Eye (2017) 31, S18–S20

www.nature.com/eye

APPENDIX

Lucentis® (ranibizumab) ABBREVIATED UK PRESCRIBING INFORMATION

Eye (2017) **31,** S18–S20; doi:10.1038/eye.2017.149

Please refer to the SmPC before prescribing Lucentis 10 mg/ml solution vial for injection, or Lucentis 10 mg/ml solution for injection in pre-filled syringe

Presentations: A glass single-use vial containing 0.23 ml solution containing 2.3 mg of ranibizumab (10 mg/ml) and a pre-filled syringe containing 0.165 ml, equivalent to 1.65 mg ranibizumab (10 mg/ml).

Indications: The treatment in adults of neovascular (wet) age-related macular degeneration (AMD), the treatment of visual impairment due to choroidal neovascularisation (CNV), the treatment of visual impairment due to diabetic macular oedema (DMO), the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).

Administration and Dosage: Available as a single-use vial and a single dose pre-filled syringe, for intravitreal use only. Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections under aseptic conditions. The recommended dose is 0.5 mg (0.05 ml).

The interval between two doses injected into the same eye should be at least four weeks.

Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity i.e. no change in visual acuity or in other signs and symptoms of the disease under continued treatment. In patients with wet AMD, DMO and RVO, initially, three or more consecutive, monthly injections may be needed. Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity, as assessed by visual acuity and/or anatomical parameters.

If, in the physician's opinion, visual and anatomic parameters indicate that the patient is not benefiting from continued treatment, Lucentis should be discontinued.

Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography).

If patients are being treated according to a treat-and-extend regimen, once maximum visual acuity is achieved and/or there are no signs of disease activity, the treatment intervals can be extended stepwise until signs of disease activity or visual impairment recur. The treatment interval should be extended by no more than two weeks at a time for wet AMD and may be extended by up to one month at a time for DMO. For RVO, treatment intervals may also be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly.

The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection. For CNV secondary to pathologic myopia (PM), many patients may only need one or two injections during the first year.

Lucentis and laser photocoagulation in DMO and in macular oedema secondary to BRVO: There is some experience of Lucentis administered concomitantly with laser photocoagulation. When given on the same day, Lucentis should be administered at least 30 min after laser photocoagulation. Lucentis can be administered in patients who have received previous laser photocoagulation.

Lucentis and Visudyne photodynamic therapy in CNV secondary to PM: There is no experience of concomitant administration of Lucentis and Visudyne.

Before treatment, evaluate the patient's medical history for hypersensitivity.

Children and adolescents: Safety and efficacy in children and adolescents below 18 years of age have not been established. Limited data is available for adolescents aged 12 to 17 years with visual impairment due to CNV.

Elderly: No dose adjustment is required in the elderly. There is limited experience in patients older than 75 years with DMO

Hepatic and renal impairment: Dose adjustment is not needed in these populations.

Contraindications: Hypersensitivity to the active substance or excipients. Patients with active or suspected ocular or periocular infections. Patients with active severe intraocular inflammation.

Special warnings and precautions for use: Lucentis is for intravitreal injection only. Intravitreal injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Monitor during week following injection for infections. Patients should be instructed to report symptoms suggestive of any of the above without delay. Transient increases in intraocular pressure (IOP) within 1 h of injection and sustained IOP increases have been identified. Both IOP and perfusion of the optic nerve head should be monitored and managed appropriately. Limited data on bilateral use of Lucentis (including same-day administration) do not suggest an increased risk of systemic adverse events compared with unilateral treatment. There is a potential for immunogenicity with Lucentis which may be greater in subjects with DMO. Patients should report an increase in severity of intraocular inflammation. Lucentis should not be administered concurrently with other anti-VEGF agents (systemic or ocular). Withhold dose and do not resume treatment earlier than the next scheduled treatment in the event of the following: a decrease in best corrected visual acuity (BCVA) of $\geq$30 letters compared with the last assessment of visual acuity; an intraocular pressure of $\geq$30 mm Hg; a retinal break; a subretinal haemorrhage involving the centre of the fovea, or if the size of the haemorrhage is $\geq$50% of the total lesion area; performed or planned intraocular surgery within the previous or next 28 days. Risk factors associated with the development of a retinal pigment epithelial (RPE) tear after anti-VEGF therapy for wet AMD include a large and/or high pigment epithelial retinal detachment. When initiating Lucentis therapy, caution should be used in patients with these risk factors for RPE tears. Discontinue treatment in cases of rhegmatogenous retinal detachment or stage 3 or 4 macular holes.

There is only limited experience in the treatment of subjects with DMO due to type I diabetes. Lucentis has not been studied in patients who have previously received intravitreal injections, in patients with active systemic infections, proliferative diabetic retinopathy, or in patients with concurrent eye conditions such as retinal detachment or macular hole. There is also no experience of treatment with Lucentis in diabetic patients with an HbA1c over 12% and uncontrolled hypertension. In PM patients there are no data on the use of Lucentis in patients with extrafoveal lesions and only limited data on its use in those who have had previous unsuccessful therapy with verteporfin photodynamic therapy. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors.

There are limited data on safety in the treatment of DMO, macular oedema due to RVO and CNV secondary to PM patients with prior history of stroke or transient ischaemic attacks. Caution should be exercised when treating such patients. There are insufficient data to conclude on the effect of Lucentis in patients with RVO presenting irreversible ischaemic visual function loss.

Interactions: No formal interaction studies have been performed. In DMO and BRVO adjunctive use of laser therapy and Lucentis was not associated with any new ocular or non-ocular safety findings. In clinical studies for the treatment of visual impairment due to DMO, the outcome with regard to visual acuity or central retinal subfield thickness (CSFT) in patients treated with Lucentis was not affected by concomitant treatment with thiazolidinediones.

Pregnancy and lactation: Women of childbearing potential should use effective contraception during treatment. No clinical data on exposed pregnancies are available. Ranibizumab should not be used during pregnancy unless the expected benefit outweighs the potential risk to the foetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving. Breast-feeding is not recommended during the use of Lucentis

Driving and using machines: The treatment procedure may induce temporary visual disturbances and patients who experience these signs must not drive or use machines until these disturbances subside.

Undesirable effects: Most adverse events are related to the injection procedure. Serious adverse events reported include endophthalmitis, blindness, retinal detachment, retinal tear and iatrogenic traumatic cataract. The safety data below include adverse events experienced following the use of Lucentis in the entire clinical trial population. Those marked * were only seen in the DMO population.
Very Common: Intraocular pressure increased, headache, vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival

haemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperaemia, eye pruritus, arthralgia, nasopharyngitis. **Common:** Urinary tract infection*, anaemia, retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous haemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site haemorrhage, eye haemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid oedema, eyelid pain, conjunctival hyperaemia, cough, nausea, allergic reactions, hypersensitivity, anxiety.

Product-class-related adverse reactions: There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the Lucentis clinical trials in patients with AMD, DMO, RVO and PM and there were no major differences between the groups treated with ranibizumab compared to control.

Please refer to the SmPC for full listing of all undesirable effects.

For UK: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis Pharmaceuticals UK Ltd on (01276) 698370 or medinfo.uk@novartis.com

Legal category: POM, **UK Basic NHS cost**: £551
Marketing authorisation number: single dose vial injection kit EU/1/06/374/001, single dose vial only pack EU/1/06/374/002, single dose vial and filter needle pack EU/1/06/374/003, single dose pre-filled syringe EU/1/06/374/003

Marketing authorisation holder: Novartis Europharm Limited, Frimley Business Park, Camberley, GU16 7SR, United Kingdom. Full prescribing information, including SmPC, is available from: Novartis Pharmaceuticals, Frimley Business Park, Frimley, Camberley, Surrey, GU16 7SR. Tel: 01276 692255; Fax: 01276 692508.

Prepared: Nov 2016
OPT17-C014 August 2017