Vedolizumab in the Management of Immune-Related Adverse Effects (irAEs)

A guide for members on the prescribing and monitoring of vedolizumab when used in the management of irAEs because of treatment immune-checkpoint inhibitors.

British Oncology Pharmacy Association in Collaboration with The Immuno-Oncology Clinical Network

Version 1.0

Nov 2024

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1. Introduction

- Vedolizumab is a monoclonal antibody directed towards the integrin $\alpha_4\beta_7$, which inhibits the intestinal homing of T lymphocytes. It acts as a gut-specific immunosuppressive agent that is approved by NICE for ulcerative colitis and Crohn's disease.

- The European Society of Medical Oncology (ESMO) and Society for Immunotherapy of Cancer (SITC) guidelines for the management of immunotherapy-related toxicities recommend consideration of vedolizumab in steroid refractory immunotherapy-related colitis.

- Evidence supporting the use of vedolizumab for immunotherapy-related colitis is currently limited to case series and retrospective reports. The largest of these was a retrospective study of 28 adults who were treated with vedolizumab for immunotherapy-related colitis which was refractory to steroids and/or infliximab (Abu-Sbeih *et al*., 2018). This identified that 86% of patients achieved and sustained clinical remission over the follow-up period, with a median of 3 doses being required to achieve remission.

- Vedolizumab can be considered for use instead of infliximab in patients where the latter is contraindicated. For example, latent tuberculosis after commencing anti-tuberculosis treatment, hepatitis virus or HIV, or moderate to severe heart failure (NYHA class III/IV)

- This document is intended to be used as a monograph to provide prescribing and monitoring advice once the decision has been made to initiate vedolizumab. It is not a clinical guideline, but a consensus view of current use of vedolizumab when used for irAEs. It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance processes.

2. Prescribing and Monitoring Advice

2.1 Contraindications

- Hypersensitivity to vedolizumab.
- Hypersensitivity to any of the excipients.
- Active severe infections such as tuberculosis (TB), sepsis, cytomegalovirus, listeriosis, and opportunistic infections such as Progressive Multifocal Leukoencephalopathy (PML).

2.2 Precautions

- Immunisations - Avoid live vaccinations, particular live oral vaccines.
- Cautioned in patients with controlled chronic severe infection or history of recurrent infection.
- Vedolizumab should be administered in a healthcare setting equipped to allow management of acute hypersensitivity reactions including anaphylaxis, if they occur.

2.3 Pregnancy Advice

- It is preferable to avoid the use of vedolizumab during pregnancy unless the benefits clearly outweigh any potential risk to both the mother and foetus.
- Women of childbearing potential should use adequate contraception to prevent pregnancy and to continue its use for at least 18 weeks after the last treatment.

2.4 Pre-treatment assessment

- Pregnancy test.
- TB screening – chest x-ray or other appropriate imaging, Quantiferon test and full TB history.
- Blood serology – check Hepatitis A, B and C and HIV status prior to initiating vedolizumab. Some clinicians may additionally check Herpes Simplex and CMV serology based on clinical judgement, although this is not a requirement for most patients.
- Immunisation history – patients should be up to date with vaccinations prior to starting vedolizumab treatment where possible.
- Check varicella zoster IgG for patients without clear history of prior infection or vaccine.

2.5 Pharmaceutical form

- Vedolizumab (Entyvio) 300 mg powder for concentration for solution for infusion

2.6 Dosage

- 300 mg fixed-dose regimen, given at 0 and 2 weeks. A third dose may be given at 6 weeks if required.
- No dose adjustments are required for elderly patients.
- The use of vedolizumab in patients with renal or hepatic impairment has not been studied by the manufacturer, so they have not made any dose recommendations for these patients.

2.7 Method of administration

- Diluted in 250 mL sodium chloride 0.9%.
- Administer by intravenous infusion over 30 minutes.

2.8 Therapeutic Drug Monitoring

- No therapeutic drug monitoring is required.

2.9 Other monitoring

- Patients should be monitored continuously during the infusion for hypersensitivity reactions. This should be followed by a 2 hour post-infusion observation period for the first 2 infusions, and 1 hour post-infusion observation for subsequent infusions.

2.10 Adverse effects

<u>Infusion related reactions (IRRs)</u>

- If a severe infusion reaction, anaphylactic reaction, or other severe reaction occurs, administration of vedolizumab must be discontinued immediately and appropriate treatment initiated (e.g. adrenaline and antihistamine).
- If a mild to moderate infusion related reaction occurs, the infusion rate can be slowed or interrupted and appropriate treatment initiated. Once the reaction subsides, continue the infusion. Physicians should consider pre-treatment (e.g. with antihistamine, hydrocortisone

and/or paracetamol) prior to the next infusion for patients with a history of mild to moderate infusion related reaction to vedolizumab, in order to minimize their risks.

- These are the most common adverse effects.
- This is not an exhaustive list. See SmPC for further details.

System	Adverse Effects
Infections and infestations	Nasopharyngitis (very common), pneumonia, clostridium difficile infection, bronchitis, gastroenteritis, upper respiratory tract infection, influenza, sinusitis, pharyngitis, herpes zoster
Nervous system disorders	Headache (very common), paraesthesia
Vascular disorders	Hypertension
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain, nasal congestion, cough
Gastrointestinal disorders	Anal abscess, anal fissure, nausea, dyspepsia, constipation, abdominal distension, flatulence, haemorrhoids, rectal haemorrhage
Skin and subcutaneous tissue disorders	Rash, pruritis, eczema, erythema, night sweats, acne
Musculoskeletal and connective tissue disorders	Arthralgia (very common), muscle spasms, muscular weakness, fatigue, pain in the extremity
General disorders and administration site conditions	Pyrexia, Infusion related reactions (including asthenia and chest discomfort), infusion site reactions (including infusion site pain and irritation)

2.11 Drug interactions

- No interaction studies have been performed.
- Live vaccines, especially live oral vaccines, should be used with caution concurrently with vedolizumab.

2.12 Advice to patients

- Advise about the need for post-dose observations to monitor for infusion-related reactions.
- Women of childbearing potential should use adequate contraception to prevent pregnancy and to continue its use for at least 18 weeks after the last vedolizumab infusion.
- Contact their acute oncology team for advice if they experience any signs of infection.

3. Appendix 1 Example Patient Information Leaflet

What is Vedolizumab?

Vedolizumab belongs to a class of medicines called 'biologics'. These are complex drugs that target a specific cell receptor within the body. Vedolizumab acts specifically to reduce inflammation in the gut. This reduces the symptoms of colitis by dampening the immune reaction in the gut which causes inflammation.

How do I take Vedolizumab?

Vedolizumab is given by intravenous infusion (infusion into a vein). This will be administered by trained healthcare staff and is usually given in hospital as an outpatient.

How long will I need to take vedolizumab for?

After the first dose, further doses can be given after 2 weeks and 6 weeks, and then every 8 weeks if necessary. The total number of doses will depend on the improvement in symptoms and will vary for different patients. Your clinical team will be monitoring your symptoms and test results to determine the right number of doses for you.

Does Vedolizumab have any side-effects?

There are several possible side effects that you may notice, although many people do not experience any of these. The most common side effects are cold-like symptoms, joint pain and headache.

Like other medicines that suppress the immune system, vedolizumab can increase the risk of infections. It is therefore very important that you tell your medical team if you have any signs of infection before or after your vedolizumab treatment. Signs of infection can include fever, chills and/or rash.

Biologics such as vedolizumab can also sometimes cause allergic reactions. You must seek immediate medical help if you experience wheezing, difficulty breathing, hives, itching, swelling, redness of the skin or pain at the infusion site.

Can I still be vaccinated?

Vedolizumab may affect the way that your body responds to vaccinations. Live vaccinations should be avoided whilst being treated with vedolizumab. You should therefore speak with your medical team before receiving any vaccinations whilst on vedolizumab treatment.

Is it safe to become pregnant while I am taking vedolizumab?

You may have already had these conversations with your oncology team before starting immunotherapy. The safety of vedolizumab treatment during pregnancy is not known. Women of childbearing potential should use effective contraception during treatment and for at least 18 weeks after the last infusion.

Can I take other medicines whilst I am taking Vedolizumab?

You should always check with your oncology team or pharmacist if you are started on any new medicines, including anything you may buy over the counter.

Who can I contact for further information?

If you have any queries about your vedolizumab, the best people to speak to are the oncology team who you are under, the team of specialists who have prescribed the vedolizumab for you, or your oncology pharmacist.

4. References

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5. Acknowledgements

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BOPA Immunotherapy Specialist Interest Group

6. Document control

Title	**Vedolizumab in the Management of Immune-Related Adverse Effects (irAEs)**
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Owner	BOPA.

Change History

Draft	**Date**	**Lead Author/Editor**	**Summary of Change**

Proposed Target Audience	Any healthcare professional involved in the care of patients treated with immune-checkpoint inhibitors
Proposed Circulation List	BOPA members, IOCN members
Contact details	Alice,tew@uhb.nhs,uk