



EUROPEAN MEDICINES AGENCY
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EPAR summary for the public

Eylea

aflibercept

This is a summary of the European public assessment report (EPAR) for Eylea. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Eylea.

What is Eylea?

Eylea is a medicine that contains the active substance aflibercept. It is available as a solution for injection into the eye in pre-filled syringes or vials.

What is Eylea used for?

Eylea is 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).

The macula provides central vision that is needed to see detail for everyday tasks such as driving, reading and recognising faces. The diseases cause the gradual loss of the central part of a person's vision.



The medicine can only be obtained with a prescription.

How is Eylea used?

Eylea must be given as an intravitreal injection (injection into the vitreous humour, the jelly-like fluid in the eye) by a qualified doctor who is experienced in giving intravitreal injections.

For wet AMD, one injection of 2 mg is given into the affected eye every month for three consecutive months, followed by one injection every two months. After one year of treatment, injections may be given less frequently depending on the response to treatment.

For macular oedema following CRVO or BRVO, treatment is started with monthly injections of 2 mg is given into the affected eye, but the interval between injections may be extended depending on the response of the patient. Further treatment should not be given if patients do not respond.

For diabetic macular oedema, one injection of 2 mg is given into the affected eye every month for five consecutive months, followed by one injection every two months. After one year of treatment, injections may be given less frequently depending on the response to treatment. If patients do not respond, treatment should be stopped.

For myopic choroidal neovascularisation, a single injection of 2 mg is given into the affected eye. Additional injections may be given if the disease persists, but the interval between injections should be at least one month.

The procedure should be carried out under sterile conditions. The syringe and the vial are for single use only. The pre-filled syringe contains more than the recommended dose, therefore when preparing the injection, the doctor must expel the excess volume and ensure the injection of the correct dose. After the injection, the pressure within the eye should be checked.

How does Eylea work?

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 (PlGF). VEGF-A and PlGF are involved in stimulating the abnormal growth of blood vessels in patients with AMD, certain types of macular oedema and myopic choroidal neovascularisation. By blocking these factors, aflibercept reduces the growth of the blood vessels and controls the leakage and swelling.

How has Eylea been studied?

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 also investigated in two other main studies involving 366 patients with macular oedema following CRVO. These compared monthly injections of Eylea 2 mg with a sham injection using a

syringe without a needle. 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.

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 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.

What benefit has Eylea shown during the studies?

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).

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 administration of Eylea between week 24 and 52.

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.

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.

What is the risk associated with Eylea?

The most common side effects (affecting at least 1 in 20 patients) reported with Eylea are conjunctival haemorrhage (bleeding from the small blood vessels on the surface of the eye at the site of injection), 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 2,200 injections) include blindness, endophthalmitis (inflammation inside the eye), cataract, 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 all side effects reported with 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 with Eylea see the package leaflet.

Why has Eylea been approved?

The CHMP noted that for wet AMD Eylea was as effective as ranibizumab in maintaining patients' vision after the first year of treatment. In addition the CHMP 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. The CHMP further noted that there were no major or unexpected safety concerns with Eylea. Therefore, the CHMP decided that Eylea's benefits are greater than its risks and recommended that it be given marketing authorisation.

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

A risk management plan has been developed to ensure that Eylea is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Eylea, including the appropriate precautions to be followed by healthcare professionals and patients.

The company that makes Eylea will also provide up-to-date educational material for doctors (to minimise the risks associated with the injection in the eye) and for patients (so they can recognise any serious side effects, and know when to seek urgent attention from their doctor). In addition, the company will carry out a study investigating extended treatment intervals with Eylea in diabetic macular oedema, as well as a study looking at the effects of Eylea treatment when given on an as-needed basis in wet AMD.

Other information about Eylea

The European Commission granted a marketing authorisation valid throughout the European Union for Eylea on 22 November 2012.

The full EPAR for Eylea can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_public_assessment_reports. For more information about treatment with Eylea, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 11-2015.