Claims

1. A ~~injectable~~ 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 ~~an amide, an ester, a carbonate, a lactam, an ether, a sulfonyl, or any combination thereof; which has a solubility in aqueous medium or body fluid ranging from insoluble to completely soluble in all proportions~~ N-methyl-2-pyrrolidone, 2-pyrrolidone, N,N-dimethylformamide, dimethyl sulfoxide, propylene carbonate, caprolactam, triacetin, PEG, or any combination thereof; and,

(c) ~~1 wt% to 30wt% of buprenorphine, a metabolite, or a prodrug thereof;~~

~~wherein the composition is transformed *in situ* into a solid implant by contact with water, body fluid or other aqueous medium~~ 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.

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 ~~about~~ from 5 wt. % to ~~about~~ 95 wt. % of the flowable composition, or is present in ~~about~~ from 15 wt. % to ~~about~~ 70 wt. % of the flowable composition, or is present in ~~about~~ from 25 wt. % to ~~about~~ 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 ~~about~~ 5,000 Daltons to ~~about~~ 40,000 Daltons of the flowable composition, or ~~about~~ 10,000 Daltons to ~~about~~ 20,000 Daltons of the flowable composition.

~~7. The flowable composition of any preceding claim wherein the biocompatible polar aprotic liquid comprises N-methyl-2-pyrrolidone, 2-pyrrolidone, N,N-dimethylformamide, dimethyl sulfoxide, propylene carbonate, caprolactam, triacetin, PEG, or any combination thereof.~~

~~8~~7. The flowable composition of any preceding claim, wherein the biocompatible polar aprotic liquid is present ~~in about~~ from 10 wt. % to ~~about~~ 90 wt. % of the flowable composition or ~~about~~ from 30 wt. % to ~~about~~ 70 wt. % of the flowable composition.

~~9~~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.

~~10~~9. The flowable composition of any preceding claim, wherein the buprenorphine, the metabolite, or the prodrug thereof is in the neutral, free-base form.

~~11~~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.

~~12~~11. The flowable composition of any preceding claim which has a volume of ~~about~~ from 0.10 ml to ~~about~~ 2.0 ml, preferably ~~about~~ from 0.20 ml to ~~about~~ 1.0 mL.

~~13~~12. The flowable composition of any preceding claim which is formulated for administration ~~about~~ once per month, or ~~about~~ once per three months, or ~~about~~ once per four months or ~~about~~ once per six months.

~~14~~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, 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.

~~15~~14. The method of claim ~~14~~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, the metabolite, or the prodrug thereof to form the flowable composition.

~~16. A biodegradable implant formed *in situ*, in a patient, by the steps comprising:~~

~~(a) injecting a composition of claim 1 into the body of the patient; and~~

~~(b) allowing the biocompatible polar aprotic liquid to dissipate to produce a solid biodegradable implant.~~

~~17. The biodegradable implant of claim 16, wherein the composition comprises an effective amount of the biodegradable thermoplastic polymer; an effective amount of the biocompatible polar aprotic liquid; and an effective amount of the buprenorphine, the metabolite, or the prodrug thereof, wherein the solid implant releases an effective amount of the buprenorphine, the metabolite, or the prodrug thereof over time as the solid implant biodegrades in the patient.~~

~~18. A method of forming a biodegradable implant *in situ*, in a living patient, comprising the steps of:~~

~~(a) injecting the flowable composition of claim 1 into the body of a patient; and~~

(b) allowing the biocompatible polar aprotic liquid to dissipate to produce a solid biodegradable implant;

wherein the solid biodegradable implant releases the effective amount of the buprenorphine, the metabolite, or the prodrug thereof by diffusion, erosion, or a combination of diffusion and erosion as the implant biodegrades in the patient.

1915. 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, a metabolite, or a prodrug thereof; wherein the syringes can be directly connected to each other.

2016. 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, a metabolite, or a prodrug thereof.

2117. A method for treatment of a patient having a medical condition, comprising administering to the patient The use of an effective amount of buprenorphine, 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.

2218. A method according to use as claimed in claim 21 17 wherein the medical condition comprises pain relief or opioid dependency or a combination thereof.

2319. A method according to use as claimed in claim 21 17 or 22 claim 18 wherein the biodegradable implant delivers a therapeutically effective dosage of the buprenorphine, metabolite, or prodrug thereof from about 0.1 to about 10 milligrams (mg) or about from 1 to about 5 milligrams (mg) per day.

~~24~~20. The ~~method of~~ use as claimed in any of claims ~~21 to 23~~17-19, wherein the dosage achieves a therapeutically effective level of the buprenorphine, metabolite, or prodrug thereof within ~~about~~ one day after administration of the implant; and wherein the therapeutically effective dosage of the buprenorphine, metabolite, or prodrug thereof is delivered for at least ~~about~~ 15 days after administration of the implant, or for at least ~~about~~ 30 days after administration of the implant, or for at least ~~about~~ 45 days after administration of the implant, or for at least ~~about~~ 60 days after administration of the implant.