Claims

1. A pharmaceutical formulation that is useful in the treatment of myelodysplastic syndrome, comprising a plurality of particles suspended in an aqueous carrier system, which particles:
   (a) have a weight-, number-, or volume-based mean diameter that is between amount 10 nm and about 700 μm; and
   (b) comprise solid cores comprising azacitidine, or a pharmaceutically-acceptable salt thereof, coated, at least in part, by a coating of inorganic material comprising mixture of:
      (i) zinc oxide; and
      (ii) one or more other metal and/or metalloid oxides,
      wherein the atomic ratio ((i):(ii)) is at least about 1:6 and up to and including about 6:1.

2. A formulation as claimed in Claim 1, wherein the atomic ratio ((i):(ii)) is at least about 1:1 and up to and including about 6:1.

3. A formulation as claimed in Claim 1, wherein the coated particles comprise:
   (a) solid cores comprising, or consisting essentially of, azacitidine, or pharmaceutically-acceptable salt thereof; and
   (b) one or more discrete layers surrounding said cores, said one or more discrete layers each comprising at least one separate mixture of zinc oxide and one or more other metal and/or metalloid oxides in a atomic ratio of between about 1:1 and about 6:1.

4. A formulation as claimed in any one of the preceding claims, wherein the weight-, number-, or volume-based mean diameter of the particles is between amount 1 μm and about 50 μm.

5. A formulation as claimed in any one of the preceding claims, wherein:

- more than one discrete layer of the mixture of oxides is applied to the core sequentially, optionally wherein between 3 and 10 discrete layers of the mixture of oxides are applied;

- the total thickness of the mixed oxide coating is between about 0.5 nm and about 2 μm;

- the ratio of zinc oxide to other metal and/or metalloid oxides is between about 2:1 and about 5:1; and/or

- the one or more other metal and/or metalloid oxides are selected from aluminium oxide and/or silicon dioxide.

6. A formulation as claimed in Claim 5, wherein the maximum thickness of an individual discrete layer of mixed oxide coating is about 1 hundredth of the weight-, number-, or volume-based mean diameter of the core, including any other discrete layers that have previously been applied to the core.

7. A formulation as claimed in any one of the preceding claims in the form of a sterile injectable and/or infusible dosage form.

8. A formulation as claimed in Claim 7 in a form that is administrable *via* a surgical administration apparatus that forms a depot formulation.

9. A process for the preparation of a formulation as defined in any one of the preceding claims, wherein the coated particles are made by applying the layer(s) of mixed oxide coating material to the cores, and/or previously-coated cores, by atomic layer deposition.

10. A process as claimed in Claim 9, wherein:
(i) solid cores are coated with a first discrete layer of mixed oxide coating material;
(ii) the coated cores from step (i) are then subjected to a deagglomeration process step;
(iii) the deagglomerated coated cores from step (ii) are then coated with a second discrete layer of mixed oxide coating material;
(iv) repeating steps (ii) and (iii) to obtain the required number of discrete layers.

11. A process as claimed in Claim 10, wherein the deagglomeration step that takes place between applications of coatings comprises sieving,

optionally wherein the sieving comprises vibrational sieving or sonic sifting.

12. A process as claimed in Claim 11, wherein the vibrational sieving comprises controlling a vibration probe coupled to the sieve.

13. A process for the preparation of a formulation as defined in any one of Claims 1 to 8 wherein the coated particles are mixed with the carrier system after coating.

14. An injectable and/or infusible dosage form comprising a formulation as defined in any one of Claims 1 to 8 contained within a reservoir that is connected to, and/or is in association with, an injection or infusion means,

optionally which is a surgical administration apparatus that forms a depot formulation.

15. A dosage form as claimed in Claim 14, wherein coated particles as defined in any one of Claims 1 to 7 and the carrier system are housed separately, and in which admixing occurs prior to and/or during injection or infusion.

16. The use of a formulation as defined in any one of Claims 1 to 8, or a dosage form as defined in Claims 14 or 15, for the manufacture of a medicament for the treatment of myelodysplastic syndrome,

optionally wherein the myelodysplastic syndrome is selected from the group refractory anaemia, refractory anaemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory cytopenia with multilineage dysplasia and ringed sideroblasts, refractory anemia with excess blasts, refractory anaemia with excess blasts in transformation, unclassified myelodysplastic syndrome and myelodysplastic syndrome associated with isolated del (5q).

17. The use as claimed in Claim 16, wherein, following injection, the formulation provides a depot formulation from which azacitidine is released over a period of time that is between 3 days and about 3 weeks.

18. The use as claimed in Claim 17, wherein the total exposure for azacitidine is at least about 50% of the total exposure obtained from a dosing regimen comprising administering 75 mg /m^2 of body surface area over seven consecutive days by injection or infusions of azacitidine,

optionally wherein the exposure in terms of the average area under the concentration vs. time curve up to infinite time is 960 ±458 ng*h/mL.

19. The use as claimed in Claims 17 or 18, wherein the average maximum concentration observed in the plasma is less than that obtained from a dosing regimen comprising administering 75 mg /m^2 of body surface area over seven consecutive days by injection or infusions of azacitidine,

optionally wherein the average maximum concentration observed in the plasma is between about 200 and about 700 ng/mL.

20. A formulation as claimed in any one of Claims 1 to 8, a dosage form as claimed in Claims 14 or 15, or the use as claimed in any one of Claims 17 to 19, wherein the dose of

azacitidine or pharmaceutically-acceptable salt thereof (calculated as the free compound) is in the range of about 200 mg to about 1000 mg per m^2 of body surface area.