



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Eylea (*aflibercept*)

An overview of Eylea and why it is authorised in the EU

What is Eylea and what is it used for?

Eylea is a medicine used to treat adults with:

- the 'wet' form of age-related macular degeneration (AMD), a disease which affects the central part of the retina (called the macula) at the back of the eye. The wet form of AMD is caused by choroidal neovascularisation (the abnormal growth of blood vessels under the macula), which may leak fluid and blood and cause swelling;
- impaired vision due to macular oedema (swelling) that follows blockage of either the main vein carrying blood from the retina (known as central retinal vein occlusion, CRVO) or of smaller branch veins (known as branch retinal vein occlusion, BRVO);
- impaired vision due to macular oedema caused by diabetes;
- impaired vision due to myopic choroidal neovascularisation (a severe type of short-sightedness where the eyeball continues to grow, becoming longer than it should be).

Eylea is also used to treat preterm infants with retinopathy of prematurity (ROP), an eye condition that can occur when a baby is born too early and blood vessels in the eye do not develop normally, causing damage to the retina. Eylea is used for specific stages of the disease: zone I (stage 1+, 2+, 3 or 3+) and zone II (stage 2+ or 3+) as well as the rapidly progressing severe form of the disease called aggressive posterior retinopathy disease.

Eylea contains the active substance aflibercept.

How is Eylea used?

Eylea is available as prefilled syringes or vials containing a solution for intravitreal injection (injection into the vitreous humour, the jelly-like fluid inside the eye). It can only be obtained with a prescription and must be given by a qualified doctor who is experienced in giving intravitreal injections.

In adults, Eylea is given as an injection of 2 mg into the affected eye, repeated as appropriate at intervals of a month or more. How often the injections are given depends on the condition being

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treated and the response of the patient to treatment.

For the treatment of preterm infants with ROP, Eylea is given as a single injection of 0.4 mg per eye. It may be injected in one eye or both eyes on the same day. If the symptoms persist, a second dose may be given in the same eye at least 4 weeks after the first dose. Up to 2 injections per eye may be given within 6 months of starting treatment.

For more information about how Eylea is used, see the package leaflet or contact your doctor or pharmacist.

How does Eylea work?

The active substance in Eylea, aflibercept is an engineered protein that has been designed to attach to and block the effects of a substance called vascular endothelial growth factor A (VEGF-A). It can also attach to other proteins such as placental growth factor (PIGF). VEGF-A and PIGF are involved in stimulating the abnormal growth of blood vessels in patients with AMD, certain types of macular oedema, myopic choroidal neovascularisation and ROP. By blocking these factors, aflibercept reduces the growth of abnormal blood vessels and controls leakage and swelling.

What benefits of Eylea have been shown in studies?

Wet AMD

Eylea was investigated in two main studies involving a total of around 2,400 patients with the wet form of AMD. The studies compared Eylea (given either as 0.5 mg every four weeks, 2 mg every four weeks or 2 mg every eight weeks, all after three initial monthly doses) with ranibizumab, another treatment for AMD which was given by injection into the eye every four weeks. The main measure of effectiveness was the proportion of patients who maintained vision (defined as losing less than 15 letters in a standard eye test) after the first year of treatment. Both studies also looked at the maintenance of the effect in the second year of treatment, during which the number of injections and the time between injections were adjusted depending on the vision and changes within the eye.

Eylea was shown to be as effective as ranibizumab in maintaining vision in patients with wet AMD: looking at the results of the two studies together, the proportions of patients who maintained vision were 96.1% (517 out of 538), 95.4% (533 out of 559) and 95.3% (510 out of 535) for 0.5 mg Eylea every four weeks, 2 mg Eylea every four weeks and 2 mg Eylea every eight weeks, respectively, compared with 94.4% (508 out of 538) of patients treated with ranibizumab every four weeks. During the second year of treatment, the effectiveness was generally maintained, with a majority of patients receiving injections at an extended dosing interval of 10 weeks, although a small number of patients occasionally needed more frequent injections (such as monthly).

Subsequent results from a supportive study indicated the effectiveness of extended treatment intervals in patients with wet AMD.

Macular oedema following retinal vein occlusion

Eylea was also investigated in two other main studies involving 366 patients with macular oedema following CRVO. Monthly injections of Eylea 2 mg were compared with a sham injection. Another main study involving 181 patients with macular oedema due to BRVO compared monthly injections of Eylea 2 mg with laser treatment. In all the studies, the main measure of effectiveness was the proportion of patients who responded and whose vision improved by 15 or more letters on an eye test after 24 weeks of treatment. The studies in patients with macular oedema following CRVO also looked at the effects of treatment on an as-needed basis after 24 weeks.

Eylea also produced a significant improvement in vision in patients with macular oedema following CRVO and BRVO. For CRVO, overall about 60% of patients given Eylea had an improvement of 15 letters or more in the eye test at week 24, compared with 17% of those given sham injections. The benefit was largely maintained with as-needed treatment up to 52 weeks, although some of the benefit seemed to be lost when patients were treated and followed up for longer periods than this. For BRVO, around 53% of patients given Eylea had an improvement of 15 letters or more in the eye test at week 24, compared with 27% of patients who received laser treatment. This effect was maintained at 52 weeks, despite less frequent injection of Eylea between week 24 and 52.

Diabetic macular oedema

Two further main studies involving 872 patients with diabetic macular oedema looked at the effect of Eylea compared with laser treatment. Eylea was either given once a month, or once every other month after the first five monthly injections. The main measure of effectiveness in both studies was the change in the number of letters that could be read in an eye test after one year of treatment.

In patients with diabetic macular oedema, the average number of letters they could read in an eye test before treatment was about 59 to 60; in patients given Eylea monthly this improved by around 12 letters, and in those given Eylea every other month by around 11 letters. In contrast, in patients given laser treatment the improvement after a year was only about 1 letter.

Myopic choroidal neovascularisation

In myopic choroidal neovascularisation, Eylea was investigated in a main study involving 122 patients, which compared Eylea with a sham injection. The main measure of effectiveness was the change in the number of letters that could be read in an eye test after 24 weeks of treatment.

In the study in myopic choroidal neovascularisation, the average number of letters patients could read in an eye test before treatment was about 56; patients given Eylea could read on average 12 more letters after 24 weeks of treatment whereas in patients given sham injections the total number of letters they could read decreased on average by 2.

Retinopathy of prematurity

In a study involving 113 infants with ROP, 24 weeks after starting treatment, about 86% of patients who received Eylea had no signs of active disease (i.e. no disease requiring treatment) and no structural abnormalities in their retina compared with 82% of patients who received laser therapy, another type of treatment for ROP. Most patients treated with Eylea received only one injection in each eye.

What are the risks associated with Eylea?

The most common side effects with Eylea (which may affect more than 1 in 20 people) are conjunctival haemorrhage (bleeding from the small blood vessels on the surface of the eye at the site of injection), retinal haemorrhage (bleeding at the back of the eye), reduced vision, eye pain, vitreous detachment (detachment of the jelly-like substance inside the eye), cataract (clouding of the lens), vitreous floaters (small particles or spots in the vision) and increased intraocular pressure (increased pressure inside the eye).

Serious injection-related side effects (which have occurred in less than 1 in around 2,000 injections in studies) are blindness, endophthalmitis (serious infection or inflammation inside the eye), cataracts, increased intraocular pressure, vitreous haemorrhage (bleeding into the jelly-like fluid in the eye, causing temporary loss of vision) and vitreous or retinal detachment. For the full list of side effects of Eylea, see the package leaflet.

Eylea must not be used in patients who have or are thought to have ocular or periocular infections (infections in or around the eyes), or in patients who have severe inflammation inside the eye. For the full list of restrictions, see the package leaflet.

Why is Eylea authorised in the EU?

The European Medicines Agency noted that, for wet AMD, Eylea was as effective as ranibizumab in maintaining patients' vision after the first year of treatment. In addition, the Agency considered that Eylea was beneficial in improving vision of patients with macular oedema resulting from CRVO, BRVO or diabetes, as well as patients with myopic choroidal neovascularisation. Eylea was found to be effective at treating the symptoms of ROP, although uncertainties remain regarding its effects beyond 2 years after treatment; this will be addressed by the submission of additional data. There were no major or unexpected safety concerns with Eylea. Therefore, the Agency decided that Eylea's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Eylea?

The company that markets Eylea will provide up-to-date educational material for doctors (to minimise the risks associated with the injection in the eye) and for adult patients (so they can recognise any serious side effects, and know when to seek urgent attention from their doctor).

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Eylea have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Eylea are continuously monitored. Side effects reported with Eylea are carefully evaluated and any necessary action taken to protect patients.

Other information about Eylea

Eylea received a marketing authorisation valid throughout the EU on 22 November 2012.

Further information on Eylea can be found on the Agency's website: ema.europa.eu/Find/medicine/Human_medicines/European_public_assessment_reports.

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