

Claims

1. A composition comprising HP-hMG for use in the treatment of infertility in a patient predicted to have a high ovarian response to controlled ovarian stimulation, wherein the treatment comprises:
 - 5 selecting a patient identified as predicted to have a high ovarian response to controlled ovarian stimulation;
conducting controlled ovarian stimulation by administering a daily dose of 75-450 IU HP-hMG to the selected patient from day one of treatment;
at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining whether
10 the patient's serum level of hCG is at a target mid-follicular threshold level of ≥ 1.5 mIU/mL;
and,
optionally, maintaining or increasing the daily dose of HP-hMG based on whether the patient's serum level of hCG is at or below the target mid-follicular threshold level.
2. A composition for use according to claim 1 wherein the treatment further comprises:
 - 15 triggering final follicular maturation when the level of hCG in the patient's serum is at, or above, a specified threshold level of from 1.5 – 2.0 mIU/mL, preferably 1.8 mIU/mL.
3. A composition comprising HP-hMG for use in the treatment of infertility in a patient predicted to have a high ovarian response to controlled ovarian stimulation, wherein the treatment comprises:
 - 20 selecting a patient identified as predicted to have a high ovarian response to controlled ovarian stimulation;
conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the selected patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);
25 at a mid-follicular stage of controlled ovarian stimulation (e.g., at stimulation day 5 or 6 or 7), determining whether the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL); and,
optionally, maintaining or increasing the daily dose of HP-hMG (e.g., by 75 IU/day)

based on whether the patient's serum level of hCG is at or below the target mid-follicular threshold level.

4. A composition comprising HP-hMG for use in the treatment of infertility in a patient predicted to have a high ovarian response to controlled ovarian stimulation, wherein the treatment comprises:
 - selecting a patient identified as predicted to have a high ovarian response to controlled ovarian stimulation;
 - conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);
 - at a mid-follicular stage of controlled ovarian stimulation (e.g., at stimulation day 5 or 6 or 7), determining if the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL); and
 - triggering final follicular maturation when the level of hCG in the patient's serum is at, or above, a specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth.
5. A composition for use according to claim 4, wherein the specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth is selected from 1.5 – 2.0 mIU/mL, more preferably 1.8 mIU/mL.
6. A composition for use according to any preceding claim, wherein the patient has a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation.
7. A composition for use according to any preceding claim, wherein the treatment further comprises, prior to stimulation, identifying the patient as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml).
8. A composition for use according to any preceding claim, wherein the patient is not anovulatory, and/or wherein the patient is 21-35 years old and has a BMI of 18-30 kg/m² at the start of treatment.

9. A composition for use according to any preceding claim, wherein the controlled ovarian stimulation comprises administering HP-hMG at a starting dose of 75 to 225 IU hMG per day, preferably 150 IU/day, e.g. from day 1 to at least day 5 of stimulation.
10. A composition for use according to any preceding claim, wherein the treatment of
5 infertility increases the probability of live birth compared to treatment with CHO cell-derived recombinant FSH.
11. A composition for use according to any preceding claim, wherein the treatment further comprises triggering final follicular maturation by administering hCG or a GnRH agonist, optionally supplemented with hCG.
- 10 12. A composition for use according to any preceding claim, wherein the treatment further comprises administering a GnRH antagonist starting on day 6 of stimulation.
13. A composition comprising HP-hMG for use in the treatment of infertility in a patient predicted to have a high ovarian response to controlled ovarian stimulation to increase the probability of live birth following fresh or frozen embryo transfer, wherein the treatment
15 comprises:
selecting a patient identified as predicted to have a high ovarian response to controlled ovarian stimulation;
conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225
20 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);
at a mid-follicular stage of controlled ovarian stimulation (e.g., at stimulation day 5 or 6 or 7), determining if the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL); and
triggering final follicular maturation when the level of hCG in the patient's serum is
25 at, or above, a specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth.
14. A composition comprising HP-hMG for use in the treatment of infertility in a patient predicted to have a high ovarian response to controlled ovarian stimulation to increase the

probability of live birth following fresh or frozen embryo transfer, wherein the treatment comprises:

selecting a patient identified as predicted to have a high ovarian response to controlled ovarian stimulation;

5 conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the selected patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);

at a mid-follicular stage of controlled ovarian stimulation (e.g., at stimulation day 5 or 6 or 7), determining whether the patient's serum level of hCG is at a target mid-follicular
10 threshold level (e.g., ≥ 1.5 mIU/mL); and,

optionally, maintaining or increasing the daily dose of HP-hMG (e.g., by 75 IU/day) based on whether the patient's serum level of hCG is at or below the target mid-follicular threshold level.

15 15. A composition for use according to any preceding claim wherein the treatment further comprises:

retrieving oocyte(s), fertilizing the oocyte(s), allowing the fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing the quality/morphology of the blastocyst(s), and implanting a fresh blastocyst (optionally selected based on, e.g., visual assessment of quality/morphology) in a uterus; or

20 retrieving oocyte(s), fertilizing the oocyte(s), allowing the fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing chromosomal quality of the blastocyst(s), freezing one or more or all blastocyst(s), and implanting a thawed-frozen blastocyst (e.g., a euploid blastocyst selected based on chromosomal assessment) in a uterus; or

retrieving oocyte(s), freezing unfertilized oocytes(s), subsequently thawing one or
25 more oocyte(s), fertilizing one or more or all thawed oocyte(s), allowing fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing the quality/morphology of the blastocyst(s), and implanting a blastocyst (optionally selected based on, e.g., visual assessment of quality/morphology) in a uterus; or

retrieving oocyte(s), freezing unfertilized oocytes(s), subsequently thawing one or
30 more frozen oocytes, fertilizing one or more or all thawed oocyte(s), allowing fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing chromosomal quality of the

blastocyst(s), freezing one or more or all blastocyst(s), and implanting a thawed-frozen blastocyst (e.g., a euploid blastocyst selected based on chromosomal assessment) in a uterus.

16. A composition comprising HP-hMG for use in the treatment of infertility in a patient
5 having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation, wherein the treatment comprises:

selecting a patient identified as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation;

conducting controlled ovarian stimulation by administering a daily dose of 75-450 IU
10 HP-hMG to the selected patient from day one of treatment;

at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining whether the patient's serum level of hCG is at a target mid-follicular threshold level of ≥ 1.5 mIU/mL; and,

optionally, maintaining or increasing the daily dose of HP-hMG based on whether the
15 patient's serum level of hCG is at or below the target mid-follicular threshold level.

17. A composition for use according to claim 16 wherein the treatment further comprises: triggering final follicular maturation when the level of hCG in the patient's serum is at, or above, a specified threshold level of from 1.5 – 2.0 mIU/mL, preferably 1.8 mIU/mL.

18. A composition comprising HP-hMG for use in the treatment of infertility in a patient
20 having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation, wherein the treatment comprises:

selecting a patient identified as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation;

conducting controlled ovarian stimulation by administering a daily dose of HP-hMG
25 to the selected patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);

at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining whether the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL); and,

30 optionally, maintaining or increasing the daily dose of HP-hMG (e.g., by 75 IU/day)

based on whether the patient's serum level of hCG is at or below the target mid-follicular threshold level.

19. A composition comprising HP-hMG for use in the treatment of infertility in a patient having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation, wherein the treatment comprises:
- 5 selecting a patient identified as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation;
- conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225
- 10 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);
- at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining if the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL);
- and
- triggering final follicular maturation when the level of hCG in the patient's serum is
- 15 at, or above, a specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth.

20. A composition for use according to claim 19, wherein the specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth is selected from 1.5 – 2.0 mIU/mL, more preferably 1.8 mIU/mL.

- 20 21. A composition for use according to any of claims 16 to 20, wherein the treatment further comprises, prior to stimulation, identifying the patient as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) .

22. A composition for use according to any of claims 16 to 21, wherein the patient is not anovulatory, and/or wherein the patient is 21-35 years old and has a BMI of 18-30 kg/m² at
- 25 the start of treatment.

23. A composition for use according to any of claims 16 to 22, wherein the controlled ovarian stimulation comprises administering HP-hMG at a starting dose of 75 to 225 IU hMG per day, preferably 150 IU/day, e.g. from day 1 to at least day 5 of stimulation.

24. A composition for use according to any of claims 16 to 23, wherein the treatment of infertility increases the probability of live birth compared to treatment with CHO cell-derived recombinant FSH.

25. A composition for use according to any of claims 16 to 24, wherein the treatment
5 further comprises triggering final follicular maturation by administering hCG or a GnRH agonist, optionally supplemented with hCG.

26. A composition for use according to any of claims 16 to 25, wherein the treatment further comprises administering a GnRH antagonist starting on day 6 of stimulation.

27. A composition comprising HP-hMG for use in the treatment of infertility in a patient
10 having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation to increase the probability of live birth following fresh or frozen embryo transfer, wherein the treatment comprises:

selecting a patient identified as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation;
15 conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);
at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining if the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL);
20 and
triggering final follicular maturation when the level of hCG in the patient's serum is at, or above, a specified threshold level of serum hCG at final follicular maturation which leads to an increased probability of live birth.

28. A composition comprising HP-hMG for use in the treatment of infertility in a patient
25 having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation to increase the probability of live birth following fresh or frozen embryo transfer, wherein the treatment comprises:

selecting a patient identified as having a serum anti-Müllerian hormone (AMH) level $\geq 35.7 \pm 0.5$ pmol/L ($\geq 5.0 \pm 0.2$ ng/ml) prior to treatment/stimulation;

conducting controlled ovarian stimulation by administering a daily dose of HP-hMG to the selected patient from day one of treatment (e.g., from 75-450 IU/day, preferably from 75-225 IU/day, more preferably 150 or 225 IU/day, most preferably 150 IU/day);

at stimulation day 5 or 6 or 7 of controlled ovarian stimulation, determining whether the patient's serum level of hCG is at a target mid-follicular threshold level (e.g., ≥ 1.5 mIU/mL); and,

optionally, maintaining or increasing the daily dose of HP-hMG (e.g., by 75 IU/day) based on whether the patient's serum level of hCG is at or below the target mid-follicular threshold level.

29. A composition for use according to any of claims 16 to 28 wherein the treatment further comprises:

retrieving oocyte(s), fertilizing the oocyte(s), allowing the fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing the quality/morphology of the blastocyst(s), and implanting a fresh blastocyst (optionally selected based on, e.g., visual assessment of quality/morphology) in a uterus; or

retrieving oocyte(s), fertilizing the oocyte(s), allowing the fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing chromosomal quality of the blastocyst(s), freezing one or more or all blastocyst(s), and implanting a thawed-frozen blastocyst (e.g., a euploid blastocyst selected based on chromosomal assessment) in a uterus; or

retrieving oocyte(s), freezing unfertilized oocytes(s), subsequently thawing one or more oocyte(s), fertilizing one or more or all thawed oocyte(s), allowing fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing the quality/morphology of the blastocyst(s), and implanting a blastocyst (optionally selected based on, e.g., visual assessment of quality/morphology) in a uterus; or

retrieving oocyte(s), freezing unfertilized oocytes(s), subsequently thawing one or more frozen oocytes, fertilizing one or more or all thawed oocyte(s), allowing fertilized oocyte(s) to develop to the blastocyst stage, optionally assessing chromosomal quality of the blastocyst(s), freezing one or more or all blastocyst(s), and implanting a thawed-frozen blastocyst (e.g., a euploid blastocyst selected based on chromosomal assessment) in a uterus.