

Ranibizumab Authorised Prescriber and Special Access Scheme

Ranibizumab (you may also have heard it referred to as Lucentis) is an investigational drug that has been developed to treat the disease called age related macular degeneration (AMD). An investigational drug is one that has not, as yet, been approved by the regulatory authorities and is therefore not available by prescription. You have been diagnosed with AMD and therefore your doctor has considered using this drug for your treatment. AMD is a progressive condition in the eye which, if left untreated, may cause you to lose central vision in your eye(s) because the central part of your retina (the film in the back of your eye) is swollen. This swelling is caused by abnormal blood vessels growing in the retina that are very fragile and therefore leak blood and fluid. It is this fluid accumulation and swelling that is mostly responsible for your vision loss. Ranibizumab blocks a molecule that is thought to be involved in the growth of new blood vessels as well as their leakage.

Before you are treated with Ranibizumab, you need to know the risks and benefits so you can make an informed decision. This "Patient Information Sheet" provides you with information about the drug Ranibizumab. It also provides details about the co-payment you are required to make in order to receive the medication. Please read this information carefully and discuss it with anyone you wish. This may include your doctor, a friend or a relative. If you have further questions regarding your treatment options, we suggest that you consult your doctor who knows your clinical history and is best able to advise you on the risks and benefits of treatments.

The investigational drug, Ranibizumab, is an experimental compound that is given by injection into the eye. It has been used in clinical trials to treat more than 900 patients who have AMD. Ranibizumab is being evaluated as a new treatment but is not yet approved currently, by any Health Authority for the treatment of macular degeneration, therefore it is not yet available anywhere in the world by prescription. However, Ranibizumab is available in Australia (and some other countries) under an Authorised Prescriber Scheme. Novartis has submitted an application to the Therapeutics Goods Administration (TGA) in Australia to register Ranibizumab so that it can be made available by prescription in the future.

The treatment of your affected eye will be performed according to your doctor's advice. The treatment takes around 10 minutes and you will lie in a reclining chair or on a bed. Before each Ranibizumab injection, your eye will be cleaned with antiseptic, and anaesthetic and antibiotic drops will be placed in your eye. A small device (speculum or eyelid clamp) will keep your eyelids open. The conjunctiva or skin over the white part of your eye will be anaesthetised with a small injection. The Ranibizumab will then be injected into the vitreous jelly inside your eye. You may feel slight pressure.

While you receive this treatment, you may have any, or none, of the side effects described below. Problems or side effects that are not yet known could also occur. Many side effects go away shortly after you discontinue therapy but, in some cases, side effects can be serious, long lasting, or permanent. Should any problem occur, you will be given appropriate care for your condition, and you may be withdrawn from further treatment.

RISKS OF TREATMENT

Ranibizumab has been studied in more than 900 patients with AMD in clinical trials already completed. A number of side effects have been considered possibly related to Ranibizumab.

The most serious were:

- Severe inflammation in the inside of the eye (uveitis) in less than 1 in 450 patients.
- Blockage of blood flow through the major vein that supplies blood to the retina (central retinal vein occlusion) in less than 1 in 900 patients.
- Infection, inside and/or outside of the treated eye (endophthalmitis) in less than 1 in 900 patients.

These complications may result in loss of vision or, in rare cases, other more serious events.

The other side effects were:

- Inflammation in the eye (anterior chamber and vitreous body).
- Mild increases of the pressure inside the eye (often as result of injection into the eye).
- If you have a history of glaucoma, you may be at more of a risk of experiencing increased pressure within your eye after injection of any substance, including Ranibizumab. To participate in this treatment, your doctor must be satisfied that your glaucoma is well controlled with your prescribed medication.
- Detachment of the jelly-like substance (vitreous) that fills your eyeball (this is called posterior vitreous detachment)
- Bleeding in the back of the eye (retinal haemorrhage),
 - or into the jelly-like substance inside your eyeball (vitreous haemorrhage),
 - or bleeding from a small blood vessel under the conjunctiva (creates

appearance of bright-red blood over the white part of your eye, called subconjunctival haemorrhage).

- Occasional vision disturbances, including decrease in vision.
- Injection-site pain, foreign body feeling in the eye after the injection, inflammation of your conjunctiva (conjunctivitis), dry eyes and pruritus (itching).

Tests have shown that low levels of Ranibizumab can reach your blood after injection into the eye. The significance of this is not well understood and the effect this might have on your body is unknown. However, you will be carefully monitored for signs of side effects. Examples of possible side effects involving the body as a whole may include slowed wound healing or a tendency to more frequent or prolonged bleeding.

There is a chance that your vision might worsen. Worsened vision could be due to the progression of your AMD, to a side effect of the injection, or to other reasons. There is a remote chance that you may experience an allergic reaction to Ranibizumab, such as skin rash, hives, or possibly a more serious problem such as breathing difficulties or shock. An allergic reaction can also cause dry or itchy eye. It is not possible to predict in advance if any of these problems will develop, but if they do, you will be promptly treated. As is true for any experimental drug, unknown and potentially serious or life-threatening side effects could occur with Ranibizumab.

Risks of Injection into the Eye

After the injection into your eye, you may have a foreign body feeling in the eye, and there might be mild redness or bleeding in the conjunctiva due to the anaesthetic injection. These will resolve over a few days.

Injecting any medication into the eye may result in

increased pressure within the eye, inflammation, or more serious side effects such as cataract formation, bleeding within the eye, damage to the retina (retinal tear or detachment), or damage to other eye structures. These side effects are rare, estimated to be around 1 in 1000 injections.

It is possible that you may get an infection within your eye (endophthalmitis) as a result of injections into the eye. The chance of an infection is low (estimated at 1 in 900 injections). An infection may lead to vision loss or, in rare cases, more serious events. Procedures will be done to minimise the risk of infection, such as the use of antibiotics.

Bleeding Associated with the use of Anticoagulant Medication

The use of certain kinds of anticoagulant (blood-thinning) medications (e.g. aspirin) is permitted during this treatment. However, these types of medication are known to increase the chance of bleeding and could possibly increase the chance of internal eye bleeding during treatment if you have an eye inflammation. Inform your doctor if you need to take anticoagulant (blood-thinning) medications (e.g. aspirin) during your treatment with Ranibizumab.

The risks to an unborn human foetus or a nursing child from Ranibizumab are not known. Women who are pregnant or nursing a child did not participate in any of the clinical trials. You must confirm that, to the best of your knowledge, you are not now pregnant and that you do not intend to become pregnant during treatment. If there is any possibility that you may become pregnant during treatment, you must inform your doctor. Your doctor will discuss appropriate birth control measures with you. If you suspect that you have become pregnant during treatment, you must notify your doctor immediately.

BENEFITS OF THE TREATMENT

There is no guarantee that you will receive any benefit from the treatment received. However, results from clinical trials in over 900 patients have shown that vision remained stable or increased in over 71-77% of patients being treated with Ranibizumab. Further, vision increased in 25-40% of patients treated with Ranibizumab such that they were able to read 3 lines more of the reading chart (that you are normally tested with) than before they started the treatment. Ask your doctor to explain these results to you. Your doctor can share with you more information about the results of the Ranibizumab clinical trials that have made him/her propose treating you with this drug.

PAYMENT FOR THE DRUG

Under the Ranibizumab Authorised Prescriber or Special Access Scheme, you will need to make co-payments at the time of the first 3 treatments. Ask your doctor to discuss the co-payments with you in further detail. After the 3 co-payments, Novartis will provide Ranibizumab for subsequent treatments free-of-charge until 31 July 2007 (when the Scheme ends). After that date, you will have to pay for any further doses of Ranibizumab.