Clinical Guideline

VEDOLIZUMAB TREATMENT FOR INFLAMMATORY BOWEL DISEASE PATIENTS

SETTING Bristol Royal Hospital for Children (BRHC)

FOR STAFF Medical, nursing and pharmacy staff

PATIENTS Children with Inflammatory Bowel Disease (IBD)

Vedolizumab is a gut-selective immunosuppressive biologic used to treat moderate to severe Crohn's disease and ulcerative colitis. Vedolizumab is not licensed for use in children under 18 years of age. However, there is experience of using vedolizumab in paediatric patients in practice.

Vedolizumab binds to α4β7 integrin, a key mediator of gastrointestinal inflammation which is expressed on the surfaces of T lymphocytes. This binding prevents the T lymphocytes from entering the gastrointestinal tract and reduces gastrointestinal inflammation which is a characteristic of Crohn's disease and ulcerative colitis.

Sections

1. Indication for vedolizumab

The decision to start vedolizumab should be made by a paediatric gastroenterologist experienced in the management of Inflammatory Bowel Disease (IBD), after discussion at a multi-disciplinary team (MDT) meeting.

A patient with all of the following can be prescribed vedolizumab:

- The patient has moderate to severely active ulcerative colitis or Crohn's disease;
- The patient has had an inadequate response with, lost response to, or was intolerant to either conventional therapy or anti-TNF treatment.

Induction of remission

Treatment should be reviewed if there is no evidence of therapeutic benefit seen:

- After 10 weeks for ulcerative colitis;
- After 14 weeks for Crohn's disease.

2. Definitions of response

The outcome criteria of disease activity will be monitored at 12 and 52 weeks, and as clinically indicated.

The decision to continue treatment depends on their disease response which is assessed using the Paediatric Ulcerative Colitis Activity Index (PUCAI) and the weighted Paediatric Crohn's Disease Activity Index (wPCDAI).

Ulcerative colitis
Clinical remission: Decrease in PUCAI to <10
Clinical response: Decrease in PUCAI by >/=20

Crohn's Disease
Clinical remission: Decrease in wPCDAI to <10
Clinical response: Decrease in wPCDAI by >12.5

The duration of use will be determined by clinical response or possible loss of response. If patients continue to respond to therapy a repeat endoscopy/colonoscopy and detailed clinical review in a MDT meeting will occur after 12 months.

3. Prior assessments & discussion

Assess risk of infection		
	Assess for risk of tuberculosis:	
		History of contact.
		History of travel to endemic areas.
		Perform Mantoux and Quantiferon test (In Bristol – high risk of dormant TB compared with other areas of the southwest). For patients outside of Bristol, follow the local TB screening advice.
	Pelvic infection:	
		If pelvic and/or perianal sepsis is suspected then ultrasound scan and MRI scan are essential prior to starting treatment with vedolizumab.
Record patient vaccination status		
		It is recommended that patients are brought up to date with all immunisations prior to starting vedolizumab. Live vaccines should be avoided whilst on treatment unless benefit outweighs risk.
Document discussion of pregnancy		
		Pregnancy should be avoided during the treatment course and for a least 18 weeks following cessation.
Document in notes discussion of indication, complications (include risk of anaphylaxis, serious infections and nervous system problems) and parental agreement		
	Complications:	
		Risk of infusion related reactions and anaphylaxis (not usually seen in practice).
		Potential increased risk of infections, in particular upper respiratory tract infections.
		To alert patients/carers to the early signs and symptoms of Progressive Multifocal Leukoencephalopathy (PML). Typical signs and symptoms include progressive unilateral weakness, vision disturbances, confusion and cognitive impairment. No cases of PML have currently been reported with vedolizumab, but there have been reports with other monoclonal antibodies.

4. Prescribing vedolizumab

Vedolizumab is administered as an intravenous infusion which should be prescribed on an inpatient chart with an added infusion chart <1 hour attached.

Vedolizumab requires online Blueteq approval to be completed by the prescriber before pharmacy can issue the treatment to the patient.

	Patients <40kg	**Patients >40kg**
Vedolizumab dose by IV infusion over 30 minutes in 250mL of sodium chloride 0.9%	6mg/kg*	300mg
Induction Regime	Administered at weeks: 0, 2 and 6	
Maintenance Regime	8 weekly infusions thereafter**	

*At the consultant's discretion the dose can be increased to 300mg, if a higher dose is considered necessary.

**Patients who experience a decrease in response to treatment may benefit from increasing the dosing interval from 8 weekly to 4 weekly.

Anaphylaxis Medication
All patients should be prescribed the following anaphylaxis medication on the when required section of the drug chart:

Adrenaline 1:1000 (1mg/ml) for IM injection Child less than 6 years: 150 micrograms (0.15ml); Child 6 – 12 years: 300 micrograms (0.3ml); Child more than 12 years: 500 micrograms (0.5ml).
Hydrocortisone (as sodium succinate) IM or slow IV injection Infant < 6 months: 25mg; Child 6 months – 6 years: 50mg; Child 6 – 12 years: 100mg; Child >12 years: 200mg.
Chlorphenamine IM or slow IV injection Infant <6 months: 250 micrograms/kg; Child 6 months – 6 years: 2.5mg; Child 6 – 12 years: 5mg; Child >12 years: 10mg.

Premedication
This may not be necessary; however this will be assessed on a patient by patient basis. Children should receive IV hydrocortisone as sodium succinate (4mg/kg; 200mg) at least 30minutes prior to infusion of vedolizumab and IV chlorphenamine and oral paracetamol if:

- History of atopy/asthma;
- Previous infusion reaction;
- Restarting vedolizumab following a treatment free interval.

Discuss with consultant if in doubt.

5. On the day of infusion

- Check parents/patients have been provided information on vedolizumab.
- Confirm documented discussion and record that verbal consent has been obtained.
- Take history to assess the risk of possible intercurrent illness. Check baseline observations including heart rate, blood pressure and temperature. Discuss with consultant gastroenterologist if concerned that patient is unwell and/or has temperature because of infection (Temperature can be because of active disease).
- Prescribe emergency drugs in case of anaphylaxis +/- prophylactic medications.
- Routine IBD blood tests (FBC, LFT, U&E, CRP, ESR) must be done prior to each infusion.
- Record disease activity score wPCDAI or PUCAI (see Appendix 2 and
- Appendix 3).
- If a further infusion is planned, this should be booked into the admission diary before the patient leaves the Clinical Investigations Unit/ward.
- See Appendix 1 - Checklist for patients receiving vedolizumab Infusions.

6. Administering vedolizumab

Available preparations: Entyvio® 300mg vial (powder for solution for infusion).

It is stored in the fridge prior to use. Allow vial to reach room temperature before use.

Reconstitution:

- Reconstitute each 300mg vial with 4.8ml of sterile water for injection.
- After reconstitution each mL contains 60mg of vedolizumab.
- Gently swirl vial for at least 15 seconds. Do not vigorously shake or invert.
- Let the vial sit for up to 20 minutes to allow for reconstitution and for any foam to settle. If not fully dissolved after 20 minutes, allow another 10 minutes for dissolution. Solution should be clear or opalescent, colourless to light yellow and free of visible particulates.

Dilution:

- Invert the vial gently three times before withdrawing the dose of the reconstituted solution.
- Add to 250ml infusion bag of sodium chloride 0.9%.
- Gently mix the contents of the bag.
- Administer reconstituted solutions immediately.

Administration:

- Give via intravenous infusion over 30 minutes, preferably using an infusion pump.
- No low protein-binding filter is required for administration.
- Do not infuse vedolizumab concomitantly in the same intravenous line with other agents.
- Flush the line with sodium chloride 0.9% after the infusion.

7. Monitoring vedolizumab

- Baseline observation (including blood pressure and temperature) should be checked prior every infusion and every 15 minutes during the infusion.
- Monitor for hypersensitivity reactions during the infusion. Infusion should be stopped immediately if signs of infusion reaction occur.
- For the first two infusions the patient should be observed for two hours after the infusion has finished for signs and symptoms of acute hypersensitivity reactions. Baseline observation should be performed every 30 minutes.

- For all subsequent infusions, observe for one hour after the infusion. Baseline observation should be performed every 30 minutes.

Appendix 1 – Checklist for patients receiving vedolizumab Infusions

Checklist with patient prior to infusion (document changes in nursing and medical notes)						
	Week 0	Week 2	Week 6	Week 14	Week 22	Week 30
Infusion Number						
Date of infusion						
Information given to parents/child (only required for first infusion)						
Documented discussion by consultant for whole treatment course (only once)						
Any new conditions, infections /antibiotics, surgery or dental extractions (2 weeks pre or post infusion)						
Any reaction to last infusion (if yes document in medical & nursing notes)						
Premedication's prescribed (if required)						
History of contact with TB ascertained. Local screening tests completed						
Document weight prior to each infusion						
Baseline observations (HR, BP and temperature)						
Activity indices documented (wPCDAI or PUCAI)						
IBD bloods (FBC, LFT, U&E, CRP, ESR) taken, prior to the infusion						
During the infusion						
Baseline observations (including HR, BP & temperature) every 15 minutes						
Monitor patient continuously for signs & symptoms of acute hypersensitivity reactions						
Post infusion checklist						
Observe patient for signs & symptoms of acute hypersensitivity reactions for 2 hours post first two infusions. Baseline observations (HR, BP & temperature) should be performed every 30 minutes						
For subsequent infusions observe patient for signs & symptoms of acute hypersensitivity reactions for 1 hour post infusion. Baseline observations (HR, BP & temperature) should be performed every 30 minutes						
Any adverse reaction documented in medical notes						

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Next infusion date arranged						

Appendix 2 – Weighted Paediatric Crohn's Disease Activity Index (wPCDAI score)

<TH> History (Recall, 1 week) </TH>
<*TB*> *Abdominal Pain* Score 0 = None. 10 = Mild: Brief, dose not interfere with activities. 20 = Moderate/Severe: Daily longer lasting, affects activities, nocturnal. _____
Patient Functioning, General Well-Being Score 0 = No limitations of activities, well. 10 = Occasional difficulty in maintaining age appropriate activities, below par. 20 = Frequent limitation of activities, very poor. _____
Stools (per day) Score 0 = 0 – 1 liquid stools, no blood. 7.5 = Up to 2 semi-formed with small blood, or 2 – 5 liquid. 20 = Gross bleeding, or ≥6 liquid, or nocturnal diarrhoea _____
Laboratory
Erythrocyte Sedimentation Rate Score 0 = < 20mm/hr. 7.5 = 20 – 50 mm/hr. 15 = >50mm/hr. _____
Albumin Score 0 = ≥3.5g/dL. 10 = 3.1 – 3.4g/dL. 20 = ≤3.0g/dL. _____
Examination
Weight Score 0 = Weight gain or voluntary weight stable/loss. 5 = Involuntary weight stable, weight loss 1-9% 10 = Weight loss ≥10% _____
Perirectal Disease Score 0 = None, asymptomatic tags 7.5 = 1 – 2 indolent fistula, scant drainage, no tenderness 15 = Active fistula, drainage tenderness, or abscess. _____
Extra-intestinal Manifestations Score (fever ≥ 38.5°C for 3 days over past week, definite arthritis, uveitis, E. nodosum, P gangrenosum) 0 = None. 10 = One or more. _____
Total score (0-125): </TB>

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Appendix 3 – Paediatric ulcerative colitis activity index (PUCAI score)

	Item	Points
1	Abdominal pain	
	No pain	0
	Pain can be ignored	5
	Pain cannot be ignored	10
2	Rectal bleeding	
	None	0
	Small amount only, in less than 50% of stools	10
	Small amount with most stools	20
	Large amount (> 50% of the stool content)	30
3	Stool consistency of most stools	
	Formed	0
	Partially formed	5
	Completely unformed	10
4	Number of stools per 24 hours	
	0 – 2	0
	3 – 5	5
	6 – 8	10
	>8	15
5	Nocturnal stools (any episode causing wakening)	
	No	0
	Yes	10
6	Activity level	
	No limitation of activity	0
	Occasional limitation of activity	5
	Severe restricted activity	10
	Sum of PUCAI (0 – 85)	

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- Emergency treatment of anaphylaxis reactions: Guidelines for healthcare providers. Resuscitations Council UK. Accessed via: http://www.resus.org.uk/pages/reaction.pdf [accessed 07/12/17]
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- C.Spray, T.Wiskin, Professor B. Sandhu et al, 2017. Clinical Guideline: Guideline for treatment of children with inflammatory bowel disease with biologics: Infliximab and adalimumab. Bristol Royal Hospital for Children.
- PUCAI Score Hospital for Sick Children, Toronto, Canada, 2006

RELATED DOCUMENTS	Clinical guideline: Anaphylaxis in Children http://nww.avon.nhs.uk/dms/download.aspx?did=14843
AUTHORISING BODY	Nurse Practice Group Children's Clinical Effectiveness Pharmacy Governance Group
SAFETY	N/A
QUERIES	Contact the Paediatric Pharmacist for Medicine on bleep 3121 during working hours Monday to Friday. Out of hours please contact the oncall emergency duty pharmacist via switchboard.

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