetable oils, corn starch, sodium stearyl fumarate, polyethylene glycols, alkyl sulfates, sodium benzoate and sodium acetate.

2. The composition according to claim 1, wherein at least 50% of the hydrocortisone equivalents of the first part are released within the first 30 min or within the first 20 min or within the first 15 min of the dissolution test.

3. The composition according to claim 1 or 2, wherein at least about 60% of the hydrocortisone equivalents of the immediate release part are released within the first 30 min of the dissolution test.

4. The composition according to any one of claims 1 to 3, wherein at least 60% of the hydrocortisone equivalents of the immediate release part are released within the first 20 min of the dissolution test.

5. The composition according to any one of claims 1 to 4, wherein at least 70% of the hydrocortisone equivalents of the immediate release part are released within the first 30 min of the dissolution test.

6. The composition according to any one of claims 1 to 5, wherein at least 70% of the hydrocortisone equivalents of the immediate release part are released within the first 20 min of the dissolution test.

7. The composition according to any one of claims 1 to 6, wherein at least 80% of the hydrocortisone equivalents of the immediate release part are released within the first 30 min of the dissolution test.

8. The composition according to any one of claims 1 to 7, wherein at least 80% of the hydrocortisone equivalents of the immediate release part are released within the first 20 min of the dissolution test.

9. The composition according to any one of claims 1 to 8, wherein at least 90% of the hydrocortisone equivalents of the immediate release part are released within the first 30 min of the dissolution test.

10. The composition according to any one of claims 1 to 9, wherein at least 90% of the hydrocortisone equivalents of the immediate release part are released within the first 20 min of the dissolution test.

11. The composition according to any one of claims 1 to 10, wherein the amount of one or more glucocorticoids of the immediate release part, expressed as hydrocortisone equivalents, is in a range of from about 20 to 40% or from 25 to 35% of the total hydrocortisone equivalents in the composition.

12. The composition according to any one of claims 1 to 11, wherein the extended release part of one or more glucocorticoids is released over an extended period of time of at least 10 hours, and wherein the release is determined in the dissolution test as defined in claim 1.

13. The composition according to any one of claims 1 to 12, wherein at least 50% of the total hydrocortisone equivalents in the composition are released within 10 hours after start of the dissolution test defined in claim 1.

14. The composition according to any one of claims 1 to 13, wherein at least 50% of the total hydrocortisone equivalents in the composition are released within 8 hours or within 6 hours or within 5 hours after start of the dissolution test defined in claim 1.

15. The composition according to any one of claims 1 to 14, wherein at least 80% of the total hydrocortisone equivalents in the composition are released within 24 hours after start of the dissolution test defined in claim 1.

16. The composition according to any one of claims 1 to 15, wherein at least 80% of the total hydrocortisone equivalents in the composition are released within 22 hours or within 20 hours after start of the dissolution test defined in claim 1.

17. The composition according to any one of claims 1 to 16, wherein from 3 to 15% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 1 to 8 hours after start of the dissolution test as defined in claim 1.

18. The composition according to any one of claims 1 to 17, wherein from 3 to 10% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 1 to 8 hours after start of the dissolution test as defined in claim 1.

19. The composition according to any one of claims 1 to 18, wherein from 3 to 15% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 1 to 10 hours or from t1 to t 12 hours after start of the dissolution test as defined in claim 1.

20. The composition according to any one of claims 1 to 19, wherein from 3 to 10% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 1 to 10 hours or from 1 to 12 hours after start of the dissolution test as defined in claim 1.

21. The composition according to any one of claims 1 to 20, wherein
i) from 3 to 15% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 1 to 6 hours,
ii) from 3 to 10% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from t 6 to 10 hours, and
iii) from 3 to 7.5% of the hydrocortisone equivalents contained in the extended release part are released per hour during a time period of from 10 to 12 hours after start of the dissolution test as defined in claim 1.

22. The composition according to any one of claims 1 to 21, wherein the amount of hydrocortisone equivalents of the extended release part of the composition is determined as (H_{total} - $H_{first\ part}$), wherein H_{total} is the total amount of hydrocortisone equivalents released within 24 hours after start of the test defined in claim 1 and $H_{first\ part}$ is the amount of hydrocortisone equivalents of the immediate release part of the composition determined as defined in claim 1.

23. The composition according to any one of claims 1 to 22, wherein the one or more glucocorticoid is selected from the group consisting of hydrocortisone, cortisone, prednisolone, prednisone, methylprednisone, triamcinolone, paramethasone, betamethasone, dexamethasone, fludrocortisone, pharmaceutically acceptable esters thereof, salts thereof and complexes thereof.

24. The composition according to any one of claims 1 to 23, wherein the one or more glucocorticoids of the immediate release and the extended release part are the same glucocorticoid or a mixture of the same glucocorticoids.

25. The composition according to any one of claims 1 to 24, wherein the one or more glucocorticoids of the immediate release and the extended release part are different glucocorticoids or a mixture of different glucocorticoids.

26. The composition according to any one of claims 1 to 25, wherein the one or more glucocorticoids of the immediate release part has an acceptable taste, is tasteless or is effectively taste-masked.

27. The composition according to any one of claims 1 to 26, wherein the one or more glucocorticoids of the immediate release part is a synthetic glucocorticoid selected from the group consisting of hydrocortisone 21-succinate, prednisolone, prednisone, methylprednisone, triamcinolone, paramethasone, betamethasone, dexamethasone, fludrocortisone, pharmaceutically acceptable esters thereof, salts thereof and complexes thereof.

28. The composition according to any one of claims 1 to 27, wherein the one or more glucocorticoid of the immediate release part is hydrocortisone or hydrocortisone 21-succinate or a pharmaceutically acceptable salt thereof.

29. The composition according to any one of claims 1 to 28, wherein the one or more glucocorticoid of the extended release part is hydrocortisone.

30. The composition according to any one of claims 1 to 29 for administration once daily in the morning.

31. The composition according to any one of claims 1 to 30, wherein the total amount of hydrocortisone equivalents in the composition is from 1 to 75 mg, from 1 to 70 mg, from 5 to 60 mg, from 5 to 50 mg, from 5 to 40 mg or from 10 to 30 mg.

32. The composition according to claim 23, wherein the one or more glucocorticoids of first and the second part are provided as pellets, granules, beads or powders.

33. A kit for once daily glucocorticoid administration comprising:

(i) a first component comprising one or more glucocorticoids and one or more pharmaceutically acceptable immediate release excipients or carriers adapted so that, the first component effects substantially immediate release of the one or more glucocorticoids, and wherein the amount of the one or more glucocorticoids in the first component, expressed as hydrocortisone equivalents, is in the range of 20-40% of the total amount of glucocorticoids in the kit, and determined as the amount released after 1 hour after start of testing of the kit in an *in vitro* dissolution test employing USP Dissolution Apparatus No. 2 (paddle), 50 rpm and simulated intestinal fluid without enzymes as dissolution medium;

(ii) a second component comprising one or more glucocorticoids and one or more pharmaceutically acceptable extended release excipients or carriers adapted so that, the second component effects extended release of the one or more glucocorticoids over a period of time of at least about 8 hours, and wherein the amount of the one or more glucocorticoids in the second component, expressed as hydrocortisone equivalents, is in the range of 60-80% of the total amount of glucocorticoids in the kit;

wherein the amount of the one or more glucocorticoids in total corresponds to a daily dose of from about 1 to 80 mg hydrocortisone equivalents;

and wherein the one or more pharmaceutically acceptable immediate release excipients or carriers are selected from the group consisting of one or more of methylcellulose, hydroxypropylmethylcelluose, hydroxypropylcellulose, acrylic polymers, ethylcellulose, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinylalcohol, sodium carboxymethylcellulose, cellulose acetate, cellulose acetate phthalate, gelatin, methacrylic acid copolymer, polyethylene glycol, shellac, sucrose, titanium dioxide, carnauba wax, microcrystalline wax, glyceryl monostearate, talc and zein;

and further wherein the one or more pharmaceutically acceptable extended release excipients or carriers are selected from the group consisting of:

a) one or more fillers or binders selected from the group consisting of lactose, microcrystalline cellulose, low substituted L-hydroxypropylcellulose, hydroxypropyl methylcellulose, methylcellulose polymers, sucrose, agarose, sorbitol, mannitol, dextrins, maltodextrins, starches or modified starches, calcium phosphate, calcium sulphate, calcium carbonate, sodium alginate and collagen; and

b) one or more glidants and/or lubricants selected from the group consisting of stearic acid, magnesium stearate, calcium stearate or other metallic stearate, talc, waxes and glycerides, light mineral oil, PEG, glyceryl behenate, colloidal silica, hydrogenated vegetable oils, corn starch, sodium stearyl fumarate, polyethylene glycols, alkyl sulfates, sodium benzoate and sodium acetate.

34. The kit according to claim 33, wherein at least 50% of the one or more glucocorticoids of the first component are released within the first 30 min or within the first 20 min or within the first 15 min of the dissolution test.

35. The kit according to claim 33 or 34, wherein at least 60% of the one or more glucocorticoids of the first component are released within the first 30 min of the dissolution test.

36. The kit according to any one of claims 33 to 35, wherein at least 60% of the one or more glucocorticoids of the first component are released within the first 20 min or within the first 15 min of the dissolution test.

37. The kit according to any one of claims 33 to 36, wherein at least 70% of the one or more glucocorticoids of the first component are released within the first 30 min of the dissolution test.

38. The kit according to any one of claims 33 to 37, wherein at least 70% of the one or more glucocorticoids of the first component are released within the first 20 min or within the first 15 min of the dissolution test.

39. The kit according to any one of claims 33 to 38, wherein at least 80% of the one or more glucocorticoids of the first component are released within the first 30 min of the dissolution test.

40. The kit according to any one of claims 33 to 39, wherein at least 80% of the one or more glucocorticoids of the first component are released within the first 20 min of the dissolution test.

41. The kit according to any one of claims 33 to 40, wherein at least 90% of the one or more glucocorticoids of the first component are released within the first 30 min of the dissolution test.

42. The kit according to any one of claims 33 to 41, wherein at least 90% of the one or more glucocorticoids of the first component are released within the first 20 min of the dissolution test.

43. The kit according to any one of claims 33 to 42, wherein the amount of one or more glucocorticoids of the first component, expressed as hydrocortisone equivalents, is in a range of from 15 to 50% or from 20 to 40% or from 25 to 35% of the total hydrocortisone equivalents in the kit.

44. The kit according to any one of claims 33 to 43, wherein the one or more glucocorticoids of the second component is released over an extended period of time of at least 10 hours and wherein the release is determined in the dissolution test as defined in claim 33.

45. The kit according to any one of claims 33 to 44, wherein from 3 to 15% of the one or more glucocorticoid of the second component is released per hour during a time period of from 1 to 8 hours after start of the dissolution test as defined in claim 33.

46. The kit according to any one of claims 33 to 45, wherein from about 3 to about 10% of the one or more glucocorticoids of the second component are released per hour during a time period of from 1 to about 8 hours after start of the dissolution test as defined in claim 33.

47. The kit according to any one of claims 33 to 46, wherein from 3 to 15% of the one or more glucocorticoids of the second component is released per hour during a time period of from 1 to 10 hours or from 1 to 12 hours after start of the dissolution test as defined in claim 39.

48. The kit according to any one of claims 33 to 47, wherein from about 3 to about 10% of the one or more glucocorticoids of the second component are released per hour during a time period of from 1 to about 10 hours or from 1 to about 12 hours after start of the dissolution test as defined in claim 33.

49. The kit according to any one of claims 33 to 48, wherein
i) from 3 to 15% of the one or more glucocorticoids of the second component are released per hour during a time period of from 1 to 6 hours,
ii) from 3 to 10% of the glucocorticoid of the second component is released per hour during a time period of from 6 to 10 hours, and
iii) from 3 to 7.5% of the one or more glucocorticoids of the second component is released per hour during a time period of from 10 to 12 hours after start of the dissolution test as defined in claim 33.

50. The kit according to any one of claims 33 to 49, wherein at least 25% of the one or more glucocorticoids of the second component is released within 8 hours after start of the dissolution test defined in claim 33.

51. The kit according to any one of claims 33 to 50, wherein at least 25% of the one or more glucocorticoids of the second component are released within 7 hours or within 6 hours after start of the dissolution test defined in claim 33.

52 The kit according to any one of claims 33 to 51, wherein at least 50% of the one or more glucocorticoids of the second component is released within 12 hours after start of the dissolution test defined in claim 33.

53. The kit according to any one of claims 33 to 52, wherein at least about 50% of the one or more glucocorticoids of the second component are released within 10 hours or within 9 hours after start of the dissolution test defined in claim 33.

54. The kit according to any one of claims 33 to 53, wherein at least 75% of the one or more glucocorticoids of the second component is released within 18 hours after start of the dissolution test defined in claim 33.

55. The kit according to any one of claims 33 to 54, wherein at least 75% of the one or more glucocorticoids of the second component are released within 17 hours, within 16 hours, within 15 hours, within 14 hours or within 13 hours after start of the dissolution test defined in claim 33.

56. The kit according to any one of claims 33 to 55, wherein the amount of one or more glucocorticoid of the second component, expressed as hydrocortisone equivalents, is in a range of from 50 to 90% of the total hydrocortisone equivalents in the kit.

57. The kit according to any one of claims 33 to 56, wherein the amount of one or more glucocorticoids of the second component, expressed as hydrocortisone equivalents, is in a range of from 60 to 80% or from 65 to 75% of the total hydrocortisone equivalents in the kit.

58. The kit according to any one of claims 33 to 57, wherein each of the first and the second component is in the form of a solid dosage form.

59. The kit according to claim 58, wherein the solid dosage form is selected from the group consisting of granules, beads, pellets and powders.

60. The kit according to any one of claims 33 to 59, wherein each of the first and the second component is in the form of a unit dosage form.

61. The kit according to claim 60, wherein the unit dosage form is a tablet, capsule or a sachet.

62. The kit according to any one of claims 33 to 61, wherein the first component is in the form of a dosage form that is adapted to administration to or via a mucosa.

63. The kit according to claim 62, wherein the mucosa is selected from the group consisting of the mucosa in the oral cavity, the mucosa of the nasal cavity, the mucosa of the rectum, the gastrointestinal mucosa, and the pulmonary, bronchial or respiratory mucosa and epithelia.

64. The kit according to claim 63, wherein the mucosa is the mucosa in the oral cavity.

65. The kit according to claim 64, wherein the first component has an acceptable taste.

66. The kit according to any one of claims 33 to 65, wherein the first component is in liquid, semi-solid or solid form.

67. The kit according to claim 60, wherein the first component is in the form of a tablet including a chewable tablet, a suckable tablet, an effervescent tablet, a sublingual tablet, a rapid-burst tablet, immediate release tablets or rapidly dissolvable tablets.

68. The kit according to claim 66, wherein the first component is in the form selected from the group consisting of a spray, a wafer, a film, a hydrogel, a bioadhesive patch, an inhaler, a powder inhaler, a sachet, a suppository, a clysma, and a solution.

69. The kit according to any one of claims 33 to 68, wherein the second component is in the form of a solid unit dosage form.

70. The kit according to claim 33, wherein the total amount of hydrocortisone equivalents in the kit is from 1 to 75 mg, from 1 to 70 mg, from 1 to 60 mg, from 5 to 50 mg, from 5 to 40 mg or from 10 to 30 mg.

71. The kit according to any one of claims 33 to 70, wherein the first and the second component are intended for substantially simultaneous administration.

72. The kit according to any one of claims 33 to 71, wherein the first and the second component are intended for sequential administration.

73. The kit according to any one of claims 33 to 72 further comprising a third component comprising one or more glucocorticoids designed for substantially immediate release of the one or more glucocorticoids.

74. Use of a first and a second amount of one or more glucocorticoids for the preparation of a pharmaceutical composition as defined in any one of claims 1 to 32 for the treatment of a glucocorticoid deficiency disorder.

75. Use of a first and a second amount of one or more glucocorticoids for the preparation of a kit as defined in any one of claims 33 to 73 for the treatment of a glucocorticoid deficiency disorder.

76. The coated tablet composition according to any one of claims 1 to 32 comprising:

(a) 1-80 mg of hydrocortisone comprised in the tablet core and the coating,

(b) said tablet core comprising hydrocortisone, one or more of a filler or binder selected from the group consisting of hydroxypropylmethylcellulose, microcrystalline cellulose and starch or modified starch, a colloidal silica glidant, and a magnesium stearate lubricant, the amount of hydrocortisone present in said core is 60% to 80% of the total amount of hydrocortisone present in said tablet composition and is released over an extended period of time of at least 8 hours; and

(c) said coating comprising hydrocortisone and at least one coating material selected from the group consisting of hydroxypropylmethylcellulose, polyvinylalcohol, polyethylene glycol, titanium dioxide and talc, with the amount of hydrocortisone present in said coating being 20% to 40% of the total amount of hydrocortisone in said tablet composition and determined as the amount of hydrocortisone released 1 hour after start of the dissolution test as defined in claim 1, wherein at least 50% of the hydrocortisone in the coating is released within the first 45 min of the dissolution test.

77. The coated tablet composition according to claim 76, wherein at least 50% of the hydrocortisone of the tablet coating is released within the first 30 min of the dissolution test.

78. The coated tablet composition according to claim 76 or 77, wherein the hydrocortisone of the tablet core is released over an extended period of time of at least 10 hours.

79. The coated tablet composition according to claim 78, wherein the release is determined in the dissolution test as defined in claim 1.

80. The coated tablet composition according to any one of claims 76 to 79, wherein at least 50% of hydrocortisone in the tablet composition is released within 10 hours after start of the dissolution test defined in claim 1, wherein at least 80% of the hydrocortisone in the dosage form is released within 24 hours after start of the dissolution test defined in claim 1.

81. The coated tablet composition according to any one of claims 76 to 80, wherein from 3 to 15% of the hydrocortisone contained in the tablet core is released per hour during a time period of from 1 to 8 hours after start of the dissolution test as defined in claim 1.

82. The coated tablet composition according to any one of claims 76 to 81, wherein

(i) from 3 to 15% of the hydrocortisone contained in the tablet core is released per hour during a time period of from 1 to 6 hours,

ii) from 3 to 10% of the hydrocortisone contained in the tablet core is released per hour during a time period of from 6 to 10 hours, and

iii) from 3 to 7.5% of the hydrocortisone contained in the tablet core is released per hour during a time period of from 10 to 12 hours, after start of the dissolution test as defined in claim 1.

83. The coated tablet composition according to any one of claims 76 to 82 for administration once daily in the morning.

84. The coated tablet composition according to any one of claims 76 to 83 in unit dosage form.

85. Use of hydrocortisone for the preparation of a coated tablet composition as defined in any one of claims 76 to 84 for the treatment of a glucocorticoid deficiency disorder.

86. A coated tablet for delivery of glucocorticoid replacement therapy, comprising:

(a) an extended release tablet core and an immediate release coating surrounding said tablet core,

(b) said tablet core comprising hydrocortisone and an excipient composition composed of (i) a combination of hydroxypropylmethylcellulose, microcrystalline cellulose and pregelatinized starch (ii) colloidal silicon dioxide, and (iii) magnesium stearate, the amount of hydrocortisone present in said tablet core being 60% to 80% of the total amount of hydrocortisone present in said tablet;

(c) said coating comprising hydrocortisone and at least one coating material selected from the group consisting of methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, acrylic polymers, ethylcellulose, cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinylalcohol, sodium carobxymethylcellulose, cellulose acetate, gelatin, methacrylic acid copolymer, polyethylene glycol, shellac, sucrose, titanium dioxide, carnauba wax, microcrystalline wax, glyceryl monostearate, talc and zein, with the amount of hydrocortisone present in said coating being 20% to 40% of the total amount of hydrocortisone present in said tablet; and

(d) said tablet being effective to deliver a daily dose of from about 5 to 40 mg of hydrocortisone.

87. The coated tablet according to claim 86, which provides a release profile of hydrocortisone that essentially mimics an endogenous release profile of hydrocortisone with circadian rhythm of a healthy subject.

88. The coated tablet according to claims 86 or 87, wherein said coating is a rapidly dissolving coating containing the hydrocortisone.

89. The coated tablet according to any one of claims 86 to 88, wherein said rapidly dissolving coating comprises a coating material selected from the group consisting of hydroxypropylmethylcellulose, hydroxypropylcellulose, polyvinylalcohol, sodium carobxymethylcellulose, gelatin, polyethylene glycol, titanium dioxide and talc.

90. The coated tablet according to any one of claims 86 to 89, wherein said coating comprises hydroxypropylmethylcellulose and talc.

91. The coated tablet according to any one of claims 86 to 90, said tablet being effective to deliver a daily dose of from 1 to 30 mg of hydrocortisone.

92. The coated tablet according to any one of clams 86 to 91, said tablet being effective to deliver a daily dose of 5 mg of hydrocortisone.

93. The coated tablet according to any one of claims 86 to 92, said tablet being effective to deliver a daily dose of 20 mg of hydrocortisone.

94. The coated tablet according to any one of claims 86 to 93 for administration once daily in the morning.

95. The coated tablet according to any one of claims 86 to 94, wherein the amount of hydrocortisone present in said tablet core is 74% of the total amount of hydrocortisone present in said coated tablet; the amount of hydrocortisone present in said coating is 26% of the total amount of hydrocortisone present in said coated tablet and the relative amounts of hydroxypropylmethylcellulose, microcrystalline cellulose, pregelatinized starch, colloidal silicon dioxide, and magnesium stearate, by weight, in said tablet core is 35.5: 54.4: 8.9: 0.55: 0.55.

96. A coated tablet for delivery of glucocorticoid replacement therapy, comprising:

(a) an extended release tablet core and an immediate release coating surrounding said tablet core,

(b) said extended release core comprising hydrocortisone and an extended release excipient composition composed of (i) a combination of hydroxypropylmethylcellulose, microcrystalline cellulose and pregelatinized starch (ii) colloidal silicon dioxide, and (iii) magnesium stearate, the amount of hydrocortisone present in said extended release core being 60% to 80% of the total amount of hydrocortisone present in said tablet;

(c) said immediate release coating comprising hydrocortisone and at least one coating material selected from the group consisting of

hydroxypropylmethylcellulose, hydroxypropylcellulose, polyvinylalcohol, sodium carboxymethylcellulose, gelatin, polyethylene glycol, said immediate release coating further comprising at least one of titanium dioxide and talc, with the amount of hydrocortisone present in said immediate release coating material being 20% to 40% of the total amount of hydrocortisone present in said tablet; and

(d) said tablet being effective to deliver a daily dose of from about 5 to about 40 mg of hydrocortisone.