

## Treatment of Diabetic Macular Edema with Iluvien (Fluocinoloneacetonide 0.19mg): Pharmacokinetics and Lipophilicity for the Primary Care Provider: Alyson Evans- Alimera Sciences, USA

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### Abstract

Diabetes mellitus is a plague worldwide. medical care providers, including advanced practice registered nurses, can play an important role in both the treatment of the disease and prevention of complications, particularly diabetic macular edema. A working comprehension of the ailment procedure and early referral is of fantastic significance, as are end of the day treatment choices patients may get from their ophthalmologist. ILUVIEN® (fluocinoloneacetonide (FAC) intravitreal embed) 0.19 mg is an embed infused into the attention (glassy) and utilized for the treatment of diabetic macular edema (DME) in patients who are previously treated with a course of corticosteroids and didn't have a clinically significant increase in pressure. The embed of ILUVIEN, a corticosteroid, gives a continuing microdose of FAC for as long as three years. One must comprehend the pharmacokinetics of a medicine as not all corticosteroids have an identical lipophilicity, water dissolvability and tissue penetration, as well as its lipophilic nature. The lipophilicity of FAC considers the ceaseless utilization of a microdose that's promptly retained into the retina, which clarifies why the FAC continuous microdose can settle or improve vision for several patients, while reducing retinal edema. It's important for the first care provider to understand the features of the drug and understand the implications of diabetic macular edema. Assertive, collaborative treatment is imperative for this patient population to take care of vision through their lifetime.

Diabetes as a National Epidemic it's been well documented that Type 2 DM (DM2) may be a national epidemic within the US. The Centers for Disease Control and Prevention estimated that in 2012, over 29 million people were diagnosed with DM2, and 1 in 4 people were undiagnosed. These statistics were even grimmer for those considered pre-diabetic: 86 million were prediabetic with 9 of 10 being unaware. Given these numbers, it's no surprise that

medical care providers (PCPs) would see more patients with a myriad of complications, including those affecting vision. Diabetic macular edema (DME) is one among them; improved appreciation of this disease process and its treatments could enable PCPs to form a timelier referral, thereby positively affecting the patient's vision over time, which when lost, may never be regained. Diabetic Macular Edema consistent with Bandello et al. DME, defined as "retinal thickening involving or approaching the middle of the macula, represents the foremost common explanation for vision loss in patients suffering from DM." DME may be a multi-factorial disease process which incorporates multiple inflammatory cytokines and biochemical factors driven by local and systemic disease processes (Figure 1). For the PCP, management of the systemic disease is a crucial part of preventing ocular complications, but early referrals to ophthalmologists and retina specialists are equally important. Understanding treatment options is critical, as some have systemic affect.

### ILUVIEN (fluocinoloneacetonide 0.19mg implant) as a Foundational Therapy for DME

ILUVIEN has been available in Europe since 2014 and within the US since 2015 (Figure 2). The US label indicates that it's for the treatment of diabetic macular edema (DME) in patients who are previously treated with a course of corticosteroids and didn't have a clinically significant rise in pressure. One trial of any ocular steroid, topical or intravitreal is sufficient to spot IOP hyper-responders. Within the FAME study, ILUVIEN met the first endpoint of proportion of patients with  $\geq 15$ -letter improvement in BCVA from baseline at month 24 with sustained improvements through 36 months. The secondary endpoint of reduced retinal thickness was also met through 36 months. Class effect of cataract development and pressure elevation were the foremost common adverse events. Similar results were also seen within the USER study (Figure 3). Reduction in treatment frequency was also noted versus other options like laser or anti angiogenic ocular injections. Pharmacokinetics and Lipophilicity ILUVIEN is

that the novel treatment option because it combines a wellknown steroid with an innovative technology. The fluocinoloneacetonide 0.19mg implant contains a lipophilic molecule which is encased during a semi-permeable, polyimide shell approximately 3.5 mm long by 0.37 mm in diameter. it's implanted through as 25G needle into the attention and may last up to 36 months. This technology allows ILUVIEN to get near zero order pharmacokinetics and treat the retina with endless microdose of steroid. the continual microdosing in turn may result in decreased frequency of treatment over time as demonstrated in Figure 3.

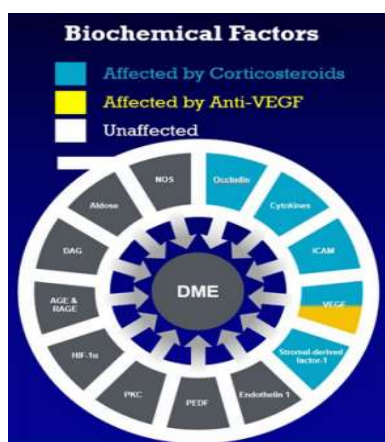


Figure 1: Biochemical Factors and therefore the Treatments that affect them in DME.

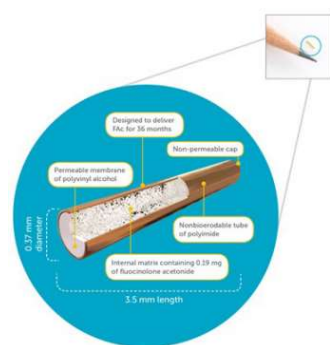


Figure 2: The ILUVIEN implant.

Implications for the PCP

Vision is of critical importance to the PCP because it affects multiple areas of patients' lives including:

- Visual-Motor Integration - Eye-hand/foot/body coordination.

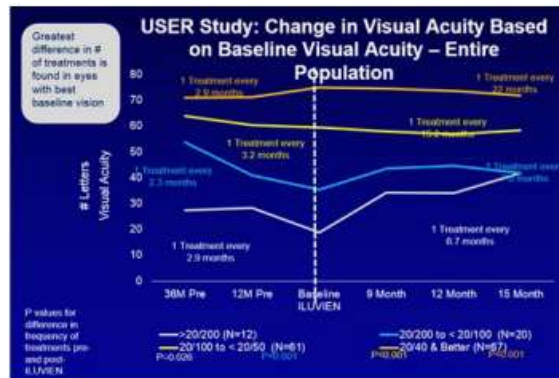


Figure 3: USER Study Visual Outcomes and Reduction in Treatment Frequency

- Visual-Auditory Integration - Associate what's seen and heard.
- Visual Memory - Remember and recall information that's seen.
- Visual Closure - Complete a visible picture supported seeing just some of the parts.
- Spatial Relationships - "Where I am" in reference to objects and space/where objects are in reference to each other .
- Figure-Ground Discrimination - Discern form and object from background. (Brainline.org).

The PCP plays an integral part in vision preservation. Systemic factors like hypertension, glycemic control, renal impairment and lipid control can have a negative impact on future vision, therefore appropriate management is vital for vision protection. As previously discussed, prompt referral and long-term collaboration with local ophthalmologists and retina specialists is a crucial part within the continuum of look after the diabetic patient. Appreciation of the pathophysiology and treatment of DME, like with ILUVIEN, can help enhance PCP competence within the care of the diabetic patient.

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