treatment has been associated with confirmed cases of progressive multifocal leukoencephalopathy (PML) in patients with Crohn's disease (and separately, multiple sclerosis) who received concomitant treatment with natalizumab and immunosupressives. PML is a potentially fatal neurological condition linked to reactivation of a polyomavirus (JC virus) and active viral replication in the brain. No known interventions can reliably prevent PML or adequately treat PML, if it occurs. One limitation of vedolizumab treatment is that it is administered intravenously which can be inconvenient for the patient and can also be associated with undesirable or adverse events, e.g., infusion site reactions. Accordingly, there is a need for improved therapeutic approaches to the treatment of gastrointestinal inflammatory disorders such as IBD, e.g., ulcerative colitis and Crohn's disease, as well as more desirable dosing regimens.

[0015] The invention described herein meets certain of the above-described needs and provides other benefits.

[0016] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety for any purpose.

SUMMARY

[0017] The methods and uses of the disclosure are based, at least in part, on the discovery that therapeutically effective amounts of integrin beta7 antagonists, such as anti-beta7 antibodies, including rhuMAb Beta7 (etrolizumab) can be administered subcutaneously as well as intravenously.

[0018] Accordingly, disclosed are methods of treating a gastrointestinal inflammatory disorder in a mammalian subject comprising administering to the subject a therapeutically effective amount of an integrin beta7 antagonist are provided.

[0018a] In one aspect, there is provided use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of between about 50 mg and about 450 mg, wherein the anti-beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;

(ii) HVR-L2 comprises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO: 19.

[0018b] In one aspect, there is provided use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder, wherein the ant-beta7 antibody or antigen-binding portion thereof is to be administered a first loading dose and at least one subsequent maintenance dose, wherein the first loading dose is a flat dose of between about 400 mg and about 450 mg and the at least one maintenance dose is a flat dose of between about 50 mg and about 350 mg, each of the first loading dose and the at least one maintenance dose is to be administered subcutaneously, wherein the anti-beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;

(ii) HVR-L2 comprises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO:19.

[0018c] In certain embodiments, the mammalian subject is a patient. In certain embodiments, the patient is human. In certain embodiments, the integrin beta7 antagonist is administered intravenously. In certain embodiments, the integrin beta7 antagonist is administered subcutaneously. In one embodiment, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In certain embodiments, the inflammatory bowel disease us ulcerative colitis (UC) or Crohn's disease (CD). In certain embodiments, the integrin beta7 antagonist is a monoclonal anti-beta7 antibody. In certain such embodiments, the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody. In certain embodiments, the anti-beta7 antibody is an antibody fragment. In certain embodiments, the anti-beta7 antibody comprises six hypervariable regions (HVRs), wherein:

H, D, and A, and/or amino acid E15 is selected from the group consisting of L and V, and/or amino acid E17 is selected from the group consisting of S and G; and

(vi) HVR-H3 comprises amino acid sequence F2-F11 wherein F2-F11 is MTGSSGYFDF (SEQ ID NO:6) or RTGSSGYFDF (SEQ ID NO:19); or comprises amino acid sequence F1-F11, wherein F1-F11 is AMTGSSGYFDF (SEQ ID NO:16), ARTGSSGYFDF (SEQ ID NO:17), or AQTGSSGYFDF (SEQ ID NO:18), or a variant of SEQ ID NOs:6, 16, 17, 18, or 19 (SEQ ID NO:30) wherein amino acid F2 is R, M, A, E, G, Q, S, and/or amino acid F11 is selected from the group consisting of F and Y. In certain such embodiments, the anti-beta7 antibody comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9;
(ii) HVR-L2 comprises SEQ ID NO:2;
(iii) HVR-L3 comprises SEQ ID NO:3;
(iv) HVR-H1 comprises SEQ ID NO:4;
(v) HVR-H2 comprises SEQ ID NO:5; and
(vi) HVR-H3 comprises SEQ ID NO:6 or SEQ ID NO:16 or SEQ ID NO:17 or SEQ ID NO:19.

[0019] Also disclosed are methods of subcutaneously administering therapeutically effective amounts of anti-beta7 antibodies at a weight-based dose are provided. In certain embodiments, the anti-beta7 antibody is administered at a dose of 0.5 mg/kg. In certain embodiments, the anti-beta7 antibody is administered at a dose of 1.5 mg/kg. In certain embodiments, the anti-beta7 antibody is administered at a dose of 3.0 mg/kg. In certain embodiments, the anti-beta7 antibody is administered at a dose of 4.0 mg/kg. In one embodiment, the anti-beta7 antibody is administered at regular intervals over time. In certain embodiments, the anti-beta7 antibody is administered once every week. In certain embodiments, the anti-beta7 antibody is administered once every two weeks. In certain embodiments, the anti-beta7 antibody is administered once every four weeks. In certain embodiments, the anti-beta7 antibody is administered once every six weeks. In certain embodiments, the anti-beta7 antibody is administered once every eight weeks. In certain embodiments, the anti-beta7 antibody is administered for a period of two months. In certain embodiments, the anti-beta7 antibody is administered for a period of three months. In certain embodiments, the anti-beta7 antibody is administered for a period of six months. In certain embodiments, the anti-beta7 antibody is administered for a period of 12 months. In certain

embodiments, the anti-beta7 antibody is administered for a period of 18 months. In certain embodiments, the anti-beta7 antibody is administered for a period of 24 months. In certain embodiments, the anti-beta7 antibody is administered for the lifetime of the subject. In certain embodiments the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

[0020] Further disclosed are methods of subcutaneously administering therapeutically-effective amounts of anti-beta7 antibodies at a flat dose are provided. In certain embodiments, the anti-beta7 antibody is administered at a flat dose between 50 mg and 450 mg. In certain embodiments, the flat dose is 50 mg. In certain such embodiments, the flat dose is 100 mg. In certain such embodiments, the flat dose is 150 mg. In certain such embodiments, the flat dose is 200 mg. In certain such embodiments, the flat dose is 300 mg. In certain embodiments, the flat dose is 350 mg. In certain such embodiments, the flat dose is 400 mg. In certain such embodiments, the flat dose is 420 mg. In certain such embodiments, the flat dose is 450 mg. In one embodiment, the anti-beta7 antibody is administered at regular intervals over time. In certain such embodiments, the anti-beta7 antibody is administered once every week. In certain embodiments, the anti-beta7 antibody is administered once every two weeks. In certain embodiments, the anti-beta7 antibody is administered once every four weeks. In certain embodiments, the anti-beta7 antibody is administered once every six weeks. In certain embodiments, the anti-beta7 antibody is administered once every eight weeks. In certain embodiments, the anti-beta7 antibody is administered for a period of two months. In certain embodiments, the anti-beta7 antibody is administered for a period of three months. In certain embodiments, the anti-beta7 antibody is administered for a period of six months. In certain embodiments, the anti-beta7 antibody is administered for a period of 12 months. In certain embodiments, the anti-beta7 antibody is administered for a period of 18 months. In certain embodiments, the anti-beta7 antibody is administered for a period of 24 months. In certain embodiments, the anti-beta7 antibody is administered for the lifetime of the subject. In certain embodiments the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

[0021] Yet further disclosed are methods of administering therapeutically-effective amounts of anti-beta7 antibodies at a flat dose are provided, wherein the administration comprises administration of a first loading dose and administration of at least one subsequent maintenance dose, wherein each of the loading dose and the at least one maintenance dose is administered at a flat dose. In certain embodiments, the loading dose of the anti-beta7 antibody is administered intravenously. In certain embodiments, the loading dose of the anti-beta7 antibody is administered subcutaneously. In certain embodiments, the at least one subsequent maintenance dose of the anti-beta7 antibody is administered intravenously. In

certain embodiments, the loading dose is 450 mg and the maintenance dose is 150 mg. In certain embodiments, the loading dose is 450 mg and the maintenance dose is 200 mg. In certain embodiments, the loading dose is 450 mg and the maintenance dose is 300 mg. In certain embodiments, the loading dose is 450 mg and the maintenance dose is 350 mg. In certain embodiments the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

[0022] Also disclosed are methods of subcutaneously administering therapeutically-effective amounts of anti-beta7 antibodies at a loading dose followed by one or more maintenance doses are provided. In certain embodiments, the first maintenance dose is administered on the same day as the loading dose. In certain embodiments, the first maintenance dose is administered one day after the loading dose. In certain embodiments, the first maintenance dose is administered one week after the loading dose. In certain embodiments, the first maintenance dose is administered two weeks after the loading dose. In certain embodiments, the first maintenance dose is administered four weeks after the loading dose. In certain embodiments, the second and each subsequent maintenance dose is administered every two weeks. In certain embodiments, the second and each subsequent maintenance dose is administered every four weeks. In certain embodiments, the second and each subsequent maintenance dose is administered every eight weeks. In certain embodiments, the first maintenance dose is administered two weeks after the loading dose, the second maintenance dose is administered two weeks after the first maintenance dose, and each subsequent maintenance dose is administered every four weeks. In certain embodiments, the anti-beta7 antibody is administered for a period of two months. In certain embodiments, the anti-beta7 antibody is administered for a period of three months. In certain embodiments, the anti-beta7 antibody is administered for a period of six months. In certain embodiments, the anti-beta7 antibody is administered for a period of 12 months. In certain embodiments, the anti-beta7 antibody is administered for a period of 18 months. In certain embodiments, the anti-beta7 antibody is administered for a period of 24 months. In certain embodiments, the anti-beta7 antibody is administered for the lifetime of the subject. In certain embodiments the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

[0023] Disclosed is an article of manufacture comprising an integrin beta7 antagonist is provided. In certain embodiments, the article of manufacture comprises a prefilled syringe or an autoinjector device comprising 2 ML (150 mg) integrin beta7 antagonist. In certain embodiments, the article of manufacture comprises a prefilled syringe or an autoinjector device comprising 1 ML (180 mg) integrin beta7 antagonist. In certain

embodiments the integrin beta7 antagonist is an anti-beta7 antibody or rhuMAb Beta7 (etrolizumab).

[0024] Disclosed are methods of subcutaneously administering therapeutically effective amounts of an integrin beta7 antagonist with at least one additional compound are provided. In certain embodiments, the at least one additional compound is selected from 5-aminosalicylic acid (5-ASA), azathioprine (AZA), 6-mercaptopurine (6-MP), and methotrexate.

[0025] Disclosed are methods of subcutaneously administering therapeutically effective amounts of an integrin beta7 antagonist where the subject or the patient previously failed at least one biological agent are provided. In certain embodiments, the biological agent is selected from adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, natalizumab, and vedolizumab. In certain embodiments the integrin beta7 antagonist is an anti-beta7 antibody or rhuMAb Beta7 (etrolizumab).

[0026] Disclosed are methods of subcutaneously administering therapeutically effective amounts of an integrin beta7 antagonist with a self-inject device are provided. In certain embodiments, the self-inject device is selected from a prefilled syringe, microneedle device, an autoinjector device and needle-free injection device. In certain embodiments the integrin beta7 antagonist is an anti-beta7 antibody or rhuMAb Beta7 (etrolizumab).

[0027] Disclosed are methods of inducing remission in an ulcerative colitis patient are provided.

[0027a] In one aspect, there is provided use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for inducing remission in a patient suffering from ulcerative colitis, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of either about 100 mg or about 300 mg every four weeks, wherein the anti-beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;

(ii) HVR-L2 comp1ises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO: 19.

[0027b] In one aspect, there is provided use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for inducing sustained remission in a patient suffering from ulcerative colitis, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of either about 100 mg or about 300 mg very four weeks, wherein remission is retained for a period of 8 weeks following induction of remission, or a period of 30 weeks following induction of remission, or a period of 50 weeks following induction of remission, or a period of 54 weeks or more following induction of remission, wherein the anti beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;

(ii) HVR-L2 comprises SEQ ID NO:2;

(iii) HVR-L3 comprises SEQ ID NO:3;

(iv) HVR-H1 comprises SEQ ID NO:4;

(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO: 19.

[0027c] Such methods and uses include administering an anti-beta7 antibody according to any of the doses or dosing regimens indicated above. In certain embodiments, the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab). In certain embodiments, remission in the patient is determined to be induced when the absolute Mayo Clinic Score ≤ 2 and no individual subscore >1, which is also referred to as clinical remission. In certain embodiments remission in the patient is induced at least by week 10 following initiation of treatment with anti-beta7 antibody. In certain embodiments, patients administered anti-beta7 antibody as described above retain clinical remission from induction and continue in remission for a certain period of time, also referred to as sustained remission. In certain such embodiments, sustained remission is for a period of 8 weeks following induction of remission, or a period of 30 weeks following induction of remission, or a period of 50 weeks following induction of remission, or a period of 54 weeks or more following induction of remission. In certain embodiments, patients administered anti-beta7 antibody according to any of the doses or dosing regimens indicated above experience sustained steroid-free remission. In certain embodiments, patients who experience sustained steroid-free remission

WHAT IS CLAIMED IS:

1. Use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of between about 50 mg and about 450 mg, wherein the anti-beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;
(ii) HVR-L2 comprises SEQ ID NO:2;
(iii) HVR-L3 comprises SEQ ID NO:3;
(iv) HVR-H1 comprises SEQ ID NO:4;
(v) HVR-H2 comprises SEQ ID NO:5; and
(vi) HVR-H3 comprises SEQ ID NO: 19.

2. The use of claim 1, wherein the flat dose is selected from the group consisting of about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 300 mg, about 350 mg, about 400 mg, about 420 mg, and about 450 mg, wherein optionally the anti-beta7 antibody or antigen-binding portion thereof is to be administered once every week, or once or every two weeks, or once every four weeks, or once every six weeks, or once every eight weeks, and wherein optionally the anti-beta7 antibody or antigen-binding portion thereof is to be administered for a period of two months, or three months, or six months, or 12 months, or 18 months, or 24 months, or for the lifetime of the patient.

3. The use of claim 1, wherein the patient is a human.

4. The use of claim 1, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease, and wherein optionally the inflammatory bowel disease is ulcerative colitis or Crohn' s disease.

5. The use of claim 1, wherein the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody.

6. The use of claim 5, wherein the anti-beta7 antibody is a humanized antibody.

7. The use of claim 1, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered at a flat dose of about 100 mg or about 300 mg every four weeks, wherein the patient suffers from ulcerative colitis, and wherein the patient experiences mucosal healing or a reduced rate of flare over time.

8. Use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for treating a gastrointestinal inflammatory disorder, wherein the ant-beta7 antibody or antigen-binding portion thereof is to be administered a first loading dose and at least one subsequent maintenance dose, wherein the first loading dose is a flat dose of between about 400 mg and about 450 mg and the at least one maintenance dose is a flat dose of between about 50 mg and about 350 mg, each of the first loading dose and the at least one maintenance dose is to be administered subcutaneously, wherein the anti-beta7 antibody or

antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;
(ii) HVR-L2 comprises SEQ ID NO:2;
(iii) HVR-L3 comprises SEQ ID NO:3;
(iv) HVR-H1 comprises SEQ ID NO:4;
(v) HVR-H2 comprises SEQ ID NO:5; and
(vi) HVR-H3 comprises SEQ ID NO:19.

9. The use of claim 8, wherein the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg.

10. The use of claim 8, wherein the maintenance dose is about 50 mg, or about 100 mg, or about 150 mg, or about 200 mg, or about 300 mg, or about 350 mg.

11. The use of claim 8, wherein the loading dose and the maintenance dose are selected from the group consisting of:

(i) the loading dose is about 400 mg and the maintenance dose is about 50 mg, or about 100 mg, or about 150 mg, or about 200 mg, or about 300 mg, or about 350 mg;

(ii) the loading dose is about 420 mg and the maintenance dose is about 50 mg, or about 100 mg, or about 150 mg, or about 200 mg, or about 300 mg, or about 350 mg;

(iii) the loading dose is about 430 mg and the maintenance dose is about 50 mg, or about 100 mg, or about 150 mg, or about 200 mg, or about 300 mg, or about 350 mg;

(iv) the loading dose is about 450 mg and the maintenance dose is about 50 mg, or about 100 mg, or about 150 mg, or about 200 mg, or about 300 mg, or about 350 mg;

(v) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 50 mg;

(vi) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 100 mg;

(vii) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 150 mg;

(viii) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 200 mg;

(ix) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 300 mg; and

(x) the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg and the maintenance dose is about 350 mg.

12. The use of claim 9, wherein the loading dose is about 420 mg.

13. The use of claim 9, wherein the loading dose is about 450 mg.

14. The use of claim 12 or 13, wherein the maintenance dose is about 350 mg.

15. The use of claim 8, wherein the first maintenance dose is to be administered one day, or one week, or two weeks, or four weeks after the loading dose, or on the same day as the loading dose.

16. The use of claim 15, wherein the second and each subsequent maintenance dose is to be administered every two weeks, or every four weeks, or every eight weeks.

17. The use of claim 8, wherein the first maintenance dose is to be administered two weeks after the loading dose, the second maintenance dose is to be administered two weeks after the first maintenance dose, and each subsequent maintenance dose is to be administered every four weeks.

18. The use of claim 8, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered for a period of two months, or four months, or six months, or 12 months, or 18 months, or 24 months, or for the lifetime of the patient.

19. The use of claim 8, wherein the patient is a human.

20. The use of claim 8, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease, and wherein optionally the inflammatory bowel disease is ulcerative colitis or Crohn' s disease.

21. The use of claim 8, wherein the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody.

22. The use of claim 21, wherein the anti-beta7 antibody is a humanized antibody.

23. The use according to any one of claims 1-22, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered with at least one additional compound selected from 5-aminosalicylic acid (5-ASA), azathioprine (AZA), 6-mercaptopmine (6-MP),and methotrexate.

24. The use according to any one of claims 1-22, wherein the patient previously failed at least one biological agent, and wherein optionally the biological agent is selected from adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, natalizumab, and vedolizumab.

25. The use according to any one of claims 1-22, wherein the anti-beta7 antibody or antigen-binding portion thereof to be administered with a self-inject device, and wherein optionally the self-inject device is selected from a prefilled syringe, microneedle device, autoinjector device and needle-free injection device.

26. Use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for inducing remission in a patient suffering from ulcerative colitis, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of either about 100 mg or about 300 mg every four weeks, wherein the anti-beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:

(i) HVR-L1 comprises SEQ ID NO:9;
(ii) HVR-L2 comp1ises SEQ ID NO:2;
(iii) HVR-L3 comprises SEQ ID NO:3;
(iv) HVR-H1 comprises SEQ ID NO:4;
(v) HVR-H2 comprises SEQ ID NO:5; and

(vi) HVR-H3 comprises SEQ ID NO: 19.

27. The use of claim 26, further comprising determining a Mayo Clinic Score and Mayo Clinic subscores, wherein the patient is determined to have an absolute Mayo Clinic Score < 2 and no individual subscore >1, and wherein optionally remission is induced at least by week 10 following the first administration of the anti-beta7 antibody or antigen-binding portion thereof.

28. Use of a monoclonal anti-beta7 antibody or an antigen-binding portion thereof in the manufacture of a medicament for inducing sustained remission in a patient suffering from ulcerative colitis, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of either about 100 mg or about 300 mg very four weeks, wherein remission is retained for a period of 8 weeks following induction of remission, or a period of 30 weeks following induction of remission, or a period of 50 weeks following induction of remission, or a period of 54 weeks or more following induction of remission, wherein the anti beta7 antibody or antigen-binding portion thereof comprises three heavy chain hypervariable region (HVR-H1-H3) sequences and three light chain hypervariable region (HVR-L1-L3) sequences, wherein:
(i) HVR-L1 comprises SEQ ID NO:9;
(ii) HVR-L2 comprises SEQ ID NO:2;
(iii) HVR-L3 comprises SEQ ID NO:3;
(iv) HVR-H1 comprises SEQ ID NO:4;
(v) HVR-H2 comprises SEQ ID NO:5; and
(vi) HVR-H3 comprises SEQ ID NO: 19.

29. The use of claim 28, wherein the remission is steroid-free remission, and wherein optionally the steroid-free remission is for 20 weeks following induction of remission, or for 24 weeks or longer following induction of remission.

30. The use of any one of claims 1-29, wherein the anti-beta7 antibody is etrolizumab.