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 in a patient, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of between 100 mg and 450 mg, and the administration comprises an administration once every week, or an administration once every two weeks, or an administration once every four weeks, or an administration once every six weeks, and/or an administration once every eight 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;
(ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;
(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;
(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;
(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
(vi) the HVR-H3 comprises the amino acid sequence set forth in 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 in a patient, wherein the ant-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a loading dose and subcutaneously at least one subsequent maintenance dose, wherein the loading dose is a flat dose of between 400 mg and 450 mg and the at least one maintenance dose is a flat dose of between 300 mg and 350 mg, and the administration comprises an administration once every two weeks, an administration once every four weeks, and/or an administration once every eight 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;

(ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;

(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;

(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;

(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and

(vi) the HVR-H3 comprises the amino acid sequence set forth in SEQ ID NO:19.

[0018c] In certain examples, the mammalian subject is a patient. In certain examples, the patient is human. In certain examples, the integrin beta7 antagonist is administered intravenously. In certain examples, the integrin beta7 antagonist is administered subcutaneously. In one example, the gastrointestinal inflammatory disorder is an inflammatory bowel disease. In certain examples, the inflammatory bowel disease us ulcerative colitis (UC) or Crohn's disease (CD). In certain examples, the integrin beta7 antagonist is a monoclonal anti-beta7 antibody. In certain such examples, the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody. In certain examples, the anti-beta7 antibody is an antibody fragment. In certain examples, 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 examples, 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 examples, the anti-beta7 antibody is administered at a dose of 0.5 mg/kg. In certain examples, the anti-beta7 antibody is administered at a dose of 1.5 mg/kg. In certain examples, the anti-beta7 antibody is administered at a dose of 3.0 mg/kg. In certain examples, the anti-beta7 antibody is administered at a dose of 4.0 mg/kg. In one example, the anti-beta7 antibody is administered at regular intervals over time. In certain examples, the anti-beta7 antibody is administered once every week. In certain examples, the anti-beta7 antibody is administered once every two weeks. In certain examples, the anti-beta7 antibody is administered once every four weeks. In certain examples, the anti-beta7 antibody is administered once every six weeks. In certain examples, the anti-beta7 antibody is administered once every eight weeks. In certain examples, the anti-beta7 antibody is administered for a period of two months. In certain examples, the anti-beta7 antibody is administered for a period of three months. In certain examples, the anti-beta7 antibody is administered for a period of six months. In certain examples, the anti-beta7 antibody is administered for a period of 12 months. In certain

examples, the anti-beta7 antibody is administered for a period of 18 months. In certain examples, the anti-beta7 antibody is administered for a period of 24 months. In certain examples, the anti-beta7 antibody is administered for the lifetime of the subject. In certain examples 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 examples, the anti-beta7 antibody is administered at a flat dose between 50 mg and 450 mg. In certain examples, the flat dose is 50 mg. In certain such examples, the flat dose is 100 mg. In certain such examples, the flat dose is 150 mg. In certain such examples, the flat dose is 200 mg. In certain such examples, the flat dose is 300 mg. In certain examples, the flat dose is 350 mg. In certain such examples, the flat dose is 400 mg. In certain such examples, the flat dose is 420 mg. In certain such examples, the flat dose is 450 mg. In one example, the anti-beta7 antibody is administered at regular intervals over time. In certain such examples, the anti-beta7 antibody is administered once every week. In certain examples, the anti-beta7 antibody is administered once every two weeks. In certain examples, the anti-beta7 antibody is administered once every four weeks. In certain examples, the anti-beta7 antibody is administered once every six weeks. In certain examples, the anti-beta7 antibody is administered once every eight weeks. In certain examples, the anti-beta7 antibody is administered for a period of two months. In certain examples, the anti-beta7 antibody is administered for a period of three months. In certain examples, the anti-beta7 antibody is administered for a period of six months. In certain examples, the anti-beta7 antibody is administered for a period of 12 months. In certain examples, the anti-beta7 antibody is administered for a period of 18 months. In certain examples, the anti-beta7 antibody is administered for a period of 24 months. In certain examples, the anti-beta7 antibody is administered for the lifetime of the subject. In certain examples 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 examples, the loading dose of the anti-beta7 antibody is administered intravenously. In certain examples, the loading dose of the anti-beta7 antibody is administered subcutaneously. In certain examples, the at least one subsequent maintenance dose of the anti-beta7 antibody is administered intravenously. In

certain examples, the at least one subsequent maintenance dose of the anti-beta7 antibody is administered subcutaneously. In certain examples, each of the loading dose and at least one subsequent maintenance dose is administered intravenously. In certain examples, each of the loading dose and at least one subsequent maintenance dose is administered subcutaneously. In certain examples, the loading dose is administered intravenously, and each of the at least one subsequent maintenance dose is administered subcutaneously. In certain examples, the loading dose is between 400 mg and 450 mg and the maintenance dose is between 50 mg and 350 mg. In certain examples, the loading dose is 400 mg. In certain examples, the loading dose is 420 mg. In certain examples, the loading dose is 430 mg. In certain examples, the loading dose is 450 mg. In certain examples, the maintenance dose is 50 mg. In certain examples, the maintenance dose is 100 mg. In certain examples, the maintenance dose is 150 mg. In certain examples, the maintenance dose is 200 mg. In certain examples, the maintenance dose is 300 mg. In certain examples, the maintenance dose is 350 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 50 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 100 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 150 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 200 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 300 mg. In certain examples, the loading dose is 400 mg and the maintenance dose is 350 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 50 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 100 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 150 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 200 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 300 mg. In certain examples, the loading dose is 420 mg and the maintenance dose is 350 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 50 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 100 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 150 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 200 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 300 mg. In certain examples, the loading dose is 430 mg and the maintenance dose is 350 mg. In certain examples, the loading dose is 450 mg and the maintenance dose is 50 mg. In certain examples, the loading dose is 450 mg and the maintenance dose is 100 mg. In

certain examples, the loading dose is 450 mg and the maintenance dose is 150 mg. In certain examples, the loading dose is 450 mg and the maintenance dose is 200 mg. In certain examples, the loading dose is 450 mg and the maintenance dose is 300 mg. In certain examples, the loading dose is 450 mg and the maintenance dose is 350 mg. In certain examples 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 examples, the first maintenance dose is administered on the same day as the loading dose. In certain examples, the first maintenance dose is administered one day after the loading dose. In certain examples, the first maintenance dose is administered one week after the loading dose. In certain examples, the first maintenance dose is administered two weeks after the loading dose. In certain examples, the first maintenance dose is administered four weeks after the loading dose. In certain examples, the second and each subsequent maintenance dose is administered every two weeks. In certain examples, the second and each subsequent maintenance dose is administered every four weeks. In certain examples, the second and each subsequent maintenance dose is administered every eight weeks. In certain examples, 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 examples, the anti-beta7 antibody is administered for a period of two months. In certain examples, the anti-beta7 antibody is administered for a period of three months. In certain examples, the anti-beta7 antibody is administered for a period of six months. In certain examples, the anti-beta7 antibody is administered for a period of 12 months. In certain examples, the anti-beta7 antibody is administered for a period of 18 months. In certain examples, the anti-beta7 antibody is administered for a period of 24 months. In certain examples, the anti-beta7 antibody is administered for the lifetime of the subject. In certain examples the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

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

examples 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 examples, 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 examples, the biological agent is selected from adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, natalizumab, and vedolizumab. In certain examples 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 examples, the self-inject device is selected from a prefilled syringe, microneedle device, an autoinjector device and needle-free injection device. In certain examples 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 about 100 mg or about 300 mg once 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;

(ii) the HVR-L2 comp1ises the amino acid sequence set forth in SEQ ID NO:2;

(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;

(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;

(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and

(vi) the HVR-H3 comprises the amino acid sequence set forth in 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 about 100 mg or about 300 mg once every 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;

(ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;

(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;

(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;

(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and

(vi) the HVR-H3 comprises the amino acid sequence set forth in 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 examples, the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab). In certain examples, 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 examples remission in the patient is induced at least by week 10 following initiation of treatment with anti-beta7 antibody. In certain examples, 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 examples, 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 examples, patients administered anti-beta7 antibody according to any of the doses or dosing regimens indicated above experience sustained steroid-free remission. In certain examples, patients who experience sustained steroid-free remission

discontinue corticosteroid use at week 30 following induction of remission and sustain remission through week 50 or week 54 or longer following induction of remission. In certain, examples, patients administered anti-beta7 antibody as described above experience a reduced time to flare or a reduced rate of flares over a given period of time. In certain examples, patients administered anti-beta7 antibody as described above experience mucosal healing. In certain examples, patients who experience mucosal healing are determined to have an endoscopy subscore of 0 or 1 as assessed by flexible sigmoidoscopy. In certain examples the anti-beta7 antibody is rhuMAb Beta7 (etrolizumab).

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] Figure 1 shows group mean serum concentration-time profiles of rhuMAb Beta7 in the Phase I study as described in Example 1. (A) Serum rhuMAb Beta7 in patients in the single ascending dose stage of the study who received study drug IV; (B) Serum rhuMAb Beta7 in patients in the single ascending dose stage of the study who received study drug at 3.0 mg/kg IV compared to patients who received the same dose of study drug SC; (C) Serum rhuMAb Beta7 in patients in the multiple ascending dose stage of the study. Each graph shows serum rhuMAb Beta7 concentration (μg/mL) on the vertical axis and time (days) on the horizontal axis.

[0029] Figure 2 shows integrin beta 7 occupancy as described in Example 1. (A) Occupancy in samples from each patient in cohort G; four patients (V, W, X, Y) received 0.5 mg/kg rhuMAb beta7 SC while one received placebo (P6); (B) Occupancy in samples from each patient in cohort H; three patients (AA, BA, DA) received 1.5 mg/kg rhuMAb beta7 SC while one received placebo (P8); (C) Occupancy in samples from each patient in cohort I; four patients (EA, FA, GA, HA) received 3.0 mg/kg rhuMAb beta7 SC while one received placebo (P9); (D) Occupancy in samples from each patient in cohort J; five patients (IA, JA, KA, LA, MA) received 4.0 mg/kg rhuMAb beta7 IV while one received placebo (P10). Each graph shows occupancy on the vertical axis and study day on the horizontal axis. Certain patients had flares during the study and this is indicated in parentheses by each patient with the day of the flare indicated.

[0030] Figure 3 shows individual changes in Mayo Clinic Score as described in Example 1. (A) Cohort G (0.5 mg/kg SC); (B) Cohort H (1.5 mg/kg SC); (C) Cohort I (3 mg/kg SC); (D) Cohort J (4 mg/kg IV); (E) placebo. For each graph, Mayo Clinic Score is shown on the

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 in a patient, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a flat dose of between 100 mg and 450 mg, and the administration comprises an administration once every week, or an administration once every two weeks, or an administration once every four weeks, or an administration once every six weeks, and/or an administration once every eight 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;
(ii) the HVR-L2 comprises the amino acid sequence set for thin in SEQ ID NO:2;
(iii) the HVR-L3 comprises the amino acid sequence set for thin in SEQ ID NO:3;
(iv) the HVR-H1 comprises the amino acid sequence set for thin in SEQ ID NO:4;
(v) the HVR-H2 comprises the amino acid sequence set for thin in SEQ ID NO:5; and
(vi) the HVR-H3 comprises the amino acid sequence set for thin in SEQ ID NO: 19.

2. The use of claim 1, wherein the flat dose is selected from 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.

3. The use of claim 1, wherein the flat dose is between 100 mg and 110 mg.

4. The use of claim 1, wherein the flat dose is 105 mg.

5. The use of claim 1, wherein the flat dose is between 200 mg and 220 mg.

6. The use of claim 1, wherein the flat dose is 210 mg.

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

8. The use of any one of claim 1-7, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered at a flat dose of between 100 mg and 110 mg once every four weeks, wherein the patient suffers from ulcerative colitis.

9. The use of claim 8, wherein the flat dose is 105 mg.

10. The use of claim 8 or 9, wherein the patient is refractory to an anti-TNF therapy.

11. The use of any one of claims 8-10, wherein the patient experiences mucosal healing or a reduced rate of flare over time.

12. The use of any one of claims 1-7, wherein the anti-beta7 antibody or antigen-binding portion thereof is to be administered at a flat dose of between 200 mg and 220 mg, wherein the patient suffers from Crohn's disease.

13. The use of claim 12, wherein the flat dose is 210 mg.

14. 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 in a patient, wherein the ant-beta7 antibody or antigen-binding portion thereof is to be administered subcutaneously at a loading dose and subcutaneously at least one subsequent maintenance dose, wherein the loading dose is a flat dose of between 400 mg and 450 mg and the at least one maintenance dose is a flat dose of between 300 mg and 350 mg, and the administration comprises an administration once every two weeks, an administration once every four weeks, and/or an administration once every eight 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;
(ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;
(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;
(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;
(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
(vi) the HVR-H3 comprises the amino acid sequence set forth in SEQ ID NO:19.

15. The use of claim 14, wherein the loading dose is about 400 mg, or about 420 mg, or about 430 mg, or about 450 mg.

16. The use of claim 14 or 15, wherein the maintenance dose is about 300 mg, or about 350 mg.

17. The use of any one of claims 14-16, wherein the loading dose and the maintenance dose are selected from:

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

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

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

(iv) the loading dose is about 450 mg and the maintenance dose is 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 300 mg; and

(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 350 mg.

18. The use of any one of claims 14-17, wherein the loading dose is about 420 mg.

19. The use of any one of claims 14-18, wherein the loading dose is about 450 mg.

20. The use of any one of claims 14-19, wherein the maintenance dose is about 350 mg.

21. The use of any one of claims 14-20, 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.

22. The use of any one of claims 14-21, 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.

23. The use of any one of claims 14-22, wherein the patient is a human.

24. The use of any one of claims 1-23, 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.

25. The use of any one of claims 1-24, wherein the gastrointestinal inflammatory disorder is an inflammatory bowel disease, and optionally wherein the inflammatory bowel disease is ulcerative colitis or Crohn' s disease.

26. The use of any one of claims 1-25, wherein the anti-beta7 antibody is selected from a chimeric antibody, a human antibody, and a humanized antibody.

27. The use of claim 26, wherein the anti-beta7 antibody is a humanized antibody.

28. The use of any one of claims 1-27, 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.

29. The use of any one of claims 1-28, wherein the patient previously failed to respond to at least one biological agent, and optionally wherein the biological agent is selected from adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, natalizumab, and vedolizumab.

30. The use of any one of claims 1-29, wherein the anti-beta7 antibody or antigen-binding portion thereof to be administered with a self-inject device, and optionally wherein the self-inject

device is selected from a prefilled syringe, microneedle device, autoinjector device and needle-free injection device.

31. 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 about 100 mg or about 300 mg once 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;
(ii) the HVR-L2 comp1ises the amino acid sequence set forth in SEQ ID NO:2;
(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;
(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;
(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
(vi) the HVR-H3 comprises the amino acid sequence set forth in SEQ ID NO: 19.

32. The use of claim 31, wherein the flat dose is 105 mg.

33. The use of claim 31 or 32, further comprising determining a Mayo Clinic Score and Mayo Clinic subscores after the patient receives the anti-beta7 antibody or antigen-binding portion thereof, wherein the patient is determined to have an absolute Mayo Clinic Score < 2 and no individual subscore >1, and optionally wherein remission is induced at least by week 10 following the first administration of the anti-beta7 antibody or antigen-binding portion thereof.

34. 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 about 100 mg or about 300 mg once every 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) the HVR-L1 comprises the amino acid sequence set forth in SEQ ID NO:9;
(ii) the HVR-L2 comprises the amino acid sequence set forth in SEQ ID NO:2;
(iii) the HVR-L3 comprises the amino acid sequence set forth in SEQ ID NO:3;
(iv) the HVR-H1 comprises the amino acid sequence set forth in SEQ ID NO:4;
(v) the HVR-H2 comprises the amino acid sequence set forth in SEQ ID NO:5; and
(vi) the HVR-H3 comprises SEQ ID NO: 19.

35. The use of claim 34, wherein the flat dose is 105 mg.

36. The use of claim 34 or 35, wherein the remission is steroid-free remission, and optionally wherein the steroid-free remission is for 20 weeks following induction of remission, or for 24 weeks or longer following induction of remission.

37. The use of any one of claims 31-36, wherein the patient is a human.

38. The use of any one of claims 1-36, wherein the anti-beta7 antibody is etrolizumab.