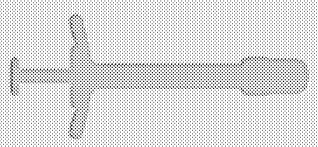
LUCENTIS
RANIBIZUMAB INJECTION

PREFILLED SYRINGE
ADMINISTRATION PREPARATION



1 PREPARE

- Make sure that your pack contains a sterile prefilled syringe in a sealed tray
- Peel the lid off the syringe tray and, using aseptic technique, remove the syringe

2 INSPECT SYRINGE

- LUCENTIS should be colorless to pale yellow
- **Do not** use the prefilled syringe if:
  - The syringe cap is detached from the Luer lock
  - The syringe is damaged
  - Particulates, cloudiness, or discoloration are visible

SNAP

3 REMOVE SYRINGE CAP

- Snap off (**do not** turn or twist) the syringe cap (see Figure 1)

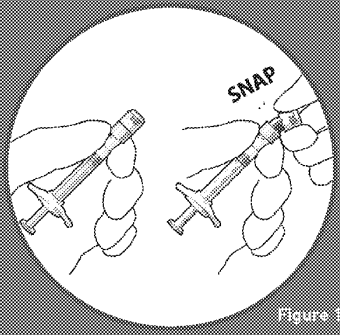


Figure 1

ATTACH

4 ATTACH NEEDLE

- Attach a 30G x ½-inch sterile injection needle firmly onto the syringe by screwing it tightly onto the Luer lock (see Figure 2)
- Carefully remove the needle cap by pulling it straight off

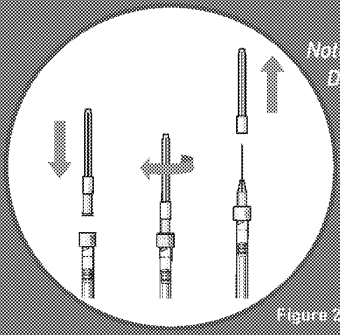


Figure 2

TAP

5 DISLODGE AIR BUBBLES

- Hold the syringe with the needle pointing up
- If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top (see Figure 3)

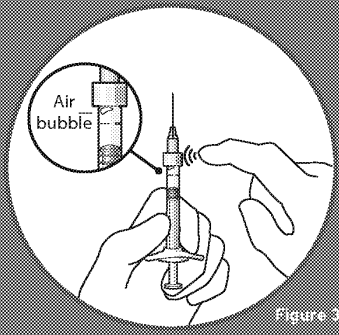


Figure 3

6 EXPEL AIR AND ADJUST DRUG DOSE

- Hold the syringe at eye level, and carefully push the plunger rod until the **edge below the dome** of the rubber stopper is aligned with the 0.05 mL dose mark (see Figure 4)

Note: The plunger rod is not attached to the rubber stopper—this is to prevent air from being drawn into the syringe.

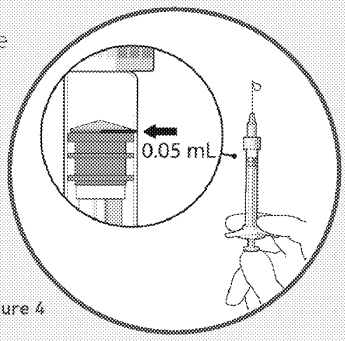


Figure 4

7 INJECT

- The injection procedure should be carried out under aseptic conditions
- Insert the needle into the injection site
- Inject slowly until the rubber stopper reaches the bottom of the syringe to deliver the volume of 0.05 mL
- After injection, **do not** recap the needle or detach it from the syringe. Dispose of the used syringe together with the needle in a sharps disposal container, or in accordance with local requirements

For Important Safety Information, please see next page and LUCENTIS full Prescribing Information.

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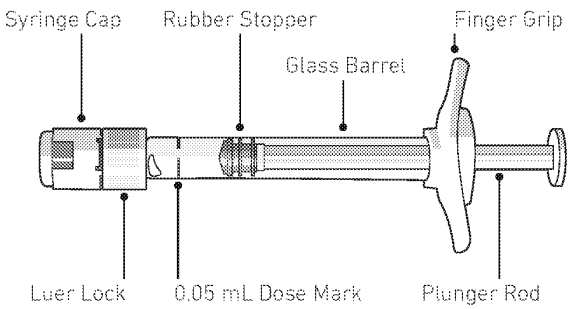
LUCENTIS® RANIBIZUMAB INJECTION

PREFILLED SYRINGE: ADMINISTRATION PREPARATION

DEVICE DESCRIPTION



TO PREPARE LUCENTIS FOR INTRAVITREAL ADMINISTRATION, PLEASE ADHERE TO THE ACCOMPANYING INSTRUCTIONS. READ ALL THE INSTRUCTIONS CAREFULLY BEFORE USING THE PREFILLED SYRINGE. PLEASE SEE THE FULL PRESCRIBING INFORMATION FOR ADMINISTRATION INFORMATION.

HOW TO STORE LUCENTIS:

- LUCENTIS should be refrigerated at 2°C-8°C (36°F-46°F). **Do not** freeze
- **Do not** use beyond the expiration date stamped on the label
- Protect LUCENTIS prefilled syringes from light and store in the original carton until time of use
- **Do not** open sealed tray until time of use

The prefilled syringe is for single-use only. The prefilled syringe is sterile. **Do not** use product if the packaging is damaged or has been tampered with.

The opening of the sealed tray and all subsequent steps should be done under aseptic conditions.

For the intravitreal injection, a 30-gauge x ½-inch sterile injection needle should be used (not provided).

NOTE: The dose must be set to 0.05 mL.

IMPORTANT SAFETY INFORMATION

INDICATIONS

LUCENTIS® (ranibizumab injection) is indicated for the treatment of patients with:

- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR)
- Myopic choroidal neovascularization (mCNV)

IMPORTANT SAFETY INFORMATION

- LUCENTIS is contraindicated in patients with ocular or periocular infections or known hypersensitivity to ranibizumab or any of the excipients in LUCENTIS. Hypersensitivity reactions may manifest as severe intraocular inflammation.
- Intravitreal injections, including those with LUCENTIS, have been associated with endophthalmitis, retinal detachment, and iatrogenic traumatic cataract.
- Increases in intraocular pressure have been noted both pre-injection and post-injection with LUCENTIS.
- Although there was a low rate of arterial thromboembolic events (ATEs) observed in the LUCENTIS clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).
- Fatal events occurred more frequently in patients with DME and DR at baseline treated monthly with LUCENTIS compared with control. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded.
- In the LUCENTIS Phase III clinical trials, the most common ocular side effects included conjunctival hemorrhage, eye pain, vitreous floaters, and increased intraocular pressure. The most common non-ocular side effects included nasopharyngitis, anemia, nausea, and cough.

For additional Safety Information, please see LUCENTIS full Prescribing Information.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

REFERENCE: 1. LUCENTIS [package insert]. South San Francisco, CA: Genentech, Inc; 2018.

Genentech
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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LUCENTIS safely and effectively. See full prescribing information for LUCENTIS.

LUCENTIS® (ranibizumab injection) for intravitreal injection
Initial U.S. Approval: 2006

----------RECENT MAJOR CHANGES----------

Indications and Usage, Diabetic Retinopathy (1.4)	04/2017
Dosage and Administration (2)	03/2018
Dosage Forms and Strengths (3)	03/2018

----------INDICATIONS AND USAGE----------

LUCENTIS, a vascular endothelial growth factor (VEGF) inhibitor, is indicated for the treatment of patients with:

- Neovascular (Wet) Age-Related Macular Degeneration (AMD) (1.1)
- Macular Edema Following Retinal Vein Occlusion (RVO) (1.2)
- Diabetic Macular Edema (DME) (1.3)
- Diabetic Retinopathy (DR) (1.4)
- Myopic Choroidal Neovascularization (mCNV) (1.5)

----------DOSAGE AND ADMINISTRATION----------

For ophthalmic intravitreal injection only (2.1)

- Neovascular (Wet) Age-Related Macular Degeneration (AMD) (2.2):

LUCENTIS 0.5 mg (0.05 mL) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

- Although not as effective, patients may be treated with 3 monthly doses followed by less frequent dosing with regular assessment.
- Although not as effective, patients may also be treated with one dose every 3 months after 4 monthly doses. Patients should be assessed regularly.

- Macular Edema Following Retinal Vein Occlusion (RVO) (2.3):

LUCENTIS 0.5 mg (0.05 mL) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

- Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR) (2.4):

LUCENTIS 0.3 mg (0.05 mL) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

- Myopic Choroidal Neovascularization (mCNV) (2.5):

LUCENTIS 0.5 mg (0.05 mL) is recommended to be initially administered by intravitreal injection once a month (approximately 28 days) for up to three months. Patients may be retreated if needed.

----------DOSAGE FORMS AND STRENGTHS----------

- Single-use prefilled syringe designed to provide 0.05 mL for intravitreal injections:
  - 10 mg/mL solution (LUCENTIS 0.5 mg) (3)
  - 6 mg/mL solution (LUCENTIS 0.3 mg) (3)

- Single-use glass vial designed to provide 0.05 mL for intravitreal injections:
  - 10 mg/mL solution (LUCENTIS 0.5 mg) (3)
  - 6 mg/mL solution (LUCENTIS 0.3 mg) (3)

----------CONTRAINDICATIONS----------

- Ocular or periocular infections (4.1)
- Hypersensitivity (4.2)

----------WARNINGS AND PRECAUTIONS----------

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be monitored following the injection (5.1).
- Increases in intraocular pressure (IOP) have been noted both pre- and post-intravitreal injection (5.2).
- There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors (5.3).
- Fatal events occurred more frequently in patients with DME and DR at baseline, who were treated monthly with LUCENTIS compared with control (5.4).

----------ADVERSE REACTIONS----------

- The most common adverse reactions (reported more frequently in LUCENTIS-treated subjects than control subjects) are conjunctival hemorrhage, eye pain, vitreous floaters, and increased IOP (6.2).

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 03/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the Full Prescribing Information are not listed.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LUCENTIS is indicated for the treatment of patients with:

1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

1.2 Macular Edema Following Retinal Vein Occlusion (RVO)

1.3 Diabetic Macular Edema (DME)

1.4 Diabetic Retinopathy (DR)

1.5 Myopic Choroidal Neovascularization (mCNV)

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

FOR OPHTHALMIC INTRAVITREAL INJECTION.
Vials: A 5-micron sterile filter needle (19-gauge x 1-1/2 inch), a 1-mL Luer lock syringe and a 30-gauge x ½ inch sterile injection needle are needed but not included.

2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

LUCENTIS 0.5 mg (0.05 mL of 10 mg/mL solution) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

Although not as effective, patients may be treated with 3 monthly doses followed by less frequent dosing with regular assessment. In the 9 months after three initial monthly doses, less frequent dosing with 4-5 doses on average is expected to maintain visual acuity while monthly dosing may be expected to result in an additional average 1-2 letter gain. Patients should be assessed regularly [*see Clinical Studies (14.1)*].

Although not as effective, patients may also be treated with one dose every 3 months after 4 monthly doses. Compared with continued monthly dosing, dosing every 3 months over the next 9 months will lead to an approximate 5-letter (1-line) loss of visual acuity benefit, on average. Patients should be assessed regularly [*see Clinical Studies (14.1)*].

2.3 Macular Edema Following Retinal Vein Occlusion (RVO)

LUCENTIS 0.5 mg (0.05 mL of 10 mg/mL solution) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

In Studies RVO-1 and RVO-2, patients received monthly injections of LUCENTIS for 6 months. In spite of being guided by optical coherence tomography and visual acuity re-treatment criteria, patients who were then not treated at Month 6 experienced on average, a loss of visual acuity at Month 7, whereas patients who were treated at Month 6 did not. Patients should be treated monthly [*see Clinical Studies (14.2)*].

2.4 Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR)

LUCENTIS 0.3 mg (0.05 mL of 6 mg/mL solution) is recommended to be administered by intravitreal injection once a month (approximately 28 days).

2.5 Myopic Choroidal Neovascularization (mCNV)

LUCENTIS 0.5 mg (0.05 mL of 10 mg/mL LUCENTIS solution) is recommended to be initially administered by intravitreal injection once a month (approximately 28 days) for up to 3 months. Patients may be retreated if needed [(*see Clinical Studies 14.5*)].

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2.6 Preparation for Administration

Prefilled Syringe:

The prefilled syringe is sterile and is for single use only. **Do not** use the product if the packaging is damaged or has been tampered with.

To prepare LUCENTIS for intravitreal administration, please adhere to these instructions for use. Read all the instructions carefully before using the prefilled syringe.

The opening of the sealed tray and all subsequent steps should be done under aseptic conditions.

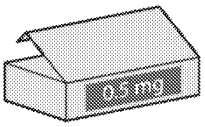
For the intravitreal injection, a 30-gauge x ½ inch sterile injection needle should be used (not provided).

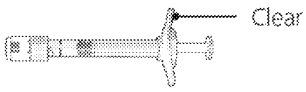
Note: the dose must be set to 0.05 mL.

Device description

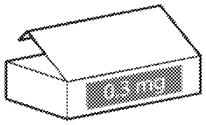
LUCENTIS prefilled syringes are available in 2 dose strengths:

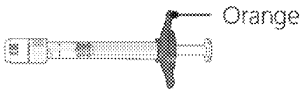
- LUCENTIS 0.5 mg prefilled syringe with a CLEAR finger grip.





- LUCENTIS 0.3 mg prefilled syringe with an ORANGE finger grip.





Check the labels on the LUCENTIS carton, syringe tray and prefilled syringe to make sure you have the correct dose strength.

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