

## Information for Patients

# Diabetic macula oedema treatment pathway

There are two main ways in which diabetes can seriously affect eyesight:

1. Diabetic macular oedema – where fluid builds up at the back of the eye.
2. Proliferative diabetic retinopathy – where new vessels grow on the retina (the back of the eye) which can bleed.

These complications are both sight threatening, and do not always lead to symptoms until the changes are very advanced. This makes early identification and treatment very important. It is therefore very important that you attend your appointments. Also please be advised your pupils will be dilated at almost every visit. So please do not drive to your eye clinic appointment.

## General measures

There are various risk factors that can lead to the above problems progressing more quickly, so it is important that these risk factors are well controlled. These are:

- Blood pressure control
- Diabetes control (measured by HbA1c)
- Treating raised cholesterol
- Stopping smoking
- Maintaining a healthy diet
- Taking regular exercise

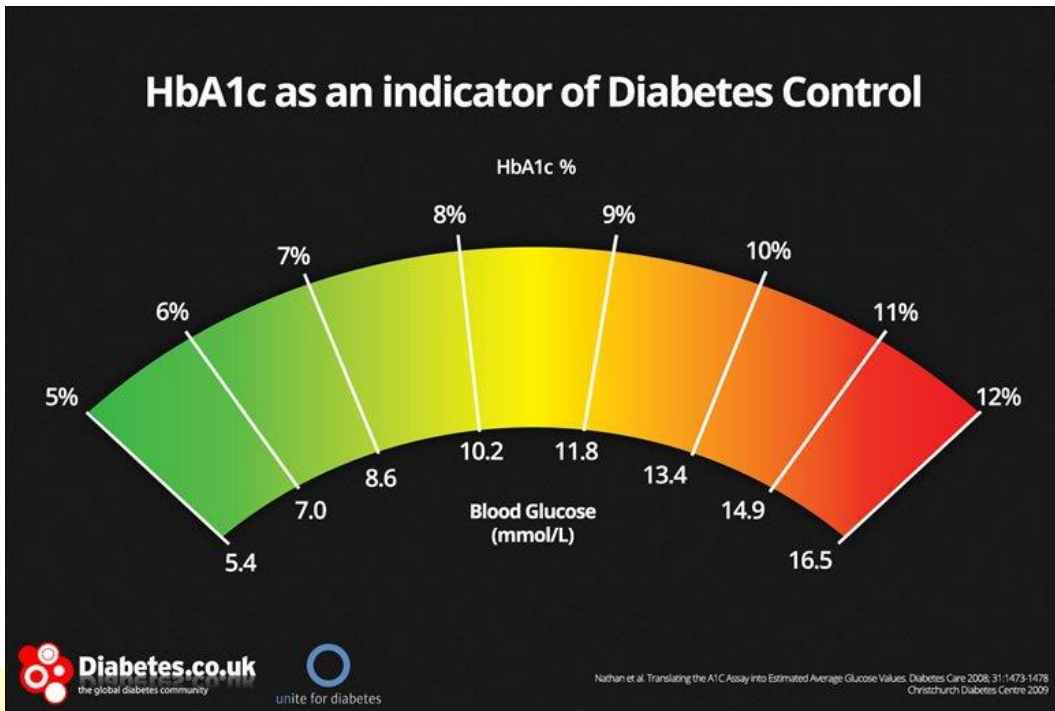


Image 1: HbA1c as an indicator of diabetes control. (Image used with permission from diabetes.co.uk)

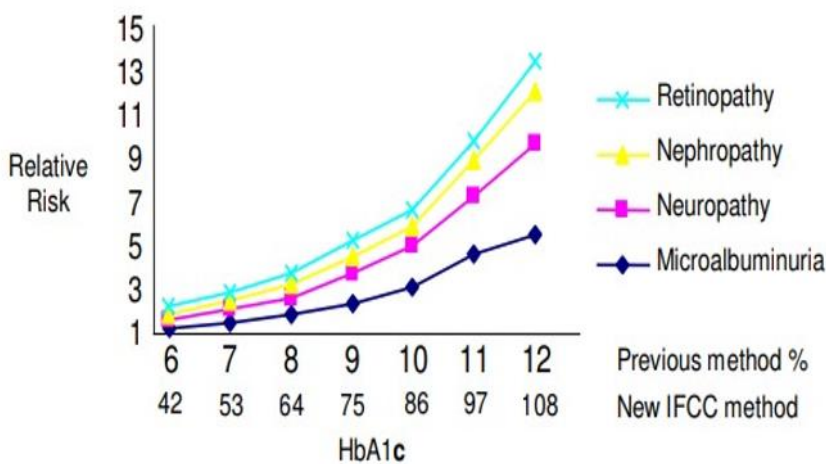
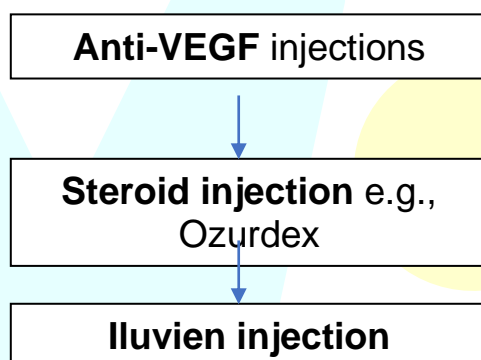


Image 2: Graph to show that worsening control of HbA1c is associated with increased risk of complications.

## Diabetic macular oedema

Normally blood sugar is very tightly controlled. Blood sugars that are outside this tight control, even if only slightly, cause damage to the control of the blood vessels at the back of the eye. This makes them leaky. Fats and fluid that are normally carried along in the bloodstream may then leak into the macula, the area responsible for our sharp, detailed central vision. Fats that have leaked are called exudates. Leaking fluid causes water logging and is called oedema. Occasionally, the blood vessels in the macular become so constricted that the macular is starved of oxygen and nutrition, causing your sight to get worse. This is called 'ischaemic maculopathy' and it does not usually respond to any type of treatment.

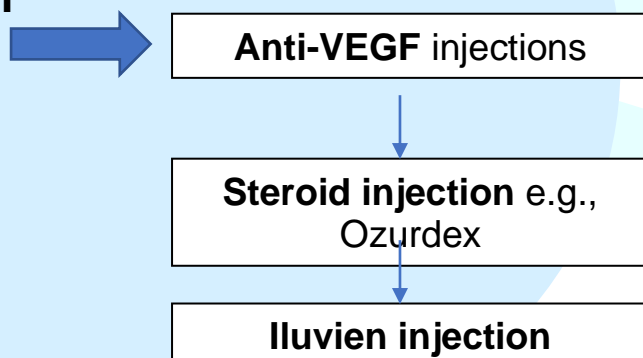
Diabetic macular oedema is managed in a stepwise approach, which is shown in the flow chart below. Each of these treatments will be discussed in more detail.



## Intravitreal injections

These are injections into the vitreous jelly inside the eye. Most patients' vision will stabilize after treatment and some patients may regain some vision lost. Drug injections may not restore vision that has already been lost and will not always prevent further loss of vision caused by the disease.

### Anti-VEGF



Anti-VEGF injections are drugs that are used to block the action of a chemical called vascular endothelial growth factor (VEGF). This is produced in excess in eyes suffering from diabetic macular oedema and plays a role in the development of leakage from retinal blood vessels. The most commonly used anti-VEGF drugs for macular oedema are Vabysmo (Faricimab) and Eylea (Aflibercept). On rare occasions, other anti-VEGF drugs like Ranibizumab biosimilar or Bevacizumab may also be considered. If you have any questions regarding choice of drug, please feel free to discuss with your medical team.

Anti-VEGF is given by injection into the eye to try and reduce the swelling at the macular. This can stop the eyesight getting worse and in some patients the eyesight can improve. Both are similar in their effect but have slightly different treatment regimens and one or the other may be more appropriate depending on the status of your eyes. These medicines may also have a beneficial effect on other changes in the retina you may have.

This is a course of treatment, and you are likely to need a number of injections at repeated intervals. Most patients will attend for assessment and injection every month for the first six months. If there is no significant improvement, your doctor may consider switching to a different type of injection in the form of a steroid based injection.

Once the fluid has resolved, the time in between injections can potentially increase up to 4-monthly intervals. If the fluid comes back at any point the interval will be reduced again. If the eye remains free from fluid, treatment will be stopped. The ability to stop treatment also depends on improved and stable control of diabetes, blood pressure and the risk factors highlighted earlier.

## How is the treatment given?

Anaesthetic drops will be put in to numb the surface of your eye. The skin around your eye and the surface of your eye is washed with an antibacterial solution to reduce the risk of infection. The drug is injected into the vitreous jelly. You may feel slight pressure on your eye when this is done, but you should not experience pain. After the injection you may have a gritty feeling in your eye, and there may be bleeding over the white of your eye. You should not worry about this; the gritty sensation will resolve within a few days and the bleeding over the white of your eye normally within 7-10 days. You might also see floaters (black spots); these will also become smaller and disappear over a couple of weeks. If you have severe pain in the injected eye or a drop in your vision, please contact your nearest eye unit as these may be signs of an infection.

Since patients with diabetes, especially those known to have diabetes for over 20 years, are at increased risk of problems with dry eyes, we would recommend the use of regular lubricants on a daily basis, to help prevent issues related to dry eyes that can occur following intravitreal injection treatment.

## What are the risks of treatment with Anti-VEGF injections?

Serious complications of the injection procedure include:

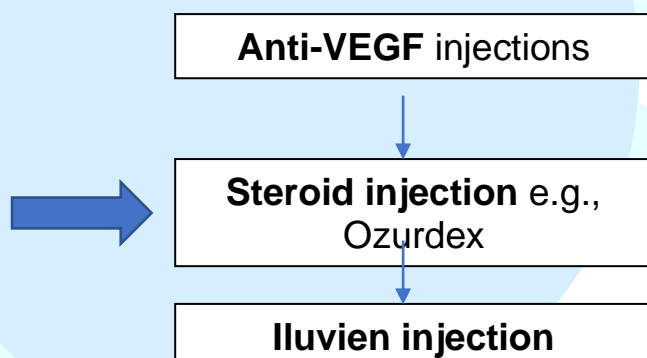
- Bleeding
- Severe infection (endophthalmitis)
- Cataract formation
- Retinal detachment
- Theoretical risk of blood clot, causing heart attack or stroke. This has not been demonstrated in clinical practice. Please see references at the end of the leaflet if you wish to read more about this.

Any of these serious complications may lead to severe, permanent loss of vision or blindness. The risks will be explained and discussed with you before you agree to treatment. Any or all of the complications described above may cause decreased vision and/or have a possibility of causing blindness. Additional procedures may be needed to treat these complications.

More common side effects may include:

- Eye pain
- Conjunctival haemorrhage (bloodshot eye)
- Floaters
- Irregularity or swelling of the cornea
- Inflammation of the eye

## Ozurdex



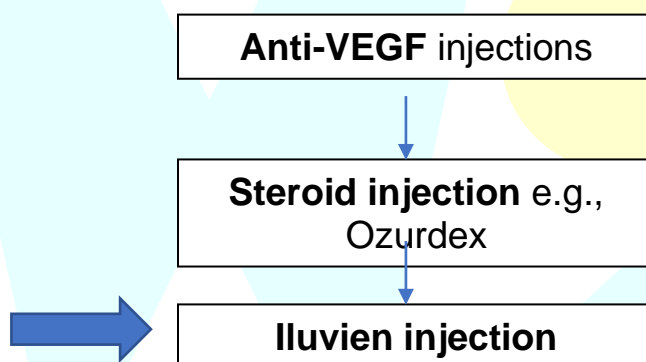
If the fluid does not respond well enough to anti-VEGF injections or if anti-VEGF is deemed unsuitable in your case, steroid injections will be considered in your management plan. Ozurdex is a short acting steroid implant that is injected in the same way as anti-VEGF. As the implant slowly dissolves in the vitreous gel it releases the steroid for up to 6 months.

You will then be reviewed to assess the response to treatment and check the pressure in the eye at 6 weeks. A repeat Ozurdex can be given between 4 to 6 months if required.

In addition to the risks discussed above for intravitreal injections, Ozurdex also carries an increased risk of cataract formation (when the lens in the eye goes cloudy) and raised pressure in the eye. The risk of eye pressure rise is 1 in 4 but is usually transient and not cumulative with subsequent treatments. It can usually be controlled with drops which are usually only needed on a temporary basis.

Due to these risks, patient with uncontrolled pre-existing glaucoma, glaucoma on more than one medication and advanced glaucoma are not eligible for this treatment.

## Iluvien



Iluvien is an anti-inflammatory drug used for the treatment of Diabetic macular oedema. It is a type of steroid, like Ozurdex, and is contained within a long-lasting implant that is injected directly inside the eye. This makes it longer acting than Ozurdex. It releases the drug over a period of up to three years. Iluvien may play an important role in addressing the inflammatory process associated with Diabetic macula oedema.

Iluvien will be offered if you have undergone a series of Ozurdex injections with good response and no safety issues, or if anti-VEGF and Ozurdex have been ineffective. The benefit entails a longer-acting (up to 3 years) drug and may significantly reduce the need for injections. However, you may still require additional one-off injections.

It is given in the same way as anti-VEGF and Ozurdex and carries a similar risk.



## Localised laser treatment

Injections are generally the most powerful way of treating macular disease but in some circumstances, laser can be useful to try and prevent leakage at the macula. Full power laser can be used especially for vessels leaking away from the centre. Lower power laser (subthreshold) may benefit if leakage is in the centre as it is less likely to cause any damage to retinal tissue.

Sometimes your doctor may also wish to combine macular laser as an adjunctive therapy with anti-VEGF injections.

## Proliferative diabetic retinopathy

This is a separate complication to diabetic macular oedema, although the two complications can co-exist. It is the development of new blood vessels on the retina. These new blood vessels are abnormal and fragile. By themselves, these blood vessels do not cause symptoms or vision loss. However, they have thin fragile walls. At this stage your sight is at risk as the vessels may bleed or may develop scar tissue. This can pull the retina away from the underlying layers of the eye, causing a 'traction retinal detachment'. Abnormal blood vessels can also grow on the front of the eye leading to rise in the eye pressure by a different mechanism.

During your treatment course the team will be assessing for any sign of new vessel development. Treatment options are as follows:

- **Panretinal laser treatment**

If new vessel growth (neo-vascularisation) has been detected, you may need more extensive laser treatment. The aim is to treat large areas of the peripheral retina with the laser. This treatment stops the retina from producing the growth factors that stimulate new blood vessels to grow.

- **Intravitreal injections**

Sometimes new vessel formation requires anti-VEGF injections as discussed earlier, to try and prevent new vessels growing and shrink the ones that have formed.

- **Surgery**

If a severe bleed occurs due to bleeding new vessels, sometimes an operation is required to remove the blood and vitreous jelly in the eye.

**If you require any further information please contact the relevant teams below:**

**Macular Treatment Centre** (0161) 276 5575/3341 Monday – Friday 8.00am - 6.00pm

**Trafford Macular Centre** (0161) 746 2626 Monday – Thursday 8.00am -5.30pm  
Friday 8.00am -1.30pm

**Specialist Eye Clinic (Civic Centre, Wythenshawe)**

(0161) 507 3765 Monday - Thursday, 8.00 - 5.30pm Friday 8.00 -1.30 pm

**Specialist Eye Clinic (Cheetham Hill)** (0161) 934 8334

Monday, Tuesday, Thursday 8.00am – 5.30pm Wednesday & Friday  
8.00am – 1.30pm

If your problem is urgent and the above departments are closed, please contact:

**Ward 55** (0161) 276 5512 available 24 hours every day.

## References

1. Porta M, Striglia E. Intravitreal anti-VEGF agents and cardiovascular risk. *Intern Emerg Med.* 2020; 15:199–210.
2. Ngo Ntjam N, Thulliez M, Paintaud G, Salvo F, Angoulvant D, Pisella PJ, Bejan-Angoulvant T. Cardiovascular Adverse Events with Intravitreal Anti-Vascular Endothelial Growth Factor Drugs: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Ophthalmol.* 2021 Apr 15;139(6):1–11.
3. Thulliez M, Angoulvant D, Pisella P-J, Bejan-Angoulvant T. Overview of systematic reviews and meta-analyses on systemic adverse events associated with intravitreal anti-vascular endothelial growth factor medication use. *JAMA Ophthalmol.* 2018;136(5):557-566.