Claims

1. A flowable composition comprising:

(a) at least one biodegradable thermoplastic polymer which is at least substantially insoluble in body fluid;

(b) a biocompatible polar aprotic organic liquid which comprises N-methyl-2-pyrrolidone, 2-pyrrolidone, N,N-dimethylformamide, dimethyl sulfoxide, propylene carbonate, caprolactam, triacetin, PEG, or any combination thereof; and,

(c) ~~buprenorphine, a metabolite, or a prodrug thereof,~~

~~wherein the flowable composition is injected into the body whereupon it transforms *in situ* into a solid implant,~~

~~and wherein the buprenorphine, the metabolite, or the prodrug thereof is present from 1 wt. % to 30 wt. % of the flowable composition~~10 wt% to 20 wt% of buprenorphine in the neutral free-base form or buprenorphine in the form of a pharmaceutically acceptable salt,

wherein the flowable composition is injected into the body whereupon it transforms in situ into a solid implant.

2. The flowable composition of claim 1 wherein the biodegradable thermoplastic polymer is a polyester of one or more hydroxycarboxylic acids, or is a polyester of a combination of one or more diols and one or more dicarboxylic acids.

3. The flowable composition of claim 2, wherein the polyester is a polylactide, a polyglycolide, a polycaprolactone, a polyorthoester, a copolymer thereof, a terpolymer thereof, or any combination thereof.

4. The flowable composition of claim 3, wherein the polyester is a 50/50, 55/45, 60/40, 65/35, 70/30, 75/25, 80/20, 85/15, 90/10, or 95/5 poly(DL-lactide-co-glycolide) having a carboxy terminal group, or is a 50/50, 55/45, 60/40, 65/35, 70/30, 75/25, 80/20, 85/15, 90/10, or 95/5 poly(DL-lactide-co-glycolide) without a carboxy terminal group.

5. The flowable composition of any of claims 2 to 4 wherein the biodegradable thermoplastic polyester is present in from 5 wt. % to 95 wt. % of the flowable composition, or is present in from 15 wt. % to 70 wt. % of the flowable composition, or is present in from 25 wt. % to 50 wt. % of the flowable composition.

6. The flowable composition of any of claims 2 to 4 wherein the biodegradable thermoplastic polyester has an average molecular weight of 5,000 Daltons to 40,000 Daltons of the flowable composition, or 10,000 Daltons to 20,000 Daltons of the flowable composition.

7. The flowable composition of any preceding claim, wherein the biocompatible polar aprotic liquid is present from 10 wt. % to 90 wt. % of the flowable composition or from 30 wt. % to 70 wt. % of the flowable composition.

8. The flowable composition of any preceding claim wherein the weight ratio of the buprenorphine~~, the metabolite, or the prodrug thereof~~ to the biodegradable thermoplastic polymer(s) is between 0.01:1 and 2:1.

9. The flowable composition of any preceding claim, wherein the buprenorphine~~, the metabolite, or the prodrug thereof is in the neutral, free-base form~~ is in the neutral, free-base form.

10. The flowable composition of any preceding claim which further comprises one or more excipients selected from the group consisting of biodegradable thermoplastic polymers, plasticizers, and porogens.

11. The flowable composition of any preceding claim which has a volume of from 0.10 ml to 2.0 ml, preferably from 0.20 ml to 1.0 mL.

12. The flowable composition of any preceding claim which is formulated for administration once per month, or once per three months, or once per four months or once per six months.

13. A method of forming a flowable composition as claimed in any one of claims 1 to 12 for use as a controlled release implant, comprising the step of mixing, in any order:

(a) a biodegradable thermoplastic polymer that is at least substantially insoluble in aqueous medium or body fluid;

(b) a biocompatible polar aprotic liquid; and

(c) buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt, ~~a metabolite, or a prodrug thereof,~~ wherein the mixing is performed for a sufficient period of time effective to form the flowable composition for use as a controlled release implant.

14. The method of claim 13, wherein the biodegradable thermoplastic polymer and the biocompatible polar aprotic liquid are mixed together to form a mixture and the mixture is mixed with the buprenorphine in the form of the neutral free-base or in the form of the pharmaceutically acceptable salt to form the flowable composition, ~~the metabolite, or the prodrug thereof to form the flowable composition~~.

15. A kit suitable for forming the composition as claimed in any one of claims 1 to 12, the kit comprising:

(a) a first syringe comprising a composition comprising a biodegradable thermoplastic polymer that is at least substantially insoluble in a body fluid and a biocompatible polar aprotic liquid; and

(b) a second syringe comprising buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt~~, a metabolite, or a prodrug thereof~~; wherein the syringes can be directly connected to each other.

16. A kit suitable for forming the composition as claimed in any one of claims 1 to 12, the kit comprising a single syringe comprising a composition comprising a biodegradable thermoplastic polymer that is at least substantially insoluble in a body fluid, a biocompatible polar aprotic liquid and buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt~~, a metabolite, or a prodrug thereof~~.

17. The use of an effective amount of buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt~~, a metabolite, or a prodrug thereof~~ in combination with an at least substantially water-insoluble biodegradable thermoplastic polymer and a biocompatible, polar, aprotic organic liquid for the preparation of a medicament to provide the composition of any one of claims 1 to 12 to form a biodegradable implant for the treatment of a medical condition.

18. A use as claimed in claim 17 wherein the medical condition comprises pain relief or opioid dependency or a combination thereof.

19. A use as claimed in claim 17 or claim 18 wherein the biodegradable implant delivers a therapeutically effective dosage of the buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt~~, metabolite, or prodrug thereof~~ from 0.1 to 10 milligrams (mg) or from 1 to 5 milligrams (mg) per day.

20. The use as claimed in any of claims 17-19, wherein the dosage achieves a therapeutically effective level of the buprenorphine, metabolite, or prodrug thereof within one day after administration of the implant; and wherein the therapeutically effective dosage of the buprenorphine in the form of a neutral free-base or in the form of a pharmaceutically acceptable salt~~, metabolite, or prodrug thereof~~ is delivered for at least 15 days after administration of the implant, or for at least 30 days after administration of the implant, or for at least 45 days after administration of the implant, or for at least 60 days after administration of the implant.

21. The flowable composition of any preceding claim, wherein the biocompatible polar aprotic organic liquid comprises N-methyl-2-pyrrolidone.

22. The flowable composition of Claim 1, wherein the biodegradable thermoplastic polymer is poly(lactide-co-glycolide) and the biocompatible polar aprotic organic liquid is N-methyl-2-pyrrolidone.