

Claims

1. A liquid formulation of recombinant human granulocyte macrophage colony stimulating factor (rhGM-CSF) for use in administration by inhalation, wherein
5 the liquid formulation comprises rhGM-CSF, a sugar alcohol or a sugar, albumin and water
2. The liquid formulation for the use according to claim 1 wherein said rhGM-CSF is molgramostim (SEQ ID NO: 1), sargramostim (SEQ ID NO: 2), or
10 regramostim.
3. The liquid formulation for the use according to any one of the preceding claims wherein said sugar is maltose, trehalose, sucrose, mannose, lactose or galactose, or wherein said sugar alcohol is mannitol or sorbitol.
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4. The liquid formulation for the use according to any one of the preceding claims wherein said albumin is recombinant human albumin.
5. The liquid formulation for the use according to any one of the preceding claims wherein the formulation further comprises polyethylene glycol (PEG), wherein
20 said PEG is selected from the group consisting of PEG 1000, PEG 1550, PEG 2000, PEG 3000, PEG 3350, PEG 4000 or PEG 8000, preferably PEG-4000.
6. The liquid formulation for the use according to any one of the preceding claims wherein the concentration of rhGM-CSF is at least 150 µg/mL.
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7. The liquid formulation for the use according to claim 6 wherein the concentration of rhGM-CSF is in the range of 150-500 µg/mL, preferably 200-300 µg/mL
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8. The liquid formulation for the use according to any one of the preceding claims wherein the concentration of the sugar alcohol is at least 25 mg/mL.

9. The liquid formulation for the use according to claim 8, wherein the concentration of the sugar alcohol is in the range 45-100 mg/mL, preferably 45-55 mg/mL.
- 5 10. The liquid formulation for the use according to any one of the preceding claims wherein the concentration of albumin is at least 0.2 mg/mL
11. The liquid formulation for the use according to any one of the preceding claims wherein the concentration of albumin is in the range 0.5-1.5 mg/mL.
- 10 12. The liquid formulation for the use according to any one of the preceding claims, wherein the concentration of the PEG is max 50, such as max 40, such as max 30, such as max 20 such as max 10 such as max 1 mg/mL.
- 15 13. The liquid formulation for the use according to any one of the preceding claims wherein the concentration of the PEG is in the range 0.05-0.15 mg/mL.
14. The liquid formulation for the use according to any one of the preceding claims wherein said rhGM-CSF is molgramostim (SEQ ID NO: 1), said sugar alcohol is mannitol, said albumin is recombinant human albumin and said PEG is PEG-4000.
- 20 15. The liquid formulation for the use according to claim 1, wherein the concentration of rhGM-CSF is at least 150 µg/mL, the concentration of mannitol is at least 25mg/mL, the concentration of recombinant human albumin is at least 0.2 mg/mL, and the concentration of PEG-4000 is max 1 mg/mL.
- 25 16. The liquid formulation for the use according to claim 15, wherein the concentration of rhGM-CSF is 200-300 µg/mL, the concentration of mannitol is 45-100 mg/mL, the concentration of recombinant human albumin is 0.5-1.50 mg/mL, and the concentration of PEG-4000 is 0.05-0.15 mg/mL.
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17. The liquid formulation for the use according to any one of the preceding claims further comprising a buffer, such as citric acid monohydrate or Na_2HPO_4 .
- 5 18. The liquid formulation for the use according to any one of the preceding claims, wherein the osmolality of the formulation is from 250 to 375 mOsm/L, preferably from 325 to 335 mOsm/L.
- 10 19. The liquid formulation for the use according to any one of the preceding claims, wherein the % of rhGM-CSF remaining after 3 months storage at 40°C is more than 60%, and/or wherein the level of impurity formation after 6 months at 25°C is less than 5%.
- 15 20. The liquid formulation for the use according to any one of the preceding claims, wherein at least 90% such as at least 95% such as at least 98% such as at least 99% biologic potency of rhGM-CSF is retained after nebulization.
- 20 21. The liquid formulation for the use according to any one of the preceding claims, wherein the formulation is storage stable for at least 18 months at 25°C.
- 25 22. The liquid formulation for the use according to any of the preceding claims, wherein the liquid formulation for inhalation is nebulized.
23. The liquid formulation for the use according to any one of the preceding claims, wherein the liquid formulation is for use in pulmonary administration.
24. The liquid formulation for the use according to any one of the preceding claims, wherein the use is for the treatment of lung infection.
- 30 25. The liquid formulation for the use according to any one of the preceding claims, wherein the use is for the treatment of bacterial, viral or fungal infection in the lungs.

26. The liquid formulation for the use according to any one of the preceding claims, wherein the use is for the treatment of autoimmune pulmonary alveolar proteinosis (aPAP) or non-tuberculous mycobacterial (NTM) infection.
- 5 27. An inhaler comprising the liquid formulation according to any one of the preceding claims.
28. The inhaler according to claim 27, wherein the inhaler is a nebulizer.
- 10 29. A pulmonary formulation of recombinant human granulocyte macrophage colony stimulating factor (rhGM-CSF) comprising rhGM-CSF, a sugar alcohol or a sugar, albumin and water.
- 15 30. A method for delivering rhGM-CSF to the lungs comprising nebulization of a liquid formulation of rhGM-CSF, wherein the liquid formulation comprises rhGM-CSF, a sugar alcohol or a sugar, albumin and water; whereby said rhGM-CSF is delivered to the lungs.