escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving weight management in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating chronic kidney disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and 10 about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating atherosclerosis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 10 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol fatty liver disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment , wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, 10 about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol steatohepatitis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is 10 to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected

from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt.

In a further aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating diabetic kidney disease in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected

from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

Description

The present invention provides novel tirzepatide dosing regimens for use in the aforementioned therapies that include a maintenance dose selected from the group consisting of: about 5.0 mg, about 10.0 mg and about 15.0 mg. In another embodiment, the present invention provides novel dosing regimens that include an escalation dose (i.e., a dose lower than the desired maintenance dose) and a maintenance dose. In another embodiment, the present invention provides novel dosing regimens that include one or more escalation doses and one or more maintenance doses. The present invention provides novel dosing regimens that include administering at least one escalation dose about once weekly for a minimum of about four weeks and thereafter at least one maintenance dose about once weekly for a minimum of about four weeks. In certain embodiment, the doses may be administered for about four weeks. In certain embodiments, the doses may be administered for more than about four weeks as determined by the nurse, patient and/or health care provider. For example, a maintenance dose may be administered for more than about four weeks. In certain embodiments of the present invention a maintenance dose may be increased to the next highest maintenance

WE CLAIM:

1. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating type 2 diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

2. The use of claim 1 for treating type 2 diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

3. The use as claimed by claim 1 or 2, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

4. The use of claim 1 or 2, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

5. The use of claim 1 or 2, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

6. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for inducing remission or regression of diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance

dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

7. The use of claim 6 to induce remission or regression of diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

8. The use of claim 6 or 7, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

9. The use of claim 6 or 7, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

10. The use of claim 6 or 7, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

11. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing diabetes in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

12. The use of claim 11 to prevent diabetes in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is

selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

13. The use of claim 11 or 12, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

14. The use of claim 11 or 12, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

15. The use of claim 11 or 12, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

16. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving weight management in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

17. The use of claim 16 to improve weight management in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

18. The use of claim 16 or 17, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

19. The use of claim 16 or 17, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

20. The use of claim 16 or 17, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

21. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating chronic kidney disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

22. The use of claim 21 for treating chronic kidney disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

23. The use of claim 21 or 22, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

24. The use of claim 21 or 22, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

25. The use of claim 21 or 22, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

26. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating atherosclerosis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be

administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt.

27. The use of claim 26 for treating atherosclerosis in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

28. The use of claim 26 or 27, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

29. The use of claim 26 or 27, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

30. The use of claim 26 or 27, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

31. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol fatty liver disease, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof, is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

32. The use of claim 31 for treating nonalcohol fatty liver disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

33. The use of claim 31 or 32, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

34. The use of claim 31 or 32, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

35. The use of claim 31 or 32, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

36. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating nonalcohol steatohepatitis, wherein an effective amount of tirzepatide or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of such treatment, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt.

37. The use of claim 36 for treating nonalcohol steatohepatitis in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg

and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

38. The use of claim 36 or 37, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

39. The use of claim 36 or 37, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

40. The use of claim 36 or 37, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

41. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

42. The use of claim 41 for treating obesity in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

43. The use of claim 41 or 42, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

44. The use of claim 41 or 42, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

45. The use of claim 41 or 42, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.

46. Use of tirzepatide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating diabetic kidney disease in a patient in need thereof, wherein: an escalation dose is to be administered once weekly for a minimum of at least two weeks and thereafter a maintenance dose is to be administered once weekly for a minimum of at least two weeks; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof.

47. The use of claim 46 for treating diabetic kidney disease in a patient in need thereof, wherein: at least one escalation dose is to be administered once weekly for a minimum of four weeks and at least one maintenance dose is to be administered once weekly for a minimum of four weeks following the escalation dose; wherein the escalation dose is selected from the group consisting of about 2.5 mg, about 7.5 mg and about 12.5 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; wherein the maintenance dose is selected from the group consisting of about 5.0 mg, about 10.0 mg and about 15.0 mg of tirzepatide, or a pharmaceutically acceptable salt thereof; and wherein the maintenance dose following an escalation dose is a 2.5 mg increment.

48. The use of claim 46 or 47, wherein the escalation dose is about 2.5 mg and the maintenance dose is about 5.0 mg.

49. The use of claim 46 or 47, wherein the escalation dose is about 7.5 mg and the maintenance dose is about 10.0 mg.

50. The use of claim 46 or 47, wherein the escalation dose is about 12.5 mg and the maintenance dose is about 15.0 mg.