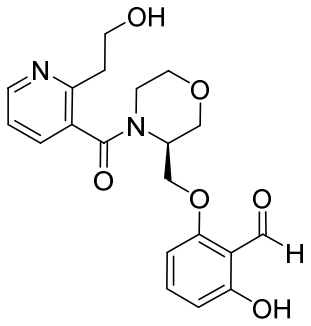
CLAIMS:

1. Use of Compound I of formula:

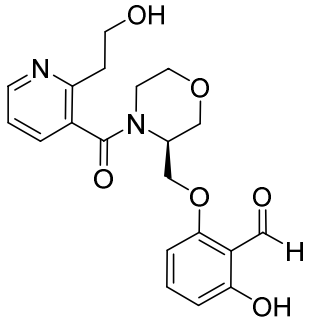


Compound I,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of sickle cell disease in a subject in need thereof, wherein the subject is to be administered a first dose of Compound I, or a pharmaceutically acceptable salt thereof, for one, two, three, four, five, six, or seven days, followed thereafter by a second dose of Compound I, or a pharmaceutically acceptable salt thereof, wherein the administrations of the first dose and the second dose provide about 25% to about 60% hemoglobin occupancy by Compound I.

2. The use of claim 1, wherein the administrations of the first dose and the second dose provide about 30% to about 50% hemoglobin occupancy by Compound I.

3. Use of Compound I of formula:

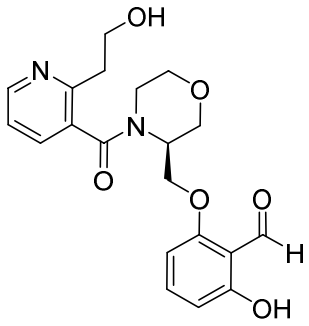


Compound I,

or a pharmaceutically acceptable salt thereof, in the manufacture of medicament for the treatment of sickle cell disease in a subject in need thereof, wherein the subject is to be administered a first dose of about 200 mg per day to about 1600 mg per day of Compound I, or a pharmaceutically acceptable salt thereof, for one, two, three, four, five, six, or seven days, followed thereafter by a

second dose of about 25 mg per day to about 500 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

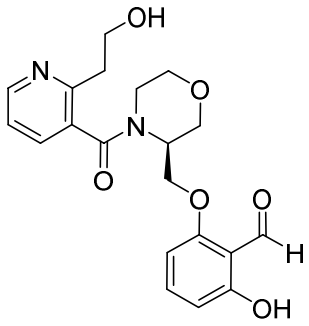
4. The use of claim 3, wherein the subject is to be administered a first dose of about 300 mg per day to about 1500 mg per day of Compound I of formula:



Compound I,

or a pharmaceutically acceptable salt thereof, for one, two, three, four, five, six, or seven days, followed thereafter by a second dose of about 25 mg per day to about 250 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

5. The use of claim 3, wherein the subject is to be administered a first dose of about 200 mg per day to about 900 mg per day of Compound I of formula:



Compound I,

or a pharmaceutically acceptable salt thereof, for one, two, three, four, five, six, or seven days, followed thereafter by a second dose of about 25 mg per day to about 250 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

6. The use of any one of claims 1-5, wherein the second dose is about 25 mg per day to about 250 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

7. The use of any one of claims 1-6, wherein the second dose is about 100 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

8. The use of any one of claims 1-6, wherein the second dose is about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

9. The use of any one of claims 1-6, wherein the second dose is about 200 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

10. The use of any one of claims 1-6, wherein the first dose is:
about 400 mg per day of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

11. The use of any one of claims 1-6, wherein the first dose is:
about 600 mg per day of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

12. The use of any one of claims 1-6, wherein the first dose is:
about 800 mg per day of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

13. The use of any one of claims 1-12, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered once daily (QD).

14. The use of any one of claims 1-12, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered twice daily (BID).

15. The use of any one of claims 1-12, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered three times daily (TID).

16. The use of any one of claims 1-12, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered four times daily (QID).

17. The use of any one of claims 1-12, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered every six hours (Q4H).

18. The use of any one of claims 1-6, wherein the first dose is:
about 200 mg twice daily (BID) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

19. The use of any one of claims 1-6, wherein the first dose is:
about 300 mg twice a day (BID) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

20. The use of any one of claims 1-6, wherein the first dose is:
about 200 mg three times daily (TID) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

21. The use of any one of claims 1-6, wherein the first dose is:
about 150 mg four times daily (QID) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

22. The use of any one of claims 1-6, wherein the first dose is:
about 150 mg every six hours (Q6H) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

23. The use of any one of claims 1-6, wherein the first dose is:

about 400 mg twice daily (BID) of Compound I, or a pharmaceutically acceptable salt thereof, to be administered for four, five, six, or seven days, followed thereafter by a second dose of about 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

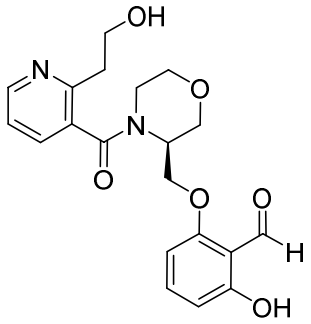
24. The use of any one of claims 1-23, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered for four days.

25. The use of any one of claims 1-23, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered for five days.

26. The use of any one of claims 1-23, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered for six days.

27. The use of any one of claims 1-23, wherein the first dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered for seven days.

28. Use of Compound I of formula:



Compound I,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of sickle cell disease in a subject in need thereof, wherein the subject is to be administered a first dose of about 300 mg twice daily (BID) of Compound I, or a pharmaceutically acceptable salt thereof, for four days, followed thereafter by a second dose of 150 mg per day of Compound I, or a pharmaceutically acceptable salt thereof.

29. The use of any one of claims 1-28, wherein the second dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered for at least one week.

30. The use of any one of claims 1-29, wherein the second dose of Compound I, or a pharmaceutically acceptable salt thereof, is to be administered once daily (QD).

31. The use of any one of claims 1-30, wherein Compound I, or a pharmaceutically acceptable salt thereof, is to be administered as a pharmaceutical composition.

32. The use of any one of claims 1-31, wherein Compound I is to be administered as a pharmaceutical composition.

33. The use of any one of claims 1-32, wherein Compound I, or a pharmaceutically acceptable salt thereof, is to be administered orally.

34. The use of any one of claims 1-33, wherein the medicament is to be conjointly administered with an additional therapeutic agent.

35. The use of claim 34, wherein the additional therapeutic agent is hydroxyurea.

36. The use of any one of claims 1-35, wherein the percent hemoglobin occupancy in the subject, as provide by the administration of Compound I, or a pharmaceutically acceptable salt thereof, reaches about 25% to about 60% after about 8 hours to about 24 hours following the completion of the first dose of Compound I, or a pharmaceutically acceptable salt thereof.

37. The use of claim 36, wherein the percent hemoglobin occupancy in the subject, as provided by the administration of Compound I, or a pharmaceutically acceptable salt thereof, reaches about 25% to about 60% after about 8 hours to about 12 hours following the completion of the first dose of Compound I, or a pharmaceutically acceptable salt thereof.

38. The use of any one of claims 1-35, wherein the percent hemoglobin occupancy in the subject, as provided by the administration of Compound I, or a pharmaceutically acceptable salt thereof, reaches about 25% to about 60% prior to administration of the second dose of Compound I, or a pharmaceutically acceptable salt thereof.

39. The use of any one of claims 1-38, wherein the administration of Compound I, or a pharmaceutically acceptable salt thereof, provides a blood concentration of Compound I of about 50 μg/mL to about 800 μg/mL.

40. The use of claim 39, wherein the administration of Compound I, or a pharmaceutically acceptable salt thereof, provides a blood concentration of Compound I of about 300 μg/mL to about 475 μg/mL.