Accelerating the Journey from Idea to Utilization

Luxturna: A Cure for Inherited Retinal Disease

About I2U

Idea to Utilization (I2U) is an initiative committed to identifying and addressing the barriers impeding the uptake of breakthrough medicines across Canada. With foundational funding from Novartis, this collaborative mechanism is being led by Santis Health and guided by an independent panel of advisory board experts. **To learn more, visit www.i2u.ca**

Abstract

Luxturna delivers a new hope for the Inherited Retinal Disease (IRD) patient community as the first therapy to address previously irreversible progressive blindness in children and adults. This case study explores the implementation challenges with administering this specialized gene therapy in Canada. Through the analysis, four key barriers were found: (1) access to genetic testing including a limited number of genetic counselors in the country; (2) access to specialized medical personnel including IRD specialists; (3) the need for additional administrative infrastructure and care coordination; and (4) a requirement for cold chain management. Reflecting on these lessons is essential to bolster Canadian health systems' ability to provide Luxturna and other gene therapies that will impose similar implementation requirements on Canadian health systems.

Luxturna: The First Treatment for Inherited Eye Dystrophies

Globally, over 2 million people are affected by Inherited Retinal Dystrophies (IRDs), a large group of rare monogenic (i.e., variation in a single gene) diseases that primarily affect the retina. IRDs collectively represent the leading cause of progressive, early-onset vision loss, and often result in complete blindness.[i] There are over 250 different mutations that have been associated with IRDs – including a mutation in both copies of the RPE65 gene that encodes a protein for chemical reactions that are essential for normal vision.[ii] This specific mutation is ultra-rare, impacting 1 in 200,000 people worldwide.[iii] Although its exact prevalence rate in Canada is uncertain, CADTH estimates that there are 129-378 individuals with RPE65-mediated IRD.

Until recently, there was no available treatment for individuals suffering from RPE65-induced IRD – resulting in a debilitating prognosis for those afflicted with this condition.

However, breakthroughs in gene therapy have altered the treatment landscape for IRDs. The development and approval of Luxturna, a one-time gene therapy designed to correct the RPE65 mutation, has generated a new hope for the IRD community as the first treatment that targets the physiology of this disease.[iv]

Mechanism and Delivery

Luxturna is a gene therapy that can be directly applied to each eye. It helps restore vision in patients using a piece of DNA that contains a working copy of the RPE65 gene, packaged inside a modified, inactivated viral vector. During treatment, Luxturna is surgically delivered via sub-retinal injection (i.e., directly into the eye beneath the retina), sending a working copy of the gene to the RPE cell nucleus and enabling production of RPE65 proteins that are needed for sight.[v]

The treatment protocol for Luxturna can be distilled into the following steps:

1. **Genetic Testing** to determine eligibility for Luxturna. This can be done through platforms specific for identifying single-gene mutations or a panel of genetic mutations (typically takes 3-4 weeks to receive test results)

2. **Optical Coherence Tomography (OCT) and Vision Function Tests** to determine viability for Luxturna (i.e., does the patient have enough remaining functional retinal cells to receive treatment and restore sight).

3. **Subretinal Injection** to deliver Luxturna to the patient. This is a surgical injection performed under anesthesia and must be administered by an experienced retinal surgeon, at a specialized, certified treatment site. One eye is treated at a time, with treatment between each eye delivered 6 days apart.

Access in Canada

Health Canada approved Luxturna in October 2020 and CADTH released its positive recommendation for the drug in November 2020. Notably, Luxturna was the first therapeutic to undergo the CADTH Review Process for Cell and Gene Therapies[vi], that was especially designed to raise the implementation challenges for the public health system. Since then, 6 provinces have approved reimbursement for Luxturna, including Nova Scotia, Quebec, Ontario, Saskatchewan, Alberta, Saskatchewan, and British Columbia.[vii] [viii]

Implementation Challenges in Canada

The following implementation challenges are key barriers for the widespread use of Luxturna in Canada:

1. Access to Genetic Testing

A key requirement for this specialized gene therapy is ensuring patient eligibility – which must first be achieved through genetic testing. In a 2021 survey from CADTH, seven public drug plans confirmed that genetic testing for detecting the RPE65 mutation was not available locally and instead could only be accessed by sending samples out-of-province or out-of-country when requested by a geneticist or other appropriate governing body.[ix] In addition to Canada's limited in-country genetic testing capabilities, there is a shortage of genetic counsellors and related infrastructure – creating a major barrier to access for diagnosis of the underlying mutation for IRDs that is essential for treatment with Luxturna.

2. Access to Specialized Medical Personnel

Another requirement for delivering Luxturna is having a retinal surgeon administer treatment as well as an inherited retinal disease specialist recommend the drug and complete post-surgical evaluation. An essential factor for patient eligibility is having enough viable retinal cells that can be treated with this gene therapy. However, measuring this is a non-trivial procedure, as standard imaging using OCT technologies does not provide enough information and there is no minimum threshold to define sufficient viable retinal cells. As a result, additional visual acuity and visual field tests must be analyzed by an IRD specialist to more accurately establish whether the patient is fit to receive treatment.

There are approximately 100 retina specialists in Canada that provide the majority of medical and surgical retina related care [x], but only an estimated 7-10 of these individuals have the niche expertise to treat IRDs. Moreover, given the variable distribution of these specialists across Canada, there is an additional access challenge that demands the creation of solutions to serve patients with providers far from their jurisdictions. [Viii]

3. The Need for Cold Chain Management Infrastructure

Like many cell and gene therapies, Luxturna must be cryopreserved prior to shipment to treatment centres. Specifically, the active ingredient and diluent must be stored frozen at ≤-65˚C and be used immediately upon thawing. [xi] As a result, there must be

systems in place starting from the manufacturer, during transport, as well as at treatment centres to maintain the integrity of this gene therapy.

4. The Additional Need for Administrative Infrastructure and Care Coordination

Luxturna can only be administered in certified treatment sites with institution-accredited staff. In addition to specialized clinicians, pharmacy staff must be trained to receive and store Luxturna using specialized handling techniques. Furthermore, to deliver this gene therapy, there must be a team-based approach between the IRD specialist and retinal surgeon to create a surgical plan, alongside coordination with the pharmacy to prepare the drug for administration.

With a limited number of treatment centres in Canada, the challenge of access to this rare disease drug is further exacerbated, as is the demand for sustainable, alternative solutions to fulfill patient need.

Conclusion

Luxturna showcases a breakthrough gene therapy with substantial benefits for patients with RPE65 mutation induced IRDs. Although this drug supports a smaller patient population, it provides a valuable snapshot on implementation challenges that will be universal to future gene therapies in the pipeline.

Canada faces several key challenges to ensure equitable and effective implementation of Luxturna, and other specialized gene therapies. There is limited access to genetic testing and associated infrastructure, including genetic counsellors to support diagnosis and patient eligibility. Next, there are few specialists in the country with the expertise to diagnose and treat inherited retinal diseases, with a particular disparity in the distribution of these clinicians across each province and territory. As a specialized gene therapy, Luxturna also requires accredited treatment sites with care coordination between pharmacists and providers to ensure a seamless patient experience and a high standard of care. Finally, the drug the requires complex cold chain management regime right from the manufacturer to the patient for its safe administration.

Luxturna provides a niche case study as the first drug to undergo CADTH's specialized review process for cell and gene therapies. With special attention given to implementation challenges during HTA evaluation, Canada's provinces and territories were made more aware of some of the system adaptations needed to effectively deliver this novel therapeutic. However, there are further reforms still needed to achieve the full value of Luxturna and future cell and gene therapies under development.

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