Claims

1. A pharmaceutical composition comprising
    a. a first composition comprising an extended release composition of an active pharmaceutical ingredient (API) selected from metoprolol and a pharmaceutically acceptable salt thereof,
    b. a second composition comprising an active pharmaceutical ingredient (API) selected from tesofensine and a pharmaceutically acceptable salt thereof, and
    c. a third composition comprising an immediate release composition of an active pharmaceutical ingredient (API) selected from metoprolol and a pharmaceutically acceptable salt thereof.

2. The composition of any of the preceding claims, wherein the metoprolol is selected from metoprolol succinate and metoprolol tartrate.

3. The composition of any of the preceding claims, wherein the tesofensine is selected from the free base, the citrate salt, and the tartrate salt.

4. The composition of any of the preceding claims, wherein the first composition comprises pellets comprising:
    a. an inert pellet core;
    b. a drug layer comprising the active pharmaceutical ingredient, which layer covers the inert core; and
    c. a controlled release layer thereon.

5. The composition of claim 4, wherein the inert pellet core comprises sugar spheres coated with a plasticized film sub-coat of a hydrophobic film coating polymer plasticized with a hydrophilic and a hydrophobic plasticizer; the drug layer comprises API and a binder; the controlled release layer comprises a plasticized film coat of a hydrophobic film coating polymer plasticized with a hydrophilic and a hydrophobic plasticizer, and wherein the pellets are mixed with a final tableting blend comprising a powder mixture of one or more of fillers, disintegrants, glidants and/or lubricants.

6. The composition of claim 5, wherein the hydrophobic film coating polymer comprises ethyl cellulose, the hydrophilic plasticizer comprises polyethylene glycol, the hydrophobic plasticizer comprises dibutyl sebacate, the API is metoprolol succinat, the binder comprises povidone, and the powder mixture comprises starlac, syloid, crospovidone and magnesium stearate.

7. The composition of claim 1, wherein the first composition comprises a controlled release layer comprising an admixture of the following components:
   a. an ethylacrylate/methylmethacrylate copolymer,
   b. a surfactant, and
   c. sodium stearyl fumarate,

   wherein the controlled release layer has been deposited from a water-containing liquid and the amount of the ethylacrylate/methylmethacrylate copolymer in the film coat is in the range of 80-99.5% (w/w).

8. The composition of any of claims 1-6, wherein the second composition is a first coating applied to the first composition.

9. The composition according to claim 8, wherein the third composition is a second coating applied to the first coating.

10. The composition of any of claims 1-6 and 8-9, wherein the first composition is coated with a coating comprising the second and third composition.

11. The composition according to any of claims 1-6 and 8-10, wherein the first composition constitutes a tablet core coated with a coating comprising the second and third composition.

12. The composition of any of claims 1-7, wherein the second and third composition comprises pellets comprising:
   a. an inert pellet core;
   b. a drug layer comprising the active pharmaceutical ingredient, which layer covers the inert core.

13. The composition of any of the preceding claims, wherein the composition is in the form of a pharmaceutical dosage form, such as a tablet or a capsule.

14. The composition of claim 13, wherein the tablet comprises an outer cosmetic film coat.

15. The composition of any of the preceding claims, wherein one dosage form comprises an amount of the first composition of 25-200 mg of API, preferably 50-150, such as 75-125, for example about 80 mg or about 100 mg.

16. The composition of any of the preceding claims, wherein one dosage form comprises an amount of the third composition of 5-100 mg API, preferably 10-75 mg, such as 10-50 mg, such as 20-30 mg or 10-20 mg, for example about 10 mg, about 15 mg, or about 25 mg.

17. The composition of any of the preceding claims, wherein the ratio of extended release metoprolol to immediate release metoprolol is 75-95:25-5, such as 75:25, 80:20, 90:10, 100:10.

18. The composition of any of the preceding claims, wherein one dosage form comprises an amount of the second composition of 0.1-1 mg API, preferably 0.2-0.8 mg, for example 0.25-0.75 mg, such as 0.4-0.6 mg for example about 0.25 mg, 0.5 mg or 0.75 mg.

19. The composition of any of claims 1-17, comprising 25-200 mg ER metoprolol, 5-50 mg IR metoprolol, and 0.1-1.5 mg tesofensine, for example 50-125 mg ER metoprolol, 10-25 mg IR metoprolol, and 0.25-0.75 mg tesofensine, for example 75-80 mg ER metoprolol, 10-15 mg IR metoprolol, and 0.25-0.75 tesofensine.

20. The composition of any of the preceding claims for use as a medicament.

21. The composition of any of the preceding claims for use in the treatment of obesity or an obesity associated disorder.

22. The composition for use of any of claims 20 to 21, for use in the treatment of diabetes.

23. The composition for use of claim 22, wherein the diabetes is type 2 diabetes.

24. The composition for use of claim 21, wherein the obesity associated disorder is prediabetes.

25. The composition for use of any of claims 20 to 21, for use in the treatment of a disorder or condition selected from the group consisting of metabolic syndrome, dyslipidemia, atherosclerosis, drug-induced obesity, overeating disorders, bulimia nervosa, binge eating disorder, compulsive over-eating, impaired appetite regulation, nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

26. The composition for use of any of claims 20 to 25, wherein the metoprolol prevents or alleviates the cardiovascular side-effects of tesofensine.

27. The composition for use of any of the claims 21 to 25, wherein the composition is to be administered once daily.

28. Use of the composition according to any of claims 1 to 19 in the manufacture of a medicament for the treatment of diabetes, obesity or an obesity associated disorder.