

Media Fact Sheet

Lucentis®

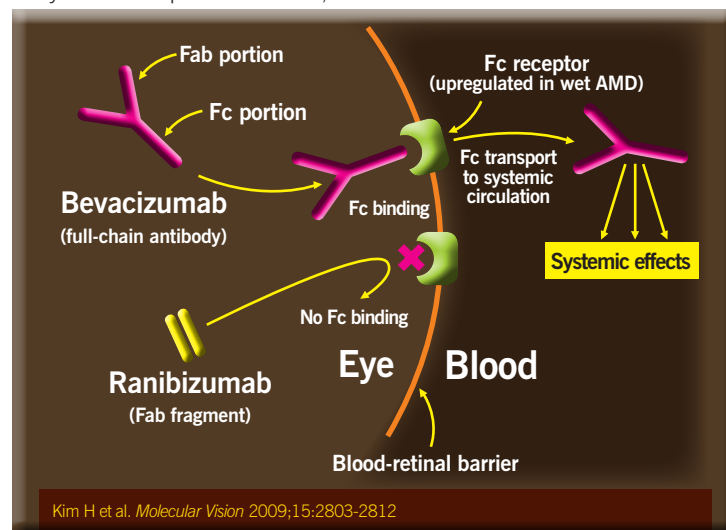
■ What is Lucentis® (ranibizumab)?

Lucentis is a humanized therapeutic antibody fragment designed to block all biologically active forms of vascular endothelial growth factor-A (VEGF-A). It has been designed and developed specifically for use in ocular diseases.¹ Since its launch, Lucentis has become the standard first-line treatment for wet age-related macular degeneration (wet AMD) where it is licensed in more than 100 countries. Lucentis is also approved in more than 100 countries for the treatment of patients with visual impairment due to diabetic macular edema (DME) and due to macular edema secondary to both branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). Further, Lucentis is approved in more than 60 countries (including the countries in the EU, Japan and Switzerland) to treat patients with visual impairment due to choroidal neovascularization (CNV) secondary to pathologic myopia (myopic CNV).

■ How does Lucentis work?

Lucentis is designed to bind and inhibit VEGF-A, a protein that drives the formation of new blood vessels (angiogenesis) and blood vessel permeability.²

■ In wet AMD,¹ pathologic blood vessels grow under the retina, which can leak blood and fluid causing rapid damage to the macula, the part of the eye that is responsible for fine, detailed central vision.³



- In visual impairment due to DME and visual impairment due to macular edema secondary to branch RVO or central RVO,¹ elevated VEGF levels are associated with blood vessels becoming increasingly permeable and leaking fluid. This causes swelling and thickening of the macula, leading to more visual impairment.^{3,4}
- VEGF also plays an important role in the pathogenesis of CNV; in patients with myopic CNV there are markedly increased VEGF levels in the aqueous humor when compared with the controls.⁵

■ What are the advantages of Lucentis due to the way the molecule was developed?

Lucentis was designed specifically for use in the eye with the following characteristics that may enhance its effectiveness and safety profile:

- The small molecular size of Lucentis allows it to penetrate all layers of the retina quickly and completely in order to reach the site of pathologic blood vessel formation.⁶
- Lucentis has been designed to bind with high affinity to VEGF-A receptors.⁷
- As an antibody fragment, Lucentis may reduce the likelihood of certain side effects.
- Lucentis lacks the Fc portion present in most biological therapies, reducing systemic exposure², and may be less likely to cause ocular inflammation.⁸
- Lucentis is rapidly cleared from the systemic circulation, which may minimize systemic side effects.⁹
- Lucentis is formulated under strict guidelines for sterile use in the eye.¹⁰

Lucentis has become the standard first-line treatment for wet AMD

Lucentis was designed specifically for use in the eye

In wet AMD, pathologic blood vessels grow under the retina

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■ What are the benefits of Lucentis for patients?

Lucentis has demonstrated transformational outcomes for patients across each of its approved indications. In clinical studies (including ANCHOR, MARINA, RESTORE, BRAVO, CRUISE and RADIANCE), patients with wet AMD, DME, BRVO, CRVO, and myopic CNV treated with Lucentis had a marked improvement in their independence (vision-related quality of life).^{11,12,13,14,15,16} Improvement was reported in near-vision activities (e.g. reading and cooking), distance activities (e.g. reading street signs and going up and down stairs at night) and vision-specific dependency (e.g. not having to stay at home most of the time).^{10, 17,18,19,20} In multiple studies, intravitreally injected inhibitors of VEGF, most notably Lucentis, were attributed to cause significant reductions in the incidence of legal blindness from wet AMD.²¹

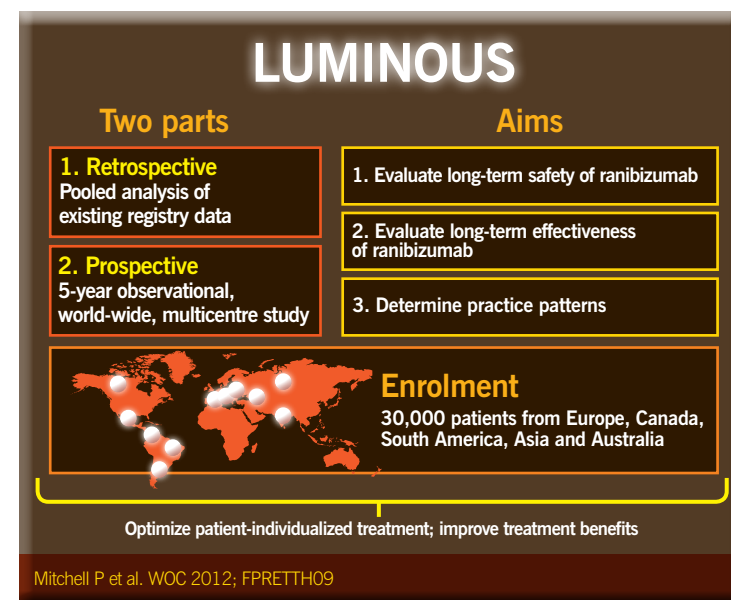
■ What is the safety profile of Lucentis?

There are more than 2.4 million patient-treatment years of exposure globally with Lucentis.²² Its safety profile has been well established in a clinical development program that enrolled more than 12,500 patients across indications.^{23,24} Mandatory continuous safety monitoring is ongoing via a systematic pharmacovigilance program. Some reported side effects of Lucentis include retinal detachment and inflammation and infections inside the eye.



In 2011, Novartis launched the LUMINOUS™ program, one of the largest observational studies in ophthalmology, aiming to recruit over 30,000 patients from clinics across Asia, Australia, Europe, and North and South America to further broaden the understanding of ocular disease and the use of Lucentis in its approved indications. LUMINOUS is a 5-year observational, international, multicenter program that will provide long-term effectiveness and safety data for Lucentis as well as assess the treatment patterns and health related quality of life issues of patients treated with Lucentis. Currently, more than 20,000 patients are enrolled in this study.

Data on nearly 4,500 patients with wet AMD treated with Lucentis were pooled for the retrospective part of LUMINOUS. The retrospective pooled analysis of European registries showed no new safety risks with Lucentis in the real-world setting and confirmed its well-characterized safety profile.²⁵



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Lucentis must meet the stringent standards required for ophthalmic injections with respect to sterility and fine particles in the solution

■ How is Lucentis administered?

Lucentis is administered via injection into the eye (also known as an intravitreal injection). Lucentis is specifically manufactured for use in the eye and must therefore meet the stringent standards required for ophthalmic injections with respect to sterility and fine particles in the solution. It is provided in sterile, single-use vials.⁹

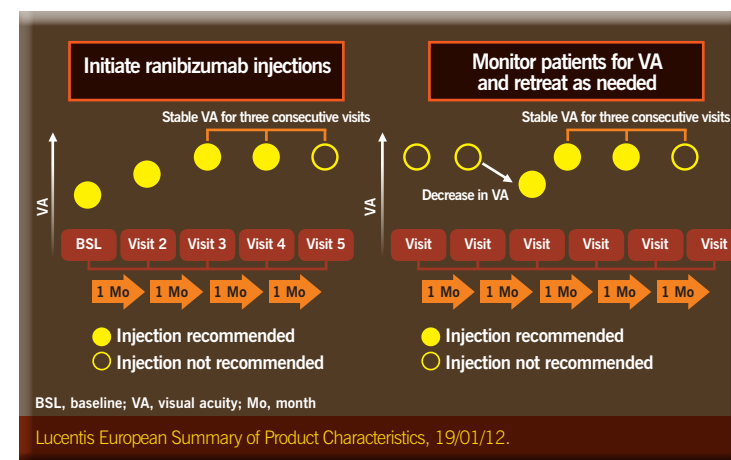
In most countries Lucentis is administered for the treatment of wet AMD, DME, BRVO, CRVO and myopic CNV to patients on an individualized basis with the goal of maximizing visual outcomes for each individual patient whilst minimizing the risks of over- or under-treating.

Roche / Genentech has the commercial rights to Lucentis in the United States and Novartis has exclusive rights in the rest of the world.

■ References

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The schematic below represents an example of the flexible, individualized dosing regimen for as needed Lucentis



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