Claims

1. A screening method for diagnosing growth hormone deficiency in pediatric patients by using macimorelin comprising:

(a) providing one to five blood samples, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) measuring the growth hormone level of each blood sample provided in step (a);

(c) comparing the measured growth hormone level obtained in step (b) with a single threshold value, wherein the single threshold value is 10.0 ng/mL or higher;

(d) determining the subject, whose highest growth hormone level in the blood samples obtained in step (b) is lower than the single threshold value, as having growth hormone deficiency, and determining the subject, whose highest growth hormone level in the blood samples obtained in step (b) is no lower than the single threshold value, as having no growth hormone deficiency.

2. The method according to claim 1, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL, preferably from about 10.2 to about 20.0 ng/mL, further preferably from about 12.0 to about 19.0 ng/mL, further preferably from about 14.0 to about 18.0 ng/mL, more preferably from about 16.0 to about 18.0 ng/mL and most preferably from about 17.0 to about 18.0 ng/mL.

3. The method according to claim 1 or 2, wherein in step (a) one to four blood samples are provided, preferably wherein in step (a) one to three blood samples are provided, more preferably wherein in step (a) two or three blood samples are provided.

4. The method according to any of claims 1 to 3, wherein in step (a) the blood samples are taken from a subject within a range from about 20 to about 100 minutes, preferably within a range from about 25 to about 100 minutes, more preferably within a range from about 25 to about 95 minutes and most preferably within a range from about 30 to about 90 minutes, following an administration of an amount of macimorelin effective for inducing growth hormone secretion.

5. The method according to any of claim 1 to 4, wherein the blood samples are taken from the subject at about 10 to about 60 minute intervals, preferably about 15 to about 30 minute intervals, if more than one blood sample is provided.

6. The method according to any of claims 1 to 5, wherein in step (a) the blood samples are serum samples or plasma samples.

7. The method according to any of claims 1 to 6, wherein in step (a) about 0.8 mg to about 1.2 mg per kg subject body weight of macimorelin is administered, preferably wherein in step (a) about 1.0 mg per kg subject body weight of macimorelin is administered.

8. The method according to any of claims 1 to 7, wherein in step (a) the administration of macimorelin is oral administration.

9. The method according to any of claims 1 to 8, wherein in step (a) one blood sample is provided, which is taken from the subject at about 60±30 minutes after administration of macimorelin.

10. The method according to any of claims 1 to 8, wherein in step (a) two blood samples are provided, which are taken from the subject at about 30±10 minutes and at about 45±10 minutes after administration of macimorelin.

11. The method according to any of claims 1 to 8, wherein in step (a) two blood samples are provided, which are taken from the subject at about 30±10 minutes and at about 60±10 minutes after administration of macimorelin.

12. The method according to any of claims 1 to 8, wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 45±10 minutes and at about 60±10 minutes after administration of macimorelin or wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 45±10 minutes and at about 90±10 minutes after administration of macimorelin or wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 60±10 minutes and at about 90±10 minutes after administration of macimorelin.

13. The method according to any of claims 1 to 12, wherein in step (a) the macimorelin is administered in a composition comprising macimorelin and optionally further pharmaceutically acceptable excipients, preferably wherein in step (a) the macimorelin is administered in a composition comprising macimorelin and optionally saccharin.

14. The method according to any of claims 1 to 13, wherein in step (a) the macimorelin is administered in a composition comprising about 3.5% (w/w) macimorelin calculated as free base, about 93.1% (w/w) spray-dried lactose monohydrate, about 2.0% (w/w) crospovidone Type A, about 0.1% (w/w) colloidal silicon dioxide, about 1.0% (w/w) sodium stearyl fumarate, and about 0.3% (w/w) saccharin sodium dehydrate.

15. The method according to any of claims 1 to 14, wherein the subject is a human child from the age of 2 to less than 18 years.

16. The method according to any of claims 1 to 15, wherein the method is a stand-alone test and does not need to be repeated and no alternative growth hormone stimulation test is required to reliably diagnose growth hormone deficiency in pediatric patients.

17. The method according to any of claims 1 to 15, wherein determining the subject as having or not having growth hormone deficiency according to step (d) is exclusively based on the growth hormone level induction by a single macimorelin administration.

18. The substance macimorelin for use in diagnosing growth hormone deficiency in pediatric patients wherein

(a) one to five blood samples are provided, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) the growth hormone level of each blood sample provided in step (a) is measured;

(c) the measured growth hormone level obtained in step (b) is compared with a single threshold value, wherein the single threshold value is 10.0 ng/mL or higher;

(d) the subject, whose highest growth hormone level in the blood samples obtained in step (b) is lower than the single threshold value, is determined as having growth hormone deficiency, and the subject, whose highest growth hormone level in the blood samples obtained in step (b) is no lower than the single threshold value, is determined as having no growth hormone deficiency.

19. The substance macimorelin for use according to claim 18, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL, preferably from about 10.2 to about 20.0 ng/mL, further preferably from about 12.0 to about 19.0 ng/mL, further preferably from about 14.0 to about 18.0 ng/mL, more preferably from about 16.0 to about 18.0 ng/mL and most preferably from about 17.0 to about 18.0 ng/mL.

20. The substance macimorelin for use according to claim 18 or 19, wherein in step (a) one to four blood samples are provided, preferably wherein in step (a) one to three blood samples are provided, more preferably wherein in step (a) two or three blood samples are provided.

21. The substance macimorelin for use according to any of claims 18 to 20, wherein in step (a) the blood samples are taken from a subject within a range

from about 20 to about 100 minutes, preferably within a range from about 25 to about 100 minutes, more preferably within a range from about 25 to about 95 minutes and most preferably within a range from about 30 to about 90 minutes, following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

22. The substance macimorelin for use according to any of claims 18 to 21, wherein the blood samples are taken from the subject at about 10 to about 60 minute intervals, preferably about 15 to about 30 minute intervals, if more than one blood sample is provided.

23. The substance macimorelin for use according to any of claim 18 to 22, wherein in step (a) the blood samples are serum samples or plasma samples.

24. The substance macimorelin for use according to any of claims 18 to 23, wherein in step (a) about 0.8 mg to about 1.2 mg per kg subject body weight of macimorelin is administered, preferably wherein in step (a) about 1.0 mg per kg subject body weight of macimorelin is administered.

25. The substance macimorelin for use according to any of claims 18 to 24, wherein in step (a) the administration of macimorelin is oral administration.

26. The substance macimorelin for use according to any of claims 18 to 25, wherein in step (a) one blood sample is provided, which is taken from the subject at about 60±30 minutes after administration of macimorelin.

27. The substance macimorelin for use according to any of claims 18 to 25, wherein in step (a) two blood samples are provided, which are taken from the subject at about 30±10 minutes and at about 45±10 minutes after administration of macimorelin.

28. The substance macimorelin for use according to any of claims 18 to 25, wherein in step (a) two blood samples are provided, which are taken from the subject at about 30±10 minutes and at about 60±10 minutes after administration of macimorelin.

29. The substance macimorelin for use according to any of claims 18 to 25, wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 45±10 minutes and at about 60±10 minutes after administration of macimorelin or wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 45±10 minutes and at about 90±10 minutes after administration of macimorelin or wherein in step (a) three blood samples are provided, which are taken from the subject at about 30±10 minutes, at about 60±10 minutes and at about 90±10 minutes after administration of macimorelin.

30. The substance macimorelin for use according to any of claims 18 to 29, wherein in step (a) the macimorelin is administered in a composition comprising macimorelin and optionally further pharmaceutically acceptable excipients, preferably wherein in step (a) the macimorelin is administered in a composition comprising macimorelin and optionally saccharin.

31. The substance macimorelin for use according to any one of claims 18 to 29, wherein in step (a) the macimorelin is administered in a composition comprising about 3.5% (w/w) macimorelin calculated as free base, about 93.1% (w/w) spray-dried lactose monohydrate, about 2.0% (w/w) crospovidone Type A, about 0.1% (w/w) colloidal silicon dioxide, about 1.0% (w/w) sodium stearyl fumarate, and about 0.3% (w/w) saccharin sodium dehydrate.

32. The substance macimorelin for use according to any of claims 18 to 31, wherein the subject is a human child from the age of 2 to less than 18 years.

33. The substance macimorelin for use according to any of claims 18 to 32, wherein the substance is used in a stand-alone test and does not need to be repeated and no alternative growth hormone stimulation test is required to reliably diagnose growth hormone deficiency in pediatric patients.

34. The substance macimorelin for use according to any of claims 18 to 33, wherein determining the subject as having or not having growth hormone

deficiency according to step (d) is exclusively based on the growth hormone level induction by a single macimorelin administration.

35. A screening method for diagnosing growth hormone deficiency in pediatric patients by using macimorelin comprising:

(a) providing at least one blood sample, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) measuring the growth hormone level of each blood sample;

(c) comparing each of the measured growth hormone level with a single threshold value, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL;

(d) diagnosing whether the subject suffers from growth hormone deficiency or not based on the comparison of growth hormone level measured in step (b) with said single threshold value in said at least one blood sample;

wherein determining the subject as having or not having growth hormone deficiency is exclusively based on the growth hormone level induction by a single macimorelin administration.

36. The method according to claim 35, wherein in step (d) the subject, whose highest growth hormone level measured in step (b) is lower than the single threshold value, is determined as having growth hormone deficiency, and the subject, whose highest growth hormone level measured in step (b) is no lower than the single threshold value, is determined as having no growth hormone deficiency

37. The method according to claim 35 or 36, wherein the single threshold value is within a range from about 10.2 to about 20.0 ng/mL, further preferably from about 12.0 to about 19.0 ng/mL, further preferably from about 14.0 to about 18.0 ng/mL, more preferably from about 16.0 to about 18.0 ng/mL and most preferably from about 17.0 to about 18.0 ng/mL.

~~38. The method according to claims 35 to 37, wherein about 0.8 mg to about 1.2 mg per kg subject body weight of macimorelin is administered, preferably about 1.0 mg per kg subject body weight of macimorelin is administered.~~

~~39. The method according to any of claims 35 to 38, wherein the subject is a human child from the age of 2 to less than 18 years.~~

1. A screening method for diagnosing growth hormone deficiency in pediatric patients by using macimorelin comprising:

(a) providing one to five blood samples, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) measuring the growth hormone level of each blood sample provided in step (a);

(c) comparing the measured growth hormone level obtained in step (b) with a single threshold value, wherein the single threshold value is 10.0 ng/mL or higher;

(d) determining the subject, whose highest growth hormone level in the blood samples obtained in step (b) is lower than the single threshold value, as having growth hormone deficiency, and determining the subject, whose highest growth hormone level in the blood samples obtained in step (b) is no lower than the single threshold value, as having no growth hormone deficiency.

2. The method according to claim 1, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL.

3. The method according to claim 1 or 2, wherein in step (a) one to four blood samples are provided.

4. The method according to claim 1 or 2 wherein in step (a) one to three blood samples are provided.

5. The method according to any of claims 1 to 4, wherein in step (a) about 0.8 mg to about 1.2 mg per kg subject body weight of macimorelin is to be administered.

6. The method according to any of claims 1 to 5, wherein the subject is a human child from the age of 2 to less than 18 years.

7. The method according to any of claims 1 to 4, wherein the subject is a human child from the age of 4 to less than 18 years

8. The method according to any of claims 1 to 7, wherein the method is a stand-alone test and does not need to be repeated and no alternative growth hormone stimulation test is required to reliably diagnose growth hormone deficiency in pediatric patients.

9. The method according to any of claims 1 to 8, wherein determining the subject as having or not having growth hormone deficiency according to step (d) is exclusively based on the growth hormone level induction by a single macimorelin administration.

10. The substance macimorelin when used in diagnosing growth hormone deficiency in pediatric patients wherein

(a) one to five blood samples are provided, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) the growth hormone level of each blood sample provided in step (a) is measured;

(c) the measured growth hormone level obtained in step (b) is compared with a single threshold value, wherein the single threshold value is 10.0 ng/mL or higher;

(d) the subject, whose highest growth hormone level in the blood samples obtained in step (b) is lower than the single threshold value, is determined

as having growth hormone deficiency, and the subject, whose highest growth hormone level in the blood samples obtained in step (b) is no lower than the single threshold value, is determined as having no growth hormone deficiency.

11. The use of substance macimorelin according to claim 10, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL.

12. The use of substance macimorelin according to claim 10 or 11, wherein in step (a) one to four blood samples are provided.

13. The use of substance macimorelin according to claim 10 or 11, wherein in step (a) one to three blood samples are provided.

14. The use of substance macimorelin according to any of claims 10 to 13, wherein in step (a) about 0.8 mg to about 1.2 mg per kg subject body weight of macimorelin is to be administered.

15. The use of substance macimorelin according to any of claims 10 to 14, wherein the subject is a human child from the age of 2 to less than 18 years.

16. The use of substance macimorelin according to any of claims 10 to 14, wherein the subject is a human child from the age of 4 to less than 18 years.

17. The use of substance macimorelin according to any of claims 10 to 16, wherein the substance is used in a stand-alone test and does not need to be repeated and no alternative growth hormone stimulation test is required to reliably diagnose growth hormone deficiency in pediatric patients.

18. The use of substance macimorelin according to any of claims 10 to 17, wherein determining the subject as having or not having growth hormone deficiency according to step (d) is exclusively based on the growth hormone level induction by a single macimorelin administration.

19. A screening method for diagnosing growth hormone deficiency in pediatric patients by using macimorelin comprising:

(a) providing at least one blood sample, taken from a subject within a range from about 15 to about 100 minutes following an administration of an amount of macimorelin effective for inducing growth hormone secretion;

(b) measuring the growth hormone level of each blood sample;

(c) comparing each of the measured growth hormone level with a single threshold value, wherein the single threshold value is within a range from about 10.0 to about 25.0 ng/mL;

(d) diagnosing whether the subject suffers from growth hormone deficiency or not based on the comparison of growth hormone level measured in step (b) with said single threshold value in said at least one blood sample; wherein determining the subject as having or not having growth hormone deficiency is exclusively based on the growth hormone level induction by a single macimorelin administration.

20. The method according to claim 19, wherein the subject is a human child from the age of 2 to less than 18 years.