CLAIMS

What is claimed is:

1. A formulation of antiretroviral drugs useful against HIV, comprising:
   a) atazanavir; and
   b) cobicistat.

2. The formulation of claim 1, wherein said atazanavir is in the form of atazanavir sulfate.

3. The formulation of claim 2, wherein said formulation is in the form of a tablet, wherein said tablet is not a monolithic tablet or a trilayer tablet, said trilayer tablet having an inert excipient layer as the middle layer.

4. The formulation of claim 3, wherein said tablet is a bilayer tablet which does not show visible cracking.

5. The formulation of claim 4, wherein said bilayer tablet delivers about 300 mg as the free base of atazanavir sulfate, and about 150 mg of cobicistat.

6. The formulation of claim 5, further comprising at least one excipient.

7. The formulation of claim 6, further comprising at least two excipients.

8. The formulation of claim 7, comprising at least three excipients.

9. The formulation of claim 8, wherein said excipients are selected from the group of stearic acid, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, crospovidone, hydroxypropyl cellulose, and croscarmellose sodium.

10. The formulation of claim 6, wherein said excipient is microcrystalline cellulose.

11. The formulation of claim 1, wherein said atazanavir comprises about 20-45% (w/w) of said formulation.

12. The formulation of claim 1, wherein said cobicistat comprises about 15-40% (w/w) of said formulation.

13. The formulation of claim 1, wherein said atazanavir and said cobicistat together comprise about 35-85% (w/w) of said formulation.

14. A method of treating HIV infection in a patient, which comprises administering to said patient the formulation as claimed in claim 1.

15. A method of treating HIV infection in a patient, which comprises administering to said patient the formulation as claimed in claim 4.

16. A method of treating HIV infection in a patient, which comprises administering to said patient the formulation as claimed in claim 5.

17. A method of treating HIV infection in a patient, which comprises administering to said patient the formulation as claimed in claim 10.

18. A method of making an atazanavir/cobicistat tablet formulation, which comprises:

a) separately admixing atazanavir together with one or more excipients, wherein at least one of said excipients is microcrystalline cellulose, wherein said atazanavir is first admixed with a first portion of said one or more excipients to produce a first atazanavir admixture, and further wherein said first admixture is then wet granulated with water and then wet milled, sized and dried, and wherein a second portion of said excipients is then admixed with said dried first admixture to produce a second atazanavir admixture;

b) separately admixing cobicistat together with one or more excipients, wherein at least one of said excipients is microcrystalline cellulose, wherein said cobicistat is first admixed with a first portion of said one or more excipients to produce a first cobicistat admixture, wherein said first admixture is then roller compacted and milled into granules,

and wherein a second portion of said excipients is then admixed with said granulated first admixture to produce a second cobicistat admixture; and

c) compressing said second atazanavir admixture and said second cobicistat admixture into a bilayer tablet.

19. The method of claim 18, wherein said formulation delivers about 300 mg as the free base of atazanavir sulfate, and about 150 mg. of cobicistat.

20. The method of claim 18, wherein in step a) said first portion of said excipients are intragranular excipients, and said second portion of said excipients are extragranular excipients; and further wherein in step b) said first portion of said excipients are intragranular excipients, and said second portion of said excipients are extragranular excipients.

21. The bilayer tablet which is produced according to the method of claim 18.

22. The bilayer tablet of claim 21, wherein said tablet has less than about 3% total cobicistat impurities after 8 weeks at 40 degrees C and 75% relative humidity.

23. The bilayer tablet of claim 22, wherein said tablet has less than about 2.5% total cobicistat impurities after 8 weeks at 40 degrees C and 75% relative humidity, and further wherein said tablet does not show visible cracking.

24. A tableted composition comprising atazanavir, cobicistat and a pharmaceutically acceptable carrier, said composition providing a blood concentration profile of atazanavir as measured by AUC(INF), that is from about 80% to 125% of 35623 ng.h/mL.

25. A tableted composition comprising atazanavir , cobicistat and a pharmaceutically acceptable carrier, said composition providing a blood concentration profile of atazanavir as measured by AUC(0-T) that is from about 80% to 125% of 34848 ng.h/mL.

26. A composition comprising atazanavir, cobicistat and a pharmaceutically acceptable carrier, said composition comprising less than or equal to about 4.0% of total cobicistat impurities.

27. A composition as claimed in claim 26, wherein said composition comprises less than about 2% total cobicistat impurities at about 12 months.

28. A composition as claimed in claim 27, wherein said composition comprises less than about 1.4% total cobicistat impurities.

29. A composition as claimed in claim 28, wherein said composition does not crack upon release from a tablet press.

30. A composition comprising atazanavir, cobicistat and a pharmaceutically acceptable carrier, said composition comprising less than or equal to about 0.2% of degradant BMT-115982 or BMT-089290.

31. A composition as claimed in claim 30, wherein said composition comprises less than or equal to about 4.0% total cobicistat impurities.

32. A composition as claimed in claim 31, wherein said composition has less than about 2% total cobicistat impurities at about 12 months.

33. A composition as claimed in claim 32, wherein said composition has less than about 1.4% cobicistat impurities at about 12 months.

34. A composition as claimed in claim 33, wherein said composition does not crack upon release from a tablet press.

35. A method of treating HIV infection in a patient, which comprises administering to said patient the composition as claimed in claim 34.

36. A tablet comprising atazanavir and cobicistat, said tablet comprising having less than about 3% total cobicistat impurities after 8 weeks at 40 ° C and 75% relative humidity.

37. The tablet as claimed in claim 36, wherein said tablet does not crack under room temperature conditions within 24 hours of being released from a tablet press.

38. The tablet as claimed in claim 36, wherein said tablet has a hardness value within the range of about 28-39 SCUs.

39. The tablet as claimed in claim 38, wherein said tablet is a bilayer tablet.

40. The tablet as claimed in claim 39, wherein said tablet has less than about 2.5% total cobicistat impurities.

41. A pharmaceutical composition comprising pharmaceutically effective amounts of atazanavir and cobicistat and a pharmaceutically acceptable carrier, wherein the composition has less than about 4% by weight cobicistat impurities.

42. A composition of claim 41 wherein said composition is a tablet.

43. A compostion of claim 42, wherein said composition has less than about 2% cobicistat impurities at about 12 months when stored at room temperature.

44. A composition of claim 42, wherein said composition has less than about 2% cobicistat impurities at about 12 months when stored at 30°C/75%RH.

45. A composition of claim 42, wherein said composition has less than about 2% cobicistat impurities at about 12 months when stored at 25°C/60%RH.

46. A composition of claim 42, wherein said composition has less than about 2% cobicistat impurities at about 12 months when stored at 5°C.

47. A compositon of claim 42, wherein said composition has less than about 3.5% cobicistat impurities at about 8 months when stored at 40° C and 75% RH.

CLAIMS

What is claimed is:

1. A tablet formulation of antiretroviral drugs useful against HIV, comprising:
   a) atazanavir; and
   b) cobicistat;

2. The formulation of claim 1, wherein said atazanavir is in the form of atazanavir sulfate.

3. The formulation of claim 2, wherein said tablet is not a monolithic tablet or a trilayer tablet, said trilayer tablet having an inert excipient layer as the middle layer.

4. The formulation of claim 3, wherein said tablet is a bilayer tablet which does not show visible cracking.

5. The formulation of claim 4, wherein said bilayer tablet delivers about 300 mg as the free base of atazanavir sulfate, and about 150 mg. of cobicistat.

6. The formulation of claim 5, further comprising at least one excipient selected from the group of stearic acid, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, crospovidone, hydroxypropyl cellulose, and croscarmellose sodium.

7. The formulation of claim 1, wherein said atazanavir and said cobicistat together comprise about 35-85% (w/w) of said formulation.

8. The formulation of claim 1 comprising atazanavir, cobicistat and a pharmaceutically acceptable carrier, said formulation comprising less than or equal to about 0.2% of degradant BMT-115982 or BMT-089290.

9. The formulation according to claim 1 comprising atazanavir, cobicistat and a pharmaceutically acceptable carrier, said formulation providing a blood concentration profile of atazanavir as measured by AUC(INF), that is from about 80% to 125% of 35623 ng.h/mL and providing a blood concentration profile of atazanavir as measured by AUC(0-T) that is from about 80% to 125% of 34848 ng.h/mL.

10. A tablet comprising atazanavir and cobicistat, said tablet having less than about 3% total cobicistat impurities after 8 weeks at 40 ° C and 75% relative humidity or less than about 2% cobicistat impurities at about 12 months when stored at room temperature, when stored at 30°C/75%RH, when stored at 25°C/60%RH or when stored at 40°C/75%RH.

11. The tablet as claimed in claim 10, wherein said tablet does not crack under room temperature conditions within 24 hours of being released from a tablet press.

12. The tablet as claimed in claim 10, wherein said tablet has a hardness value within the range of about 28-39 SCUs.

13. The tablet as claimed in claim 12, wherein said tablet is a bilayer tablet.

14. The use of the composition as claimed in any one of claims 1 to 13 in the manufacture of a medicament for the treatment of HIV infection in a patient, said use comprising administering to said patient said medicament.

15. A method of making an atazanavir/cobicistat tablet formulation, which comprises:

a) separately admixing atazanavir together with one or more excipients, wherein at least one of said excipients is microcrystalline cellulose, wherein said atazanavir is first admixed with a first portion of said one or more excipients to produce a first atazanavir admixture, and further wherein said first admixture is then wet granulated with water and then wet milled, sized and dried, and wherein a second portion of said excipients is then admixed with said dried first admixture to produce a second atazanavir admixture;

b) separately admixing cobicistat together with one or more excipients, wherein at least one of said excipients is microcrystalline cellulose, wherein said cobicistat is first

admixed with a first portion of said one or more excipients to produce a first cobicistat admixture, wherein said first admixture is then roller compacted and milled into granules, and wherein a second portion of said excipients is then admixed with said granulated first admixture to produce a second cobicistat admixture; and

c) compressing said second atazanavir admixture and said second cobicistat admixture into a bilayer tablet.

16. The method of claim 15, wherein in step a) said first portion of said excipients are intragranular excipients, and said second portion of said excipients are extragranular excipients; and further wherein in step b) said first portion of said excipients are intragranular excipients, and said second portion of said excipients are extragranular excipients.