[0017a] In another aspect, there is provided a container comprising one or more dosage forms as described herein.

[0017b] In another aspect, there is provided a use of a dosage form as described herein in the manufacture of a medicament for treating nephropathy, wherein the medicament is to be administered once daily to a human subject susceptible to or suffering from nephropathy.

[0017c] In another aspect, there is provided a use of a dosage form as described herein in the manufacture of a medicament for treating chronic kidney disease, wherein the medicament is to be administered once daily to a human subject susceptible to or suffering from chronic kidney disease.

WE CLAIM:

1. A stable solid pharmaceutical dosage form comprising:

(a) about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof; wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.05 weight percent to about 2.0 weight percent on an atrasentan free base equivalent weight basis;

(b) a pharmaceutically acceptable anti-oxidant; wherein the molar ratio of the anti-oxidant to atrasentan, or pharmaceutically acceptable salt thereof, is from about 10:1 to about 1:10; and

(c) a pharmaceutically acceptable diluent;

wherein degradation of atrasentan in the dosage form is less than degradation of atrasentan in an otherwise identical dosage form lacking the anti-oxidant when the dosage forms are stored for a storage period of six months at about 40°C and about 75% relative humidity.

2. The dosage form of claim 1, wherein the anti-oxidant has an oxidation reduction potential less than the oxidation reduction potential of atrasentan and greater than about 550 mV.

3. The dosage form of claim 1, wherein the anti-oxidant is L-cysteine, or a pharmaceutically acceptable salt or ester thereof.

4. The dosage form of claim 1, wherein the weight percent of the anti-oxidant in the dosage form is from about 0.05 weight percent to about 1.0 weight percent.

5. The dosage form of claim 1, wherein the dosage form further comprises a binder.

6. The dosage form of claim 5, wherein the binder is selected from the group consisting of hydroxymethylpropylcellulose, hydroxyethylpropylcellulose, and hydroxypropylcellulose.

7. The dosage form of claim 5, wherein the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 2:1 to about 25:1 on an atrasentan free base equivalent weight basis.

8. The dosage form of claim 5, wherein the weight percent of the binder in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

9. The dosage form of claim 1, wherein:

the molar ratio of the anti-oxidant to atrasentan, or pharmaceutically acceptable salt thereof, is from about 5:1 to about 1:5; and

the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 1:1 to about 20:1 on an atrasentan free base equivalent weight basis.

10. The dosage form of claim 9, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the anti-oxidant is from about 60:1 to about 3:1.

11. The dosage form of claim 10, wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.3 weight percent to about 0.8 weight percent on an atrasentan free base equivalent weight basis.

12. The dosage form of claim 1, wherein the dosage form comprises:

from about 0.05 weight percent to about 1.0 weight percent of the anti-oxidant; and

from about 1.0 weight percent to about 10.0 weight percent of the binder.

13. The dosage form of claim 1, wherein the dosage form comprises:

(a) about 0.05 weight percent to about 1.0 weight percent of the anti-oxidant;

(b) about 75 weight percent to about 99 weight percent of the diluent;

(c) about 1.0 weight percent to about 10.0 weight percent of a pharmaceutically acceptable binder;

(d) optionally, about 1.0 weight percent to about 10.0 weight percent of a pharmaceutically acceptable disintegrant;

(e) optionally, about 0 weight percent to about 1.5 weight percent of a pharmaceutically acceptable glidant; and

(f) optionally, about 0 weight percent to about 5.0 weight percent of a pharmaceutically acceptable lubricant;

wherein the cumulative weight percent for all components of the dosage form equals 100 percent.

14. The dosage form of claim 1, wherein the dosage form is a tablet.

15. The dosage form of claim 1, wherein the dosage form is packaged in a semi-permeable container.

16. A stable solid pharmaceutical dosage form comprising:

(a) about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof; wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.05 weight percent to about 2.0 weight percent on an atrasentan free base equivalent weight basis;

(b) L-cysteine, or a pharmaceutically acceptable salt or ester thereof; wherein the molar ratio of the L-cysteine, or a pharmaceutically acceptable salt or ester thereof, to atrasentan, or pharmaceutically acceptable salt thereof, is from about 10:1 to about 1:10; and

(c) a pharmaceutically acceptable diluent;

wherein degradation of atrasentan in the dosage form is less than degradation of atrasentan in an otherwise identical dosage form lacking the L-cysteine, or a pharmaceutically acceptable salt or ester thereof, when the dosage forms are stored for a storage period of six months at about 40°C and about 75% relative humidity.

17. The dosage form of claim 16, wherein the dosage form further comprises a polymeric binder selected from the group consisting of hydroxymethylpropylcellulose, hydroxyethylpropylcellulose, and hydroxypropylcellulose.

18. The dosage form of claim 17, wherein the polymeric binder is hydroxypropyl methylcellulose.

19. The dosage form of claim 16, wherein the weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof, in the dosage form is from about 0.05 weight percent to about 1.0 weight percent.

20. The dosage form of claim 17, wherein the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 2:1 to about 25:1 on an atrasentan free base equivalent weight basis.

21. The dosage form of claim 17, wherein the weight percent of the binder in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

22. The dosage form of claim 16, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the L-cysteine, or pharmaceutically acceptable salt or ester thereof, is from about 60:1 to about 3:1.

23. The dosage form of claim 17, wherein:

the molar ratio of the L-cysteine, or pharmaceutically acceptable salt or ester thereof, to atrasentan, or pharmaceutically acceptable salt thereof, is from about 5:1 to about 1:5; and

the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 1:1 to about 20:1 on an atrasentan free base equivalent weight basis.

24. The dosage form of claim 23, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the L-cysteine, or pharmaceutically acceptable salt or ester thereof, is from about 60:1 to about 3:1.

25. The dosage form of claim 17, wherein the dosage form comprises:

from about 0.05 weight percent to about 1.0 weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof; and

from about 1.0 weight percent to about 10.0 weight percent of the binder.

26. The dosage form of claim 25, wherein the dosage form further comprises a disintegrant; wherein the weight percent of the disintegrant in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

27. The dosage form of claim 26, wherein the dosage form comprises from about 0.40 mg to about 0.85 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

28. The dosage form of claim 17, wherein the dosage form comprises:

(a) about 0.05 weight percent to about 1.0 weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof;

(b) about 75 weight percent to about 99 weight percent of the diluent;

(c) about 1.0 weight percent to about 10.0 weight percent of the binder;

(d) optionally, about 1.0 weight percent to about 10.0 weight percent of a pharmaceutically acceptable disintegrant;

(e) optionally, about 0 weight percent to about 1.5 weight percent of a pharmaceutically acceptable glidant; and

(f) optionally, about 0 weight percent to about 5.0 weight percent of a pharmaceutically acceptable lubricant;

wherein the cumulative weight percent for all components of the dosage form equals 100 percent.

29. The dosage form of any of claim 28, wherein the polymeric binder is hydroxypropyl methylcellulose.

30. The dosage form of claim 16, wherein the dosage form is a tablet.

31. The dosage form of claim 16, wherein the dosage form is packaged in a semi-permeable container.

32. The dosage form of any of claims 1 to 31, wherein the dosage form further comprises a second therapeutic agent.

33. A kit comprising a first dosage form and a second dosage form, wherein the first dosage form is a stable solid pharmaceutical dosage form of any of claims 1 to 31, and the second dosage form comprises a second therapeutic agent.

34. A container comprising one or more dosage forms of any of claims 1 to 31.

35. A method of treating nephropathy, comprising administering a dosage form of any of claims 1 to 31 once daily to a human subject susceptible to or suffering from nephropathy.

36. A method of treating chronic kidney disease, comprising administering a dosage form of any of claims 1 to 31 once daily to a human subject susceptible to or suffering from chronic kidney disease.

WE CLAIM:

1. A stable solid pharmaceutical dosage form comprising:

(a) about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof; wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.05 weight percent to about 2.0 weight percent on an atrasentan free base equivalent weight basis;

(b) a pharmaceutically acceptable anti-oxidant; wherein the molar ratio of the anti-oxidant to atrasentan, or pharmaceutically acceptable salt thereof, is from about 10:1 to about 1:10; and

(c) a pharmaceutically acceptable diluent;

wherein degradation of atrasentan in the dosage form is less than degradation of atrasentan in an otherwise identical dosage form lacking the anti-oxidant when the dosage forms are stored for a storage period of six months at about 40°C and about 75% relative humidity.

2. The dosage form of claim 1, wherein the anti-oxidant has an oxidation reduction potential less than the oxidation reduction potential of atrasentan and greater than about 550 mV.

3. The dosage form of claim 1, wherein the anti-oxidant is L-cysteine, or a pharmaceutically acceptable salt or ester thereof.

4. The dosage form of claim 1, wherein the weight percent of the anti-oxidant in the dosage form is from about 0.05 weight percent to about 1.0 weight percent.

5. The dosage form of claim 1, wherein the dosage form further comprises a binder.

6. The dosage form of claim 5, wherein the binder is selected from the group consisting of hydroxymethylpropylcellulose, hydroxyethylpropylcellulose, and hydroxypropylcellulose.

7. The dosage form of claim 5, wherein the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 2:1 to about 25:1 on an atrasentan free base equivalent weight basis.

8. The dosage form of claim 5, wherein the weight percent of the binder in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

9. The dosage form of claim 5, wherein:

the molar ratio of the anti-oxidant to atrasentan, or pharmaceutically acceptable salt thereof, is from about 5:1 to about 1:5; and

the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 1:1 to about 20:1 on an atrasentan free base equivalent weight basis.

10. The dosage form of claim 9, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the anti-oxidant is from about 60:1 to about 3:1.

11. The dosage form of claim 10, wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.3 weight percent to about 0.8 weight percent on an atrasentan free base equivalent weight basis.

12. The dosage form of claim 5, wherein the dosage form comprises:

from about 0.05 weight percent to about 1.0 weight percent of the anti-oxidant; and

from about 1.0 weight percent to about 10.0 weight percent of the binder.

13. The dosage form of claim 5, wherein the dosage form comprises:

(a) about 0.05 weight percent to about 1.0 weight percent of the anti-oxidant;

(b) about 75 weight percent to about 99 weight percent of the diluent;

(c) about 1.0 weight percent to about 10.0 weight percent of the pharmaceutically acceptable binder;

(d) optionally, about 1.0 weight percent to about 10.0 weight percent of a pharmaceutically acceptable disintegrant;

(e) optionally, about 0 weight percent to about 1.5 weight percent of a pharmaceutically acceptable glidant; and

(f) optionally, about 0 weight percent to about 5.0 weight percent of a pharmaceutically acceptable lubricant;

wherein the cumulative weight percent for all components of the dosage form equals 100 percent.

14. The dosage form of claim 1, wherein the dosage form is a tablet.

15. The dosage form of claim 1, wherein the dosage form is packaged in a semi-permeable container.

16. A stable solid pharmaceutical dosage form comprising:

(a) about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof; wherein the weight percent of atrasentan, or pharmaceutically acceptable salt thereof, in the dosage form is from about 0.05 weight percent to about 2.0 weight percent on an atrasentan free base equivalent weight basis;

(b) L-cysteine, or a pharmaceutically acceptable salt or ester thereof; wherein the molar ratio of the L-cysteine, or a pharmaceutically acceptable salt or ester thereof, to atrasentan, or pharmaceutically acceptable salt thereof, is from about 10:1 to about 1:10; and

(c) a pharmaceutically acceptable diluent;

wherein degradation of atrasentan in the dosage form is less than degradation of atrasentan in an otherwise identical dosage form lacking the L-cysteine, or a pharmaceutically acceptable salt or ester thereof, when the dosage forms are stored for a storage period of six months at about 40°C and about 75% relative humidity.

17. The dosage form of claim 16, wherein the dosage form further comprises a polymeric binder selected from the group consisting of hydroxymethylpropylcellulose, hydroxyethylpropylcellulose, and hydroxypropylcellulose.

18. The dosage form of claim 17, wherein the polymeric binder is hydroxypropyl methylcellulose.

19. The dosage form of claim 16, wherein the weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof, in the dosage form is from about 0.05 weight percent to about 1.0 weight percent.

20. The dosage form of claim 17, wherein the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 2:1 to about 25:1 on an atrasentan free base equivalent weight basis.

21. The dosage form of claim 17, wherein the weight percent of the binder in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

22. The dosage form of claim 16, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the L-cysteine, or pharmaceutically acceptable salt or ester thereof, is from about 60:1 to about 3:1.

23. The dosage form of claim 17, wherein:

the molar ratio of the L-cysteine, or pharmaceutically acceptable salt or ester thereof, to atrasentan, or pharmaceutically acceptable salt thereof, is from about 5:1 to about 1:5; and

the weight to weight ratio of the binder to atrasentan, or pharmaceutically acceptable salt thereof, is from about 1:1 to about 20:1 on an atrasentan free base equivalent weight basis.

24. The dosage form of claim 23, wherein the dosage form further comprises a disintegrant; wherein the weight to weight ratio of the disintegrant to the L-cysteine, or pharmaceutically acceptable salt or ester thereof, is from about 60:1 to about 3:1.

25. The dosage form of claim 17, wherein the dosage form comprises:

from about 0.05 weight percent to about 1.0 weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof; and

from about 1.0 weight percent to about 10.0 weight percent of the binder.

26. The dosage form of claim 25, wherein the dosage form further comprises a disintegrant; wherein the weight percent of the disintegrant in the dosage form is from about 1.0 weight percent to about 10.0 weight percent.

27. The dosage form of claim 26, wherein the dosage form comprises from about 0.40 mg to about 0.85 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

28. The dosage form of claim 17, wherein the dosage form comprises:

(a) about 0.05 weight percent to about 1.0 weight percent of the L-cysteine, or pharmaceutically acceptable salt or ester thereof;

(b) about 75 weight percent to about 99 weight percent of the diluent;

(c) about 1.0 weight percent to about 10.0 weight percent of the binder;

(d) optionally, about 1.0 weight percent to about 10.0 weight percent of a pharmaceutically acceptable disintegrant;

(e) optionally, about 0 weight percent to about 1.5 weight percent of a pharmaceutically acceptable glidant; and

(f) optionally, about 0 weight percent to about 5.0 weight percent of a pharmaceutically acceptable lubricant;

wherein the cumulative weight percent for all components of the dosage form equals 100 percent.

29. The dosage form of any of claim 28, wherein the polymeric binder is hydroxypropyl methylcellulose.

30. The dosage form of claim 16, wherein the dosage form is a tablet.

31. The dosage form of claim 16, wherein the dosage form is packaged in a semi-permeable container.

32. The dosage form of any of claims 1 to 31, wherein the dosage form further comprises a second therapeutic agent.

33. A kit comprising a first dosage form and a second dosage form, wherein the first dosage form is a stable solid pharmaceutical dosage form of any of claims 1 to 31, and the second dosage form comprises a second therapeutic agent.

34. A container comprising one or more dosage forms of any of claims 1 to 31.

35. Use of a dosage form of any of claims 1 to 31 in the manufacture of a medicament for treating nephropathy, wherein the medicament is to be administered once daily to a human subject susceptible to or suffering from nephropathy.

36. Use of a dosage form of any of claims 1 to 31 in the manufacture of a medicament for treating chronic kidney disease, wherein the medicament is to be administered once daily to a human subject susceptible to or suffering from chronic kidney disease.