Claims

1. A once daily pharmaceutical dosage form comprising a core comprising 22 mg of tofacitinib, or an equivalent amount of tofacitinib in the form of a pharmaceutically acceptable salt thereof, and an osmagen,

and a semi-permeable membrane coating surrounding the core wherein said coating comprises a water-insoluble polymer,

wherein said dosage form is a sustained release dosage form, and when added to a test medium comprising 900 mL of 0.05M pH 6.8 potassium phosphate buffer at 37º C. in a standard USP rotating paddle apparatus and the paddles are rotated at 50 rpm, dissolves not more than 30% of the tofacitinib, or pharmaceutically acceptable salt thereof, in 1 hour, and not less than 35% and not more than 75% of the tofacitinib, or pharmaceutically acceptable salt thereof, in 2.5 hours and not less than 75% of the tofacitinib, or pharmaceutically acceptable salt thereof, in 5 hours and wherein said dosage form delivers the tofacitinib, or pharmaceutically acceptable salt thereof, to a subject primarily by osmotic pressure and wherein the water-insoluble polymer is a cellulose derivative that sustains release of the tofacitinib, or pharmaceutically acceptable salt thereof.

2. A once daily pharmaceutical dosage form comprising

a core comprising 22 mg of tofacitinib, or an equivalent amount of tofacitinib in the form of a pharmaceutically acceptable salt thereof, and an osmagen,

and a semi-permeable membrane coating surrounding the core wherein said coating comprises a water-insoluble polymer,

wherein the dosage form is a sustained release dosage form and when administered orally to a subject provides an AUC in the range of 80% to 125% of the AUC of 10 mg of tofacitinib or an equivalent amount of tofacitinib in the form of a pharmaceutically acceptable salt thereof administered as an immediate release formulation BID and provides a ratio of geometric mean plasma Cmax to Cmin from about 10 to about 100 and wherein the dosage form delivers the tofacitinib, or pharmaceutically acceptable salt thereof, to the

subject primarily by osmotic pressure and wherein the water-insoluble polymer is a cellulose derivative that sustains release of the tofacitinib or pharmaceutically acceptable salt thereof.

3. The pharmaceutical dosage form of claim 2, wherein the AUC range is 90% to 110% and the geometric mean plasma concentration Cmax to Cmin from about 20 to about 40.

4. The pharmaceutical dosage form of claim 3, wherein the geometric mean plasma concentration Cmax to Cmin from about 20 to about 30.

5. The pharmaceutical dosage form of claim 2, wherein when the dosage form is administered orally to the subject provides a mean plasma Cmax in the range of 70% to 125% of the mean plasma Cmax of tofacitinib administered as the immediate release formulation BID at steady state.

6. The pharmaceutical dosage form of claim 2, wherein when the dosage form is administered orally to the subject provides a drug holiday in the range of 80% to 110% of the drug holiday of tofacitinib administered as the immediate release formulation BID over a 24 hour period.

7. The pharmaceutical dosage form of claim 2, having a drug holiday from about 15 to about 18 hours over the 24 hour period.

8. A once daily pharmaceutical dosage form comprising

a core comprising 22 mg of tofacitinib, or an equivalent amount of tofacitinib in the form of a pharmaceutically acceptable salt thereof, and an osmagen,

and a semi-permeable membrane coating surrounding the core wherein said coating comprises a water-insoluble polymer,

wherein said dosage form is a sustained release dosage form, and when administered to a subject has a mean area under the plasma concentration versus time curve following administration from about 17 ng-hr/mL per mg of tofacitinib dosed to about 42 ng-hr/mL per mg of tofacitinib dosed and a ratio of

geometric mean plasma Cmax to Cmin from about 10 to about 100 and wherein said dosage form delivers the tofacitinib, or pharmaceutically acceptable salt thereof, to the subject primarily by osmotic pressure and wherein the water-insoluble polymer is a cellulose derivative that sustains release of the tofacitinib, or pharmaceutically acceptable salt thereof.

9. The pharmaceutical dosage form of claim 8, wherein the ratio of geometric mean plasma Cmax to Cmin from about 20 to about 40.

10. The pharmaceutical dosage form of claim 9, wherein the ratio of geometric mean plasma Cmax to Cmin from about 20 to about 30.

11. The pharmaceutical dosage form of claim 8, wherein the subject has a single, continuous time above about 17 ng/ml from about 6 to about 15 hours and a single, continuous time below about 17 ng/ml from about 9 to about 18 hours over a dosing 24 hours interval.

12. The pharmaceutical dosage form of claim 11, wherein the subject has a single, continuous time above about 17 ng/ml from about 6 to about 9 hours.

13. The pharmaceutical dosage form of claim 11, wherein the subject has a single, continuous time below about 17 ng/ml from about 15 to about 18 hours.

14. The pharmaceutical dosage form of claim 11, wherein the subject has a single, continuous time above about 17 ng/ml from about 11 to about 15 hours.

15. The pharmaceutical dosage form of claim 11, wherein the subject has a single, continuous time below about 17 ng/ml from about 9 to about 13 hours.

16. The pharmaceutical dosage form of claim 8, wherein the subject has a mean maximum plasma concentration (Cmax) from about 3 ng/mL per mg to about 6 ng/mL per mg of tofacitinib dosed.

17. The pharmaceutical dosage form of claim 8, wherein said dosage form delivers the tofacitinib, or pharmaceutically acceptable salt thereof, by a system selected from the group consisting of an extrudable core system, a swellable core system, and an asymmetric membrane technology.

18. The pharmaceutical dosage form of claim 8, wherein said cellulose derivative is cellulose acetate.

19. The pharmaceutical release dosage form of claim 8, wherein said coating further comprising a water soluble polymer having an average molecular weight between 2000 and 100,000 daltons.

20. The pharmaceutical dosage form of claim 19, wherein said water soluble polymer is selected from the group consisting of water soluble cellulose derivatives, acacia, dextrin, guar gum, maltodextrin, sodium alginate, starch, polyacrylates, and polyvinyl alcohols.

21. The pharmaceutical dosage form of claim 20, wherein said water soluble cellulose derivatives comprises hydroxypropylcellulose, hydroxypropylmethylcellulose or hydroxyethylcellulose.

22. The pharmaceutical dosage form of claim 8, wherein the osmagen is a sugar.

23. The pharmaceutical dosage form of claim 22, wherein the sugar is sorbitol.

24. The once daily pharmaceutical dosage form of claim 8, wherein the subject has a mean steady-state minimum plasma concentration (Cmin) less than about 0.3 ng/mL per mg of tofacitinib dosed.

25. The once daily pharmaceutical dosage form of claim 8, wherein when administered orally to the subject has a mean fed/fasted ratio of the area under the plasma concentration versus time curve from about 0.7 to about 1.4 and a

mean fed/fasted ratio of the maximum plasma concentration (Cmax) from about 0.7 to about 1.4.