What is claimed is:

1. A method of inducing immune tolerance in a subject in need of treatment with a therapeutic, comprising administering to the subject an effective amount of methotrexate in a single cycle, thereby inducing immune tolerance toward the therapeutic in the subject.

2. A method of inhibiting antibody responses to a protein therapeutic in a subject in need of treatment with the therapeutic, comprising administering to the subject an effective amount of methotrexate in a single cycle, thereby inhibiting antibody responses to the therapeutic in the subject.

3. A method of alleviating an infusion reaction to a therapeutic in a subject in need of treatment with the therapeutic, comprising administering to the subject an effective amount of methotrexate, thereby alleviating an infusion reaction to the protein therapeutic in the subject.

4. A method of reducing secondary autoimmunity in an autoimmune subject in need of treatment with a therapeutic, comprising administering to the subject an effective amount of methotrexate, thereby reducing secondary autoimmunity in the subject.

5. A method of increasing the efficacy of a therapeutic in a subject in need of treatment with the therapeutic, comprising administering to the subject an effective amount of methotrexate, thereby increasing the efficacy of the protein therapeutic in the subject.

6. A method of increasing the percentage of T regulatory cells in the T cell population in a subject in need of treatment with a therapeutic, comprising administering to the subject an effective amount of methotrexate, thereby increasing said percentage in said subject.

7. The method of any one of claims 1-6, wherein the therapeutic is a protein therapeutic.

8. A method of increasing the percentage of B regulatory cells in the B cell population in a subject in need of treatment with an antibody therapeutic, comprising administering to the subject an effective amount of methotrexate, thereby increasing said percentage in said subject.

9. The method of any one of claims 3-8, wherein the effective amount of methotrexate is administered in a single cycle

10. A method of prolonging the pharmacokinetics of a therapeutic agent in a subject, comprising administering methotrexate to the subject, before or during or after administration of the therapeutic agent, in an amount effective to prolong the pharmacokinetics of the therapeutic agent.

11. The method of any one of claims 1-10, wherein the subject is a human.

12. The method of any one of claims 1-10, wherein the therapeutic is an antibody therapeutic.

13. The method of claim 12, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

14. The method of any one of claims 12 or 13, wherein the antibody therapeutic is a lymphocyte-depleting agent.

15. The method of claim 14, wherein the antibody therapeutic is alemtuzumab.

16. The method of claim 15, wherein the subject is a multiple sclerosis patient.

17. The method of claim 12, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

18. The method of claim 17, wherein the antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

19. The method of claim 18, wherein the subject is a human patient who is in need of organ transplantation, has aplastic anemia, and/or has or is at risk of having graft-versus-host disease.

20. The method of any one of claims 1-11, wherein the therapeutic is an enzyme.

21. The method of claim 21, wherein the enzyme is human alpha-galactosidase A.

22. The method of claim 22, wherein the enzyme is human acid alpha-glucosidase.

23. The method of any one of claims 1-22, wherein the effective amount is 0.1 mg/kg to 5 mg/kg.

24. The method of any one of claims 1-22, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

25. The method of any one of claims 1-22, wherein the single cycle of methotrexate is administered between 48 hours prior to and 48 hours after the onset of the therapeutic treatment.

26. A method of depleting lymphocytes in a human patient in need thereof, comprising:

treating the patient with a lymphocyte-depleting agent, and

administering methotrexate to the patient, before or during or after the treatment with the lymphocyte-depleting agent, in an amount effective to induce immune tolerance in the patient toward the lymphocyte-depleting agent.

27. The method of claim 26, wherein the effective amount of methotrexate is administered in a single cycle.

28. The method of any one of claims 26 or 27, wherein the lymphocyte-depleting agent is a monoclonal antibody therapeutic.

29. The method of any one of claims 26 or 27, wherein the lympocyte-depleting agent is a polyclonal antibody therapeutic.

30. The method of claim 28, wherein the monoclonal antibody therapeutic is alemtuzumab.

31. The method of claim 28, wherein the monoclonal antibody therapeutic is rituximab.

32. The method of any one of claims 26-31, wherein the patient is a multiple sclerosis patient.

33. The method of claim 32, wherein the patient has remitting-relapsing multiple sclerosis.

34. The method of claim 29, wherein the polyclonal antibody therapeutic is anti-thymocyte globulin polyclonal antibody.

35. A method of inducing immune tolerance in a subject in need of tissue transplantation, comprising administering to the subject an effective amount of methotrexate, thereby inducing immune tolerance toward the transplanted tissue in the subject.

36. The method of claim 35, wherein the effective amount of methotrexate is administered in a single cycle.

37. The method of any one of claims 35 or 36, wherein the transplanted tissue is renal tissue or cardiac tissue.

38. The method of claim 37, wherein the subject also receives another agent for immune modulation.

39. The method of claim 38, wherein the agent for immune modulation is an immunosuppressant.

40. The method of claim 38, wherein the agent for immune modulation is polyclonal anti-thymocyte globulin antibody.

41. A method of inhibiting T cell responses in a subject in need of a therapeutic or tissue transplantation, comprising administering to the subject an effective amount of methotrexate prior to, concurrently with, or after, treating the subject with the therapeutic or tissue transplantation, thereby inhibiting T cell responses in the subject.

42. The method of claim 41, wherein the effective amount of methotrexate is administered in a single cycle.

43. The method of any one of claims 41 or 42, wherein the therapeutic is a protein therapeutic.

44. The method of any claim 43, wherein the protein therapeutic is an antibody therapeutic.

45. The method of claim 44, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

46. The method of any one of claims 44 or 45, wherein the antibody therapeutic is a lymphocyte-depleting agent.

47. The method of claim 46, wherein the antibody therapeutic is alemtuzumab.

48. The method of claim 47, wherein the subject is a multiple sclerosis patient.

49. The method of claim 44, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

50. The method of claim 49, wherein the polyclonal antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

51. The method of claim 43, wherein the transplanted tissue is renal tissue or cardiac tissue.

52. The method of claim 51, wherein the subject also receives another agent for immune modulation.

53. The method of claim 52, wherein the agent for immune modulation is an immunosuppressant.

CLAIMS

1. Use of an effective amount of methotrexate for the manufacture of a medicament for inducing immune tolerance in a subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby inducing immune tolerance toward the therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

2. Use of an effective amount of methotrexate for the manufacture of a medicament for inhibiting antibody responses to a protein therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby inhibiting antibody responses to the therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

3. Use of an effective amount of methotrexate for the manufacture of a medicament for alleviating an infusion reaction to a therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby alleviating an infusion reaction to the protein therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

4. Use of an effective amount of methotrexate for the manufacture of a medicament for reducing secondary autoimmunity in an autoimmune subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby reducing secondary autoimmunity in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

5. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the efficacy of a therapeutic in a subject in need of treatment with the therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing the efficacy of the protein

therapeutic in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

6. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the percentage of T regulatory cells in the T cell population in a subject in need of treatment with a therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing said percentage in said subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

7. The use of any one of claims 1-6, wherein the therapeutic is a protein therapeutic.

8. The use of any one of claims 1-6, wherein the subject is suffering from a disease selected from from multiple sclerosis, Fabry disease, Gaucher disease, Mucopolysaccharidosis I, Pompe disease, host-vs-graft disease, graft-vs-host disease, rheumatoid arthritis, psoriasis, diabetes, lupus, sclerodoma, chronic B-cell lymphocytic leukaemia, vasculitis, thyroid autoimmunity, thrombocytopenic purpura, immune thrombocytopenia, Goodpasture's disease, autoimmune neutropenia, autoimmune hemolytic anemia, and autoimmne lymphopenia.

9. The use of any one of claims 1-6, wherein the subject is in need of tissue transplantation.

10. Use of an effective amount of methotrexate for the manufacture of a medicament for increasing the percentage of B regulatory cells in the B cell population in a subject in need of treatment with an antibody therapeutic, wherein the methotrexate is administered in a single cycle thereby increasing said percentage in said subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

11. The use of claim 10, wherein the subject is suffering from a disease selected from from multiple sclerosis, Fabry disease, Gaucher disease, Mucopolysaccharidosis I, Pompe disease, host-vs-graft

disease, graft-vs-host disease, rheumatoid arthritis, psoriasis, diabetes, lupus, sclerodoma, chronic B-cell lymphocytic leukaemia, vasculitis, thyroid autoimmunity, thrombocytopenic purpura, immune thrombocytopenia, Goodpasture's disease, autoimmune neutropenia, autoimmune hemolytic anemia, and autoimmne lymphopenia.

12. The use of claim 10, wherein the subject is in need of tissue transplantation.

13. Use of an effective amount of methotrexate for the manufacture of a medicament for prolonging the pharmacokinetics of a therapeutic agent in a subject, wherein the methotrexate is administered to the subject before or during or after administration of the therapeutic agent, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

14. The use of any one of claims 1-13, wherein the subject is a human.

15. The use of any one of claims 1-13, wherein the therapeutic is an antibody therapeutic.

16. The use of claim 15, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

17. The use of any one of claims 15 or 16, wherein the antibody therapeutic is a lymphocyte-depleting agent.

18. The use of claim 17, wherein the antibody therapeutic is alemtuzumab.

19. The use of claim 18, wherein the subject is a multiple sclerosis patient.

20. The use of claim 15, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

21. The use of claim 20, wherein the antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

22. The use of claim 21, wherein the subject is a human patient who is in need of organ transplantation, has aplastic anemia, and/or has or is at risk of having graft-versus-host disease.

23. The use of any one of claims 1-14, wherein the therapeutic is an enzyme.

24. The use of claim 23, wherein the enzyme is human alpha-galactosidase A.

25. The use of claim 23, wherein the enzyme is human acid alpha-glucosidase.

26. The use of any one of claims 1-25, wherein the effective amount is 0.1 mg/kg to 5 mg/kg.

27. The use of any one of claims 1-25, wherein the single cycle of methotrexate is administered between 48 hours prior to and 48 hours after the onset of the therapeutic treatment.

28. Use of an effective amount of methotrexate for the manufacture of a medicament for depleting lymphocytes in a human patient in need thereof, wherein the methotrexate is administered to the patient in a single cycle, before or during or after the treatment with the lymphocyte-depleting agent to induce immune tolerance in the patient toward the lymphocyte-depleting agent, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

29. The use of claim 28, wherein the lymphocyte-depleting agent is a monoclonal antibody therapeutic.

30. The use of claim 28, wherein the lympocyte-depleting agent is a polyclonal antibody therapeutic.

31. The use of claim 29, wherein the monoclonal antibody therapeutic is alemtuzumab.

32. The use of claim 29, wherein the monoclonal antibody therapeutic is rituximab.

33. The use of any one of claims 28-32, wherein the patient is a multiple sclerosis patient.

34. The use of claim 33, wherein the patient has remitting-relapsing multiple sclerosis.

35. The use of claim 30, wherein the polyclonal antibody therapeutic is anti-thymocyte globulin polyclonal antibody.

36. Use an effective amount of methotrexate for the manufacture of a medicament for inducing immune tolerance in a subject in need of tissue transplantation, wherein the methotrexate is administered in a single cycle thereby inducing immune tolerance toward the transplanted tissue in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

37. The use of claim 36, wherein the transplanted tissue is renal tissue or cardiac tissue.

38. The use of claim 37, wherein the subject also receives another agent for immune modulation.

39. The use of claim 38, wherein the agent for immune modulation is an immunosuppressant.

40. The use of claim 38, wherein the agent for immune modulation is polyclonal anti-thymocyte globulin antibody.

41. Use of an effective amount of methotrexate for the manufacture of a medicament for inhibiting T cell responses in a subject in need of a therapeutic or tissue transplantation, wherein the methotrexate is administered in a single cycle prior to, concurrently with, or after, treating the subject with the therapeutic or tissue transplantation thereby inhibiting T cell responses in the subject, wherein the single cycle of methotrexate consists of 1 day of methotrexate administration or 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 consecutive days of methotrexate administration.

42. The use of claim 41, wherein the therapeutic is a protein therapeutic.

43. The use of claim 42, wherein the protein therapeutic is an antibody therapeutic.

44. The use of claim 43, wherein the antibody therapeutic is a monoclonal antibody therapeutic.

45. The use of any one of claims 43 or 44, wherein the antibody therapeutic is a lymphocyte-depleting agent.

46. The use of claim 45, wherein the antibody therapeutic is alemtuzumab.

47. The use of claim 46, wherein the subject is a multiple sclerosis patient.

48. The use of claim 43, wherein the antibody therapeutic is a polyclonal antibody therapeutic.

49. The use of claim 48, wherein the polyclonal antibody therapeutic is polyclonal rabbit anti-thymocyte globulin antibody.

50. The use of claim 42, wherein the transplanted tissue is renal tissue or cardiac tissue.

51. The use of claim 50, wherein the subject also receives another agent for immune modulation.

52. The use of claim 51, wherein the agent for immune modulation is an immunosuppressant.