Claims

1. A PTH compound for use in the treatment of hypoparathyroidism, wherein the treatment comprises single daily administrations of the PTH compound to a patient and titrating the patient off of standard of care within four weeks from the time the first dose of the PTH compound was administered.

2. The PTH compound for use of claim 1, wherein the patient is titrated off standard of care within three weeks from the time the first dose of the PTH compound is administered.

3. The PTH compound for use of any one of claims 1 to 3, wherein the patient is titrated off standard of care within two weeks from the time the first dose of the PTH compound is administered.

4. The PTH compound for use of any one of claims 1 to 3, wherein the single daily dose of the PTH compound is below 31 µg/day.

5. The PTH compound for use of any one of claims 1 to 4, wherein the single daily dose of the PTH compound is selected from 15mg/day, 18 µg/day and 21 µg/day.

6. The PTH compound for use of any one of claims 1 to 5, wherein the patient is a human patient.

7. The PTH compound for use of any one of claims 1 to 6, wherein administration is by subcutaneous injection.

8. The PTH compound for use of any one of claims 1 to 7, wherein administration is with a pen injector.

9. The PTH compound for use of any one of claims 1 to 7, wherein titrating the patient off of standard of care is performed according to the following the titration scheme

   (i) Visit 1: Decrease active vitamin D dose by 33-50%;

   (ii) Day 3-4: Discontinue active vitamin D;

(iii) Day 6-7: Decrease calcium supplementation by 50%;

(iv) Day 9-10: If daily nutritional calcium exceeds 750 mg/day, discontinue calcium supplements; if daily nutritional calcium intake is <750 mg/day, a calcium supplement to achieve the RDA can be maintained at the discretion of the physician.

10. The PTH compound for use of any one of claims 1 to 8, wherein titrating the patient off of standard of care is performed according to the following the titration scheme

(i) Visit 1: Decrease active vitamin D dose by 33-50%

(ii) Day 3-4: Discontinue active vitamin D;

(iii) Day 6-7: If taking calcium ≤2000 mg/day, decrease calcium by ≥50% (≥400 mg/day); if on calcium >2000 mg/day, decrease calcium by ≥800 mg/day;

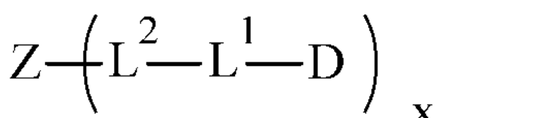
(iv) Day 9-10: If on calcium ≤2000 mg/day discontinue; if dietary calcium <750 mg/day maintain calcium at 400 or 500 mg/day or decrease calcium to ≤500 mg/day; if on calcium >2000 mg/day, decrease calcium by ≥800 mg/day.

11. The PTH compound for use of any one of claims 1 to 10, where 4 weeks after administration of the first dose of the PTH compound a statistically significant change in the Short Form-36 Physical Component Summary, in the SF-36 Mental Component Summary or both the SF-36 PCS and SF-36 MCS is achieved.

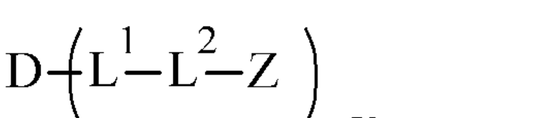
12. The PTH compound for use of any one of claims 1 to 11, wherein the PTH compound is a conjugate or a pharmaceutically acceptable salt thereof comprising at least one moiety -D conjugated via at least one moiety $-L^1-L^2-$ to at least one moiety Z, wherein the linkage between -D and $-L^1-$ is reversible and wherein a moiety $-L^2-$ is conjugated to Z, wherein each -D is independently a PTH moiety; each $-L^1-$ is independently a reversible linker moiety; each $-L^2-$ is independently a single chemical bond or a spacer moiety; and each Z is independently a polymeric moiety or a C_{8-24} alkyl moiety.

13. The PTH compound for use of any one of claims 1 to 12, wherein the PTH compound comprises a PTH moiety having the sequence of SEQ ID NO:51.

14. The PTH compound for use of any one of claims 1 to 13, wherein the PTH compound is a compound of formula (Ia) or (Ib) or a pharmaceutically acceptable salt thereof



(Ia)



(Ib),

wherein

-D is a PTH moiety;

-L^1- is a linker moiety reversibly and covalently connected to the PTH moiety -D through a functional group of PTH;

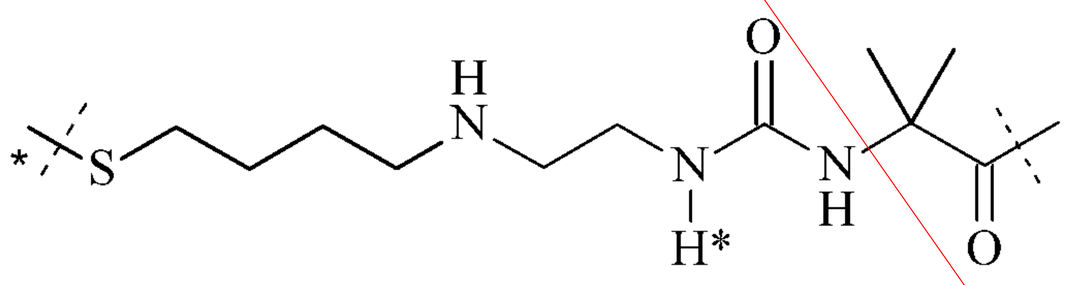
-L^2- is a single chemical bond or a spacer moiety;

-Z is a polymer moiety or a C_{8-24} alkyl moiety;

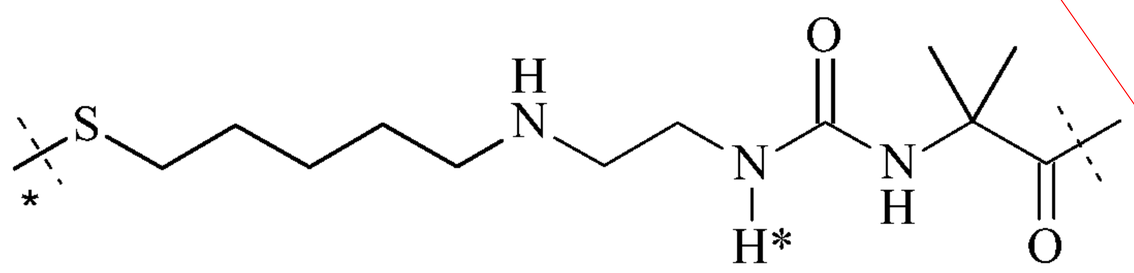
x is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16; and

y is an integer selected from the group consisting of 2, 3, 4 and 5.

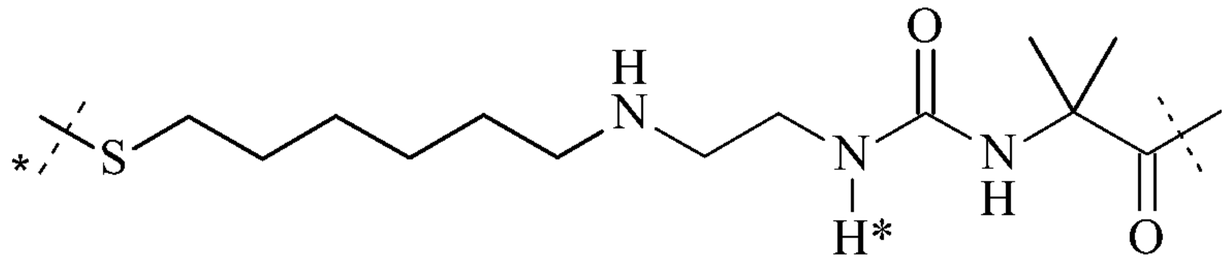
15. The PTH compound for use of any one of claims 12 to 14, wherein the moiety -L^1-L^2- is selected from the group consisting of



(IIcb-i),



(IIcb-ii) and



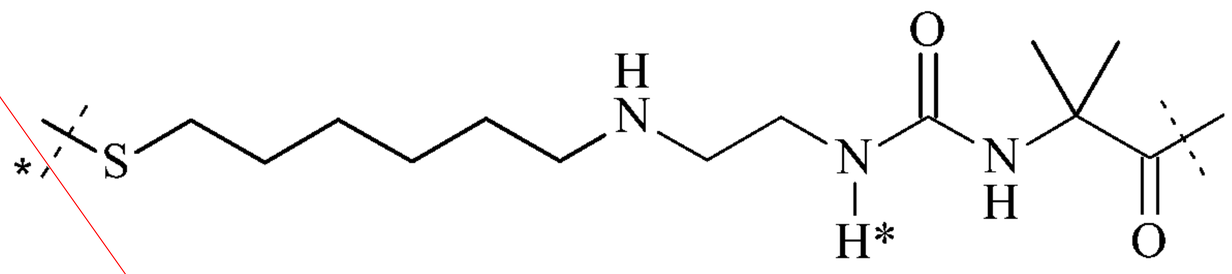
(IIcb-iii);

wherein

the unmarked dashed line indicates the attachment to a nitrogen of -D which is a PTH moiety by forming an amide bond; and

the dashed line marked with the asterisk indicates attachment to -Z.

16. The PTH compound for use of any one of claims 12 to 15, wherein the PTH compound is of formula (IIf-i):

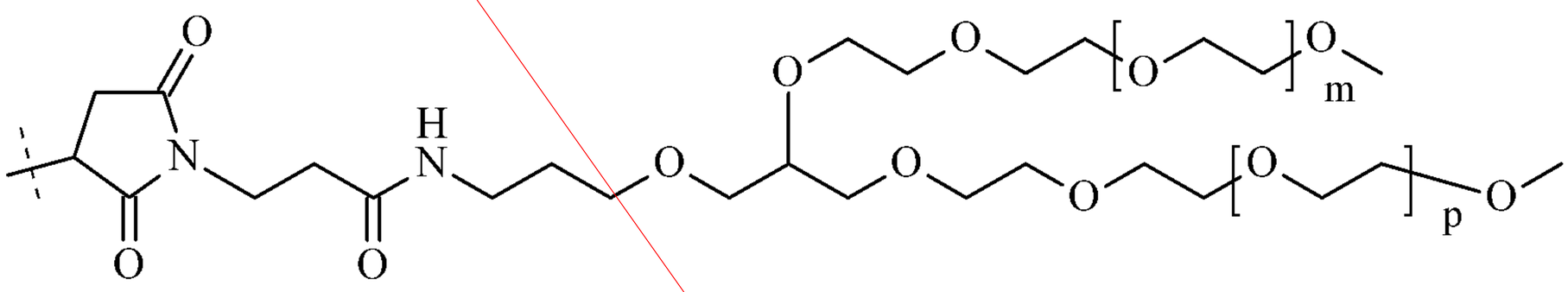


(IIf-i),

wherein

the unmarked dashed line indicates the attachment to a nitrogen of -D which is a PTH moiety by forming an amide bond; and

the dashed line marked with the asterisk indicates attachment to a moiety



wherein

m and p are independently an integer ranging from and including 400 to 500.

Claims

1. Use of a PTH compound in the manufacture of a medicament for the treatment of hypoparathyroidism, wherein single daily administrations of the medicament are to be administered to a patient and titrating the patient off of standard of care within four weeks from the time the first dose of the medicament was administered.

2. The use of claim 1, wherein the patient is titrated off standard of care within three weeks from the time the first dose of the medicament is administered.

3. The use of any one of claims 1 to 3, wherein the patient is titrated off standard of care within two weeks from the time the first dose of the medicament is administered.

4. The use of any one of claims 1 to 3, wherein the single daily dose of the PTH compound is below 31 µg/day.

5. The use of any one of claims 1 to 4, wherein the single daily dose of the PTH compound is selected from 15 µg/day, 18 µg/day and 21 µg/day.

6. The use of any one of claims 1 to 5, wherein the patient is a human patient.

7. The use of any one of claims 1 to 6, wherein administration is by subcutaneous injection.

8. The use of any one of claims 1 to 7, wherein administration is with a pen injector.

9. The use of any one of claims 1 to 7, wherein titrating the patient off of standard of care is performed according to the following the titration scheme
   (i) Visit 1: Decrease active vitamin D dose by 33-50%;
   (ii) Day 3-4: Discontinue active vitamin D;
   (iii) Day 6-7: Decrease calcium supplementation by 50%;
   (iv) Day 9-10: If daily nutritional calcium exceeds 750 mg/day, discontinue calcium supplements; if daily nutritional calcium intake is <750 mg/day, a calcium supplement to achieve the RDA can be maintained at the discretion of the physician.

10. The use of any one of claims 1 to 8, wherein titrating the patient off of standard of care is performed according to the following the titration scheme

(i) Visit 1: Decrease active vitamin D dose by 33-50%

(ii) Day 3-4: Discontinue active vitamin D;

(iii) Day 6-7: If taking calcium ≤2000 mg/day, decrease calcium by ≥50% (≥400 mg/day); if on calcium >2000 mg/day, decrease calcium by ≥800 mg/day;

(iv) Day 9-10: If on calcium ≤2000 mg/day discontinue; if dietary calcium <750 mg/day maintain calcium at 400 or 500 mg/day or decrease calcium to ≤500 mg/day; if on calcium >2000 mg/day, decrease calcium by ≥800 mg/day.

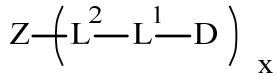
11. The use of any one of claims 1 to 10, wherein 4 weeks after administration of the first dose of the medicament a statistically significant change in the Short Form-36 Physical Component Summary, in the SF-36 Mental Component Summary or both the SF-36 PCS and SF-36 MCS is achieved.

12. The use of any one of claims 1 to 11, wherein the PTH compound is a conjugate or a pharmaceutically acceptable salt thereof comprising at least one moiety -D conjugated via at least one moiety $-L^1-L^2-$ to at least one moiety Z, wherein the linkage between -D and $-L^1-$ is reversible and wherein a moiety $-L^2-$ is conjugated to Z, wherein each -D is independently a PTH moiety; each $-L^1-$ is independently a reversible linker moiety; each $-L^2-$ is independently a single chemical bond or a spacer moiety; and each Z is independently a polymeric moiety or a C_{8-24} alkyl moiety.

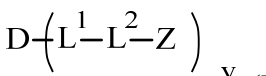
13. The use of any one of claims 1 to 12, wherein the PTH compound comprises a PTH moiety having the sequence SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114 or SEQ ID NO:115.

14. The use of any one of claims 1 to 13, wherein the PTH compound comprises a PTH moiety having the sequence of SEQ ID NO:51.

15. The use of any one of claims 1 to 14, wherein the PTH compound is a compound of formula (Ia) or (Ib) or a pharmaceutically acceptable salt thereof



(Ia)



(Ib),

wherein

-D is a PTH moiety;

-L^1- is a linker moiety reversibly and covalently connected to the PTH moiety -D through a functional group of PTH;

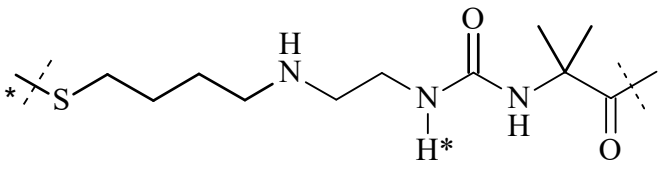
-L^2- is a single chemical bond or a spacer moiety;

-Z is a polymer moiety or a C_{8-24} alkyl moiety;

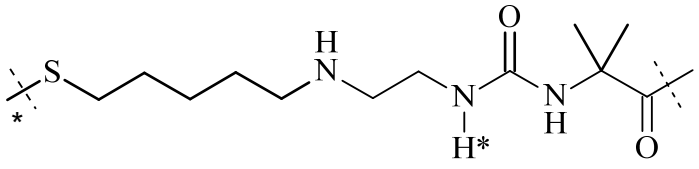
x is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16; and

y is an integer selected from the group consisting of 2, 3, 4 and 5.

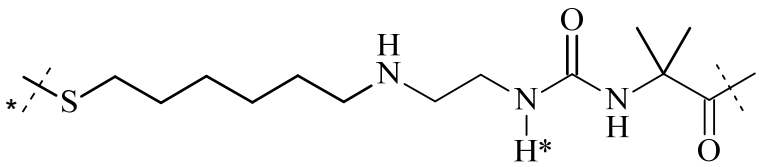
16. The use of any one of claims 12 to 15, wherein the moiety -L^1-L^2- is selected from the group consisting of



(IIcb-i),



(IIcb-ii) and



(IIcb-iii);

wherein

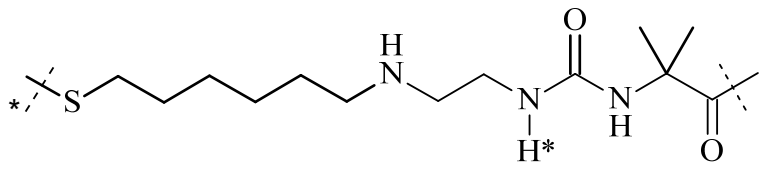
the unmarked dashed line indicates the attachment to a nitrogen of -D which is a PTH moiety by forming an amide bond; and

the dashed line marked with the asterisk indicates attachment to -Z.

17. The use of any one of claims 12 to 16, wherein -Z is a PEG-based polymer.

18. The use of any one of claims 12 to 17, wherein -Z is a branched PEG-based polymer.

19. The use of any one of claims 12 to 18, wherein the PTH compound is of formula (IIf-i):

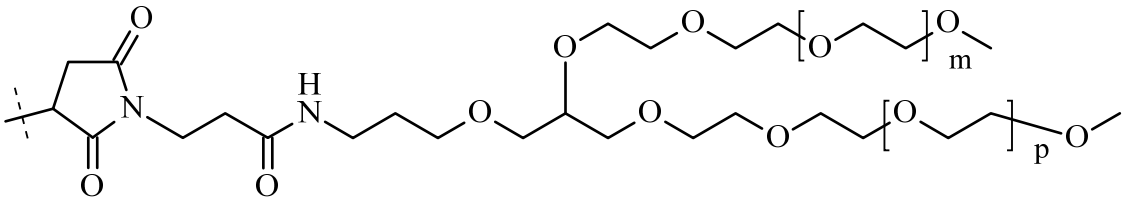


(IIf-i),

wherein

the unmarked dashed line indicates the attachment to a nitrogen of -D which is a PTH moiety by forming an amide bond; and

the dashed line marked with the asterisk indicates attachment to a moiety



wherein

m and p are independently an integer ranging from and including 400 to 500.