New drugs

Aflibercept

Approved indication: neovascular age-related macular degeneration

Eylea (Bayer)

single-use vials containing 40 mg/mL solution for intravitreal injection

Australian Medicines Handbook Appendix A

Neovascular or 'wet' age-related macular degeneration is the most severe form of the disease (see Aust Prescr 2012;35:90-3). Although it only accounts for 10% of all cases of age-related disease, it is responsible for 90% of severe visual loss. It occurs when abnormal blood vessels develop under the macula and leak fluid and blood. This eventually leads to scarring and permanent loss of central vision.

Vascular endothelial growth factor A (VEGF-A) is a key mediator in neovascular age-related macular degeneration. The standard VEGF inhibitor used in this disease is ranibizumab, a monoclonal antibody fragment (see Aust Prescr 2007;30:79-82). Aflibercept is a fusion protein that blocks the binding of VEGF-A to its receptors by acting as a soluble decoy receptor. Aflibercept also blocks placental growth factor which is thought to play a role in the disease.

The approval of aflibercept is based on two 52-week comparative trials with ranibizumab – VIEW 1 and VIEW 2. In summary, over 2400 patients were equally randomised to one of four treatment regimens (see Table). The primary outcome of the trials was the percentage of patients who maintained their vision. This was defined as losing less than 15 letters of visual acuity on the chart used in the Early Treatment Diabetic Retinopathy Study. The chart consists of 14 rows of 5 letters each. The efficacy of aflibercept 2 mg given by intravitreal injections at four or eight week intervals and 0.5 mg monthly was similar to monthly ranibizumab 0.5 mg (Table). The recommended dose of aflibercept is 2 mg every eight weeks following three initial monthly injections.

Adverse effects in the trials were mainly ophthalmic. The most common were conjunctival haemorrhage (24.7%), cataract (6.8%), eye pain (8.7%), vitreous detachment (6%), vitreous floaters (5.9%) and increased ocular pressure (5.2%). The incidence of these events was similar with ranibizumab.

Although rare, endophthalmitis has been reported after intravitreal injection with aflibercept so correct aseptic technique should always be used. Aflibercept is contraindicated in patients with ocular or periocular infection or severe intraocular inflammation.

Although aflibercept has not been tested in pregnant or lactating women, fetal abnormalities have occurred in animals when it was given systemically. Aflibercept is not recommended in pregnancy or lactation.

The safety and efficacy of aflibercept injected every eight weeks (following three initial monthly injections) for 12 months seems to be comparable to ranibizumab injected every four weeks, so patients may prefer it. Adverse effects were confined to the eye and appeared to be related to the intravitreal injections.

[T] manufacturer provided the product information

REFERENCES *†A

None

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The Transparency score ([T]) is explained in 'New drugs: T-score for transparency', Aust Prescr 2011;34:26–7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm)

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Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Table **Efficacy of aflibercept in the VIEW 1 and 2 clinical trials**

Treatment (52 weeks)	Proportion of patients who lost fewer than 15 letters of visual acuity	
	VIEW 1	VIEW 2
Aflibercept 2 mg every month for 3 months then every 8 weeks	94.4%	95.4%
Aflibercept 2 mg every 4 weeks	95.1%	94.5%
Aflibercept 0.5 mg every 4 weeks	95.0%	95.3%
Ranibizumab 0.5 mg every 4 weeks	93.8%	94.9%

Values taken from the Australian Public Assessment Report (AusPAR)