

CLAIMS

1. A pharmaceutical composition or kit for use in treating cancer in a mammal comprising asparaginase and methioninase for at least one sequential administration with
5 methioninase being administered before asparaginase.

2. The composition for the use of claim 1, wherein methioninase and asparaginase are under free form, pegylated form or encapsulated inside erythrocytes.

3. The composition for the use of claim 1, wherein methioninase is under free form or is pegylated and the delay between the end of methioninase administration and the initiation
10 of asparaginase administration is between about 1 h and about 7 days, in particular between about 3 h and about 6 days, preferably between about 1 day and about 5 days.

4. The composition for the use of claim 1, wherein methioninase is encapsulated into erythrocytes and the delay between the end of methioninase administration and the initiation
15 of asparaginase administration is between about 1h and about 30 days, in particular between about 1 day and about 20 days, preferably between about 1 day and about 10 days.

5. The composition for the use of any one of the preceding claims, wherein methioninase is administered once or more in an amount of between about 100 and about 100 000 IU, in particular between about 500 and about 50 000 IU, preferably between about 500 and about 5000 IU.

20 6. The composition for the use of any one of the preceding claims, wherein asparaginase is administered once or more in an amount of between about 500 and about 100 000 IU, in particular between about 1000 and about 50 000 IU, preferably between about 5000 and about 30 000 IU.

25 7. A pharmaceutical composition comprising asparaginase for use in treating cancer in a mammal that has been administered methioninase.

8. The composition for the use of claim 7, wherein methioninase is under free form or pegylated form and the delay between methioninase and asparaginase administration is between about 1 h and about 7 days, in particular between about 3 h and about 6 days, preferably between about 1 day and about 5 days.

30 9. The composition for the use of claim 7, wherein methioninase is encapsulated inside erythrocytes and the delay between the end of methioninase administration and the initiation of asparaginase administration is between about 1h and about 30 days, in particular between about 1 day and about 20 days, preferably between about 1 day and about 10 days.

35 10. The composition for the use of any one of claims 7-9, wherein methioninase is administered once or more in an amount of between about 100 and about 100 000 IU, in particular between about 500 and about 50 000 IU, preferably between about 500 and about 5000 IU.

11. The composition for the use of any one of claims 7-10, wherein asparaginase is administered once or more in an amount of between about 500 and about 100 000 IU, in particular between about 1000 and about 50 000 IU, preferably between about 5000 and about 30 000 IU.

5 12. The composition for the use of any one of claims 1 to 11, further comprising PLP or a PLP precursor for simultaneous, separate or sequential administration with the methioninase..

10 13. The composition for the use of claim 12, comprising methioninase encapsulated inside erythrocytes and a non-phosphate precursor of PLP for separate or sequential administration.

15 14. The composition for the use of any one of claims 1 to 11, wherein methioninase encapsulated inside erythrocytes is administered at least once or twice before asparaginase encapsulated inside erythrocytes is administered, and each methioninase administration is followed by administration of a solution of non-phosphate precursor of PLP before asparaginase is administered.

 15. The composition for the use of any one of the preceding claims, for treating liquid or solid tumors.

 16. The composition for the use claim 15, for treating leukemia or gastric cancer.

20 17. A method for treating cancer in a mammal in need thereof, the method comprising administering to the mammal in need thereof, a composition comprising methioninase and then a composition containing asparaginase.

25 18. A method for treating cancer in a mammal in need thereof, the method comprising administering to the mammal in need thereof, a composition comprising methioninase encapsulated inside erythrocytes and then a composition containing asparaginase encapsulated inside erythrocytes.

 19. The method of claim 18, wherein the delay between the end of methioninase administration and the initiation of asparaginase administration is between 1h and 30 days.

 20. The method of claim 18, wherein methioninase is administered once or more in an amount of between 100 and 100 000 IU.

30 21. The method of claim 18, wherein asparaginase is administered once or more in an amount of between 500 and 100 000 IU.

35 22. The method of claim 18, wherein methioninase encapsulated inside erythrocytes is administered at least once or twice before asparaginase encapsulated inside erythrocytes is administered, and each methioninase administration is accompanied by administration of PLP or a precursor of PLP before asparaginase is administered.

 23. The method of claim 22, wherein a solution of non-phosphate precursor of PLP is administered once or more after each administration of encapsulated methioninase.

24. The method of claim 23, wherein a solution of non-phosphate precursor of PLP is administered once a day, or twice or more per day, during the time of methioninase treatment.

25. The method of claim 18, wherein the cancer is leukemia or gastric cancer.