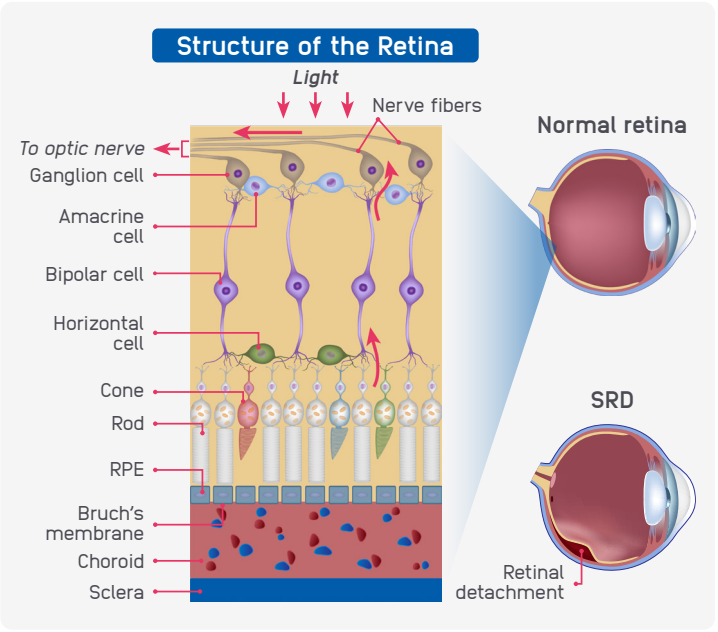
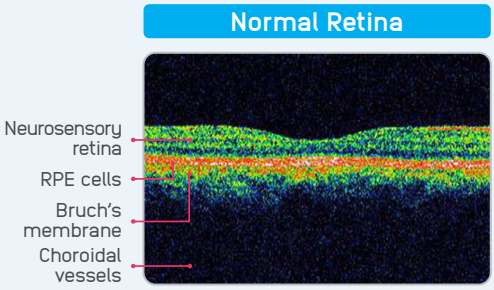
Pemazyre™ (pemigatinib): Overview of Ocular Toxicities and Guidance for Screening and Management

Serous Retinal Detachment (SRD)

- The **retinal pigment epithelium** (RPE) is a single layer of cells attached to the underlying Bruch's membrane that protects the retina from an excess of incoming light
- SRD occurs when fluid accumulates between the neurosensory retina and the RPE
- Symptoms include:
  - **Blurred vision**
  - **Visual floaters**
  - **Photopsia**
- Fibroblast growth factor (FGF) and its receptors play a role in normal cellular processes, such as the development of the eyes and corneas.[1,2] As FGFR is present throughout the retina, including the RPE, inhibition of FGFR may lead to interference with the integrity of the RPE[3]

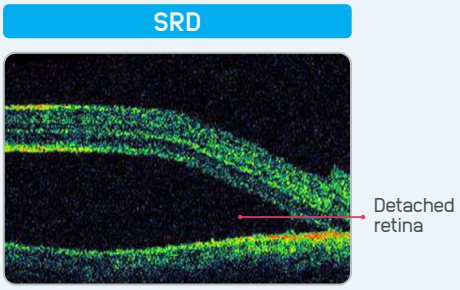


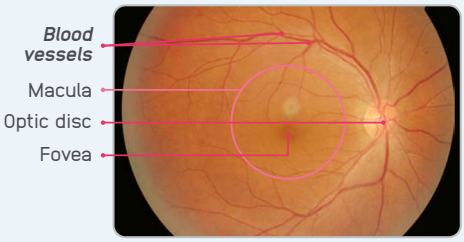
Assessing and Diagnosing SRD



Optical coherence tomography (OCT)[4,5]

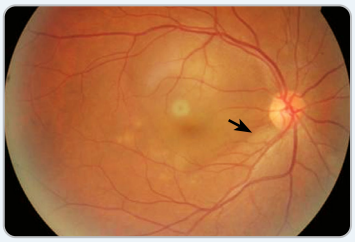
A noninvasive imaging test that delivers high-resolution cross-sectional images of the retina, anterior segment, optic nerve head, and retinal nerve fiber layer. It uses low-coherence interferometry of near-infrared light to acquire views of the eye, which resemble histological sections.





Fundoscopy (also known as ophthalmoscopy)[5,6]

A test conducted using an ophthalmoscope, which illuminates the retina through the pupil, usually dilated. This procedure allows for visualization of structures within the innermost parts of the eye (eg, retina, retinal blood vessels, optic nerve head).



Grading SRD

Increasing severity[7,8]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic	Exudative and visual acuity 20/40 or better	Rhegmatogenous or exudative detachment; operative intervention indicated; decline in vision (worse than 20/40 but better than 20/200)	Blindness (20/200 or worse) in the affected eye

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Incidence of Ocular Events in Pemigatinib Clinical Studies (N=466)[9]

SRD

7.5% (n=33) of patients experienced SRD (grade 3/4, 0.6% [n=3])[a]

Percentage of patients requiring a change in pemigatinib treatment:
1.7% dose interruption | 0.4% dose reduction | 0.4% permanent discontinuation

Almost all cases occurred within the first 6 months of exposure. The probability of having onset of SRD after the first 6 months of exposure was close to 0%

SRD resolved or proved self-limiting after dose interruption, reduction, or discontinuation in 50% of patients experiencing an SRD event

Dry eye

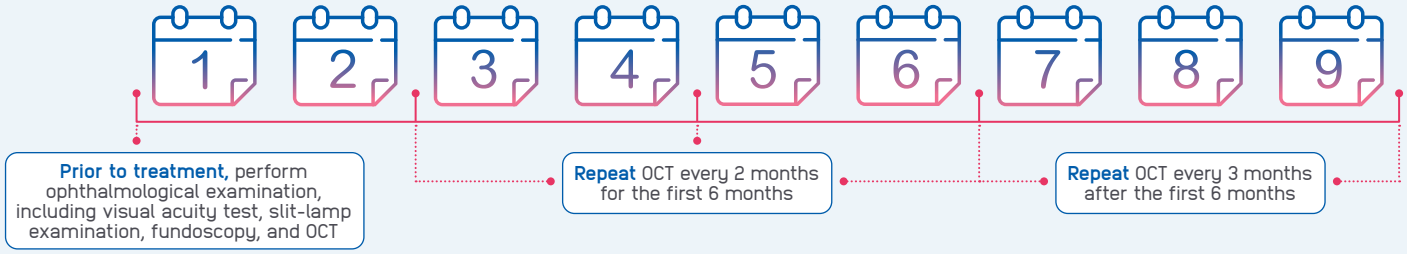
19.5% (n=91) of patients experienced dry eye (grade 3/4, 0.4% [n=2])

Symptoms may include recurrent burning, tearing, light sensitivity, and a sensation of a foreign body in the eye

Eyelash growth

Grade 1/2 growth of eyelashes (4.3%), trichiasis (4.9%), and trichomegaly (1.7%) have been reported with pemigatinib. One patient had grade 3/4 eyelash growth

Monitoring for and Managing Ocular Events With Pemigatinib



- Physicians should **inquire about visual symptoms at every patient visit.** If not too burdensome for the patient, an Amsler grid test may be administered at baseline and at each patient visit for more objective monitoring
- **For onset of visual symptoms, refer patients for urgent ophthalmologic evaluation,** with follow-up every 3 weeks until resolution or discontinuation of pemigatinib
- Additional educational material to assist healthcare professionals with the diagnosis and management of SRD is available through the manufacturer

Management of Ocular Events

SRD	
Asymptomatic	Continue pemigatinib at current dose. Monitor as described above
Moderate decrease in visual acuity (best corrected visual acuity 20/40 or better or ≤3 lines of decreased vision from baseline); limiting instrumental activities of daily living	Withhold pemigatinib until resolution. If decrease resolves within 3 weeks, resume at the next lower dose level
Marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or >3 lines of decreased vision from baseline up to 20/200); limiting activities of daily living	Withhold pemigatinib until resolution. If decrease resolves within 3 weeks, may resume at 2 dose levels lower. If decrease recurs, consider permanent discontinuation
Visual acuity worse than 20/200 in affected eye; limiting activities of daily living	Permanently discontinue
Dry eye	
Ocular demulcents (artificial tear drops) as needed	

Patient Counseling Tips

- Inform patients that pemigatinib may cause ocular toxicity, including dry eye and SRD
- Tell them to immediately alert their healthcare provider if they experience any visual changes (eg, blurred vision, flashes of light, or seeing black spots). These symptoms may require an urgent visit to an eye specialist
- Advise patients to use artificial tears or something similar to prevent or treat dry eye

For more information on SRD with pemigatinib, please consult the Product Monograph or contact Incyte at **1-833-309-2759** or **MedInfoCanada@incyte.com**

[a]Events categorized as SRD were chorioretinal folds, chorioretinal scar, chorioretinopathy, detachment of the retinal pigment epithelium, macular edema, maculopathy, retinal detachment, retinal disorder, retinal exudates, retinal edema, retinal pigmentation, retinal thickening, retinopathy, serous retinal detachment, and subretinal fluid.

References: 1. Raju R, et al. *J Signal Transduction*. 2014;104:1-16. **2.** Zhang J, et al. *PLoS One*. 2015;10(1):e0117089. **3.** van der Noll R, et al. *Cancer Treat Rev*. 2013;39:664-672. **4.** American Academy of Ophthalmology. Accessed June 2021. https://www.aao.org/eye-health/treatments/what-is-optical-coherence-tomography. **5.** Kim J, et al. *Korean J Opthal*. 2010;24:245-248. **6.** Schneiderman H. The Fundoscopic Examination. Walker HK, Hall WD, Hurst JW, eds. In: *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd ed. Butterworths; 1990:573-580. **7.** Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03. Accessed June 2020. https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf **8.** Abou-Alfa GK, et al. *Lancet Oncol*. 2020;21:671-684. **9.** Data on file, Incyte Corporation.

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