Suprachoroidal Injection of Pharmacologic Agents

**Number: 0777**

**Policy History**

- **Last Review**: 01/16/2020
- **Effective**: 02/06/2009
- **Next Review**: 08/27/2020

**Background**

Aetna considers suprachoroidal injection of pharmacologic agents experimental and investigational for all indications because the effectiveness of this approach has not been established.

Treatment of diseases of the posterior segment of the eye such as choroidal neovascularization presents a major challenge in ophthalmology. The posterior segment of the eye, including the retina, macula, and optic nerve, is difficult to access due to the recessed location within the orbital cavity.

Current drug delivery techniques to access the posterior segment of the eye include intra-vitreal injections, peri-ocular injections (i.e., subconjunctival, subtenon, or juxtascleral), and intra-vitreal implants. Drug delivery by injection into the...
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The suprachoroidal space is another technique that has recently been proposed in the treatment of posterior segment disease. The suprachoroidal space provides a potential route of access from the anterior region of the eye to the posterior region. The iScience Surgical Ophthalmic Microcannula, or iTrack (iScience Surgical Corporation, Menlo Park, CA) is designed to access ocular structures such as Schlemm’s canal, subretinal space, vitreous cavity, and the suprachoroidal space. The iTrack received 510(k) clearance from the U.S. Food and Drug Administration on June 22, 2004 as a flexible microcannula for atraumatic cannulation of spaces in the eye such as the anterior chamber and posterior segment, for infusion and aspiration of fluids during surgery, including saline and viscoelastics. The microcannula incorporates an optical fiber to allow transmission of light to the microcannula tip for surgical illumination and guidance.

There is inadequate evidence regarding the clinical utility of suprachoroidal injection of pharmacologic agents for the treatment of any ophthalmologic condition. Clinical outcome studies published in the peer-reviewed medical literature are needed to determine the value of this drug delivery method in the management of patients with diseases of the posterior segment of the eye.

In a pilot study, Rizzo et al (2012) evaluated the safety, feasibility, and preliminary effectiveness of suprachoroidal drug delivery with a microcatheter for the treatment of severe subfoveal hard exudates (SHE) in retinal vasculopathies. A total of 6 eyes of 6 patients with central or branch retinal vein occlusion or diffuse diabetic macular edema accompanied by massive refractory SHE underwent a single treatment with bevacizumab and triamcinolone administered to the submacular suprachoroidal space via a microcatheter introduced at the pars plana and advanced posteriorly. The main outcome measures included best-corrected visual acuity, vascular leakage, macular thickness, extent of SHE, and...
complications. Mean follow-up was 12 months; 3 eyes had central retinal vein occlusion, 1 had branch retinal vein occlusion, and 2 had chronic diabetic macular edema. Best-corrected visual acuity improved by greater than or equal to 2 lines in 4 eyes and remained stable in 2 eyes. At 1 month to 2 months post-procedure, SHE was almost completely resolved in all eyes and macular edema was significantly reduced. There were no surgical or post-operative complications. The authors concluded that suprachoroidal infusion of drugs can be effective in reabsorbing massive SHE. The findings of this pilot study needs to be validated by well-designed studies.

Tetz et al (2012) examined the safety and feasibility of using a microcatheter for drug delivery in the suprachoroidal space in eyes with advanced, exudative, age-related macular degeneration (ARMD) unresponsive to conventional therapy. A unique microcatheter was used to deliver a drug combination consisting of bevacizumab and triamcinolone to the submacular suprachoroidal space. A total of 21 eyes of 21 patients with choroidal neovascularization (CNV) secondary to advanced, exudative ARMD were followed over a 6-month post-procedure period. The microcatheter was successfully and atraumatically inserted into the suprachoroidal space of all eyes. No serious intra-operative or postoperative complications including suprachoroidal hemorrhages were encountered. Post-surgically, complications consisted of 1 eye experiencing a transient elevation in intra-ocular pressure at 3 months, which was medically controlled, and 2 eyes (10.5 %) with an apparent increase in nuclear sclerotic cataracts. The authors concluded that suprachoroidal drug administration was achieved without serious complication using a novel microcatheter. They noted that direct drug delivery to the choroid can potentially increase local tissue drug levels and drug effectiveness for the treatment of ARMD and other diseases associated with CNV. These preliminary findings need to be validated by further studies.
Rai and colleagues (2015) stated that the development of safe and convenient drug delivery strategies for treatment of posterior segment eye diseases is challenging. Although intra-vitreal injection has wide acceptance among clinicians, its use is associated with serious side-effects. Recently, the suprachoroidal space (SCS) has attracted the attention of ophthalmologists and pharmaceutical formulators as a potential site for drug administration and delivery to the posterior segment of the eye. These investigators reviewed the major constraints of drug delivery to the posterior eye segment, key anatomical and physiological features of the SCS and drug delivery applications of this route with emphasis on micro-needles along with future perspectives.

Pearce and associates (2015) noted that emerging developments and research for drug delivery to the posterior segment of the eye offer a promising future for the treatment of vitreo-retinal disease. As new technologies enter the market, clinicians should be aware of new indications and ongoing clinical trials. These researchers summarized the advantages and shortcomings of the most commonly used drug delivery methods, including vitreous dynamics, physician sustainability and patient preferences. Currently available, intra-vitreal, corticosteroid-release devices offer surgical and in-office management of retinal vascular disease and posterior uveitis. The SCS offers a new anatomic location for the delivery of lower dose medications directly to the target tissue. Implantable drug reservoirs would potentially allow for less frequent intra-vitreal injections reducing treatment burdens and associated risks. Newer innovations in encapsulated cell technology offer promising results in early clinical trials. The authors concluded that although pars plana intra-vitreal injection remains the mainstay of therapy for many vitreo-retinal diseases, targeted delivery and implantable eluting devices are rapidly demonstrating safety and efficacy. They stated that these therapeutic modalities offer promising options for the vitreo-retinal therapeutic landscape.
Venkatesh and Takkar (2017) noted that the prevalence of myopia and its severe/progressive visually impairing forms is increasing worldwide. Most of the preliminary clinical research has focused on rehabilitation and treatment of its complications. Pharmacological prevention of myopic progression has shown encouraging results recently and currently the scleral structure is believed to be responsible for disease progression. These investigators hypothesized injecting a biological cement in the potential space between the choroid and the sclera to halt the progressive elongation of the eye while preventing complications related to myopia.

In a prospective cohort study within a randomized, controlled phase-II clinical trial, Willoughby and colleagues (2018) evaluated choroidal and supra-choroidal changes following supra-choroidal injection of triamcinolone acetonide injectable suspension (CLS-TA), in eyes with macular edema due to retinal vein occlusion (RVO). Enhanced depth imaging optical coherence tomography (EDI-OCT) images were analyzed from 38 eyes of 38 treatment-naive patients with macular edema due to RVO, enrolled in the prospective Suprachoroidal Injection of Triamcinolone Acetonide with Intravitreal Aflibercept in Subjects with Macular Edema Due to Retinal Vein Occlusion (TANZANITE) study who received either a supra-choroidal injection of CLS-TA with an intra-vitreal (IVT) injection of aflibercept (combination arm) or only an IVT injection of aflibercept (monotherapy arm), followed by monthly IVT aflibercept injections in both arms based on pro re nata criteria. Macular choroidal thickness measured to the outer choroidal vessel lumen (vascular choroidal thickness, VCT), outer choroid stroma (stromal choroidal thickness, SCT), or inner scleral border (total choroidal thickness, TCT) showed no significant changes over 3 months in both study arms (p = 0.231 to 0.342). Eyes that received combination therapy showed a trend toward thickening of the supra-choroidal space (SCS) compared with monotherapy alone (13.4 μm versus 5.3 μm at 3 months; p = 0.077). In the 15 eyes that showed a
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Supra-choroidal CLS-TA injection (16.2 μm to 27.8 μm at 3 months; p = 0.033). The authors concluded that supra-choroidal injection of CLS-TA did not alter choroidal thickness in eyes with macular edema due to RVO, but may result in expansion of the SCS.

Hartman and Kompella (2018) noted that even though the very thought of an injection into the eye may be frightening, an estimated 6 million IVT injections were made in the U.S. during 2016. With the introduction of new therapeutic agents, this number is expected to increase. In addition, drug products that are injectable in ocular compartments other than the vitreous humor are expected to enter the back of the eye market in the not so distant future. Besides the IVT route, some of the most actively investigated routes of invasive administration to the eye include peri-ocular, sub-retinal, and SC routes. While clinical efficacy is the driving force behind new injectable drug product development for the eye, safety is also being improved with time. In the case of IVT injections, the procedural guidelines have evolved over the years to improve patient comfort and reduce injection-related injury and infection. Similar advances are anticipated for other routes of administration of injectable products to the eye. In addition to procedural improvements, the design of needles, particularly those with smaller diameters, length, and controlled bevel angles are expected to improve overall safety and acceptance of injected ophthalmic drug products. A key development in this area is the introduction of microneedles of a length less than a millimeter that can target the SC space. In the future, needles with smaller diameters and lengths, potentially approaching nano-dimensions, are expected to revolutionize ophthalmic disease management.

Suprachoroidal Corticosteroid for the Treatment of Non-Infectious Uveitis / Chorio-Retinal Diseases
In a phase I/II open-label, clinical trial, Goldstein and colleagues (2016) evaluated the safety, tolerability, and preliminary efficacy of suprachoroidal injection of triamcinolone acetonide (TA) in patients with non-infectious uveitis. A single suprachoroidal injection of 4-mg TA in 100 μl was performed in the study eye of patients with non-infectious intermediate, posterior, or pan-uveitis, and follow-up obtained for 26 weeks. A total of 9 individuals with chronic uveitis were enrolled. There were 38 reported adverse events (AEs); most were mild or moderate in severity. Approximately 50% of the AEs were ocular. The most common AE was reported by 4 subjects who experienced ocular pain at or near the time of the injection. All systemic AEs were unrelated to study drug. No steroid-related increases in intra-ocular pressure (IOP) were observed and no subject required IOP-lowering medication. All 8 efficacy-evaluable subjects had improvements in visual acuity (VA); 4 subjects, who did not need additional therapy, had on average a greater than 2-line improvement in VA through week 26; 3 of 4 had macular edema at baseline, and 2 of 3 had at least a 20% reduction in macular edema at week 26. The authors concluded that the safety and preliminary efficacy data support further investigations of suprachoroidally administered TA as a therapeutic option for the treatment of non-infectious uveitis.

Habot-Wilner and colleagues (2019) stated that delivery of pharmaceuticals to the posterior segment presents challenges that arise from the anatomy and clearance pharmacokinetics of the eye. Systemic and several local administration options [topical, peri-ocular, IVT and sub-retinal] are in clinical use, each with a unique benefit-to-risk profile shaped by factors including the administered agent, frequency of dosing, achievable pharmaceutical concentrations within posterior segment structures versus elsewhere in the eye or the body, invasiveness of the procedure and the inherent challenges with some administration methods. The use of the SCS, which is the region between the sclera and the choroid, is being explored as a potential approach to target pharmacotherapies to the posterior segment via a minimally invasive injection.
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Pre-clinical data on agents such as vascular endothelial growth factor (VEGF) inhibitors and triamcinolone acetonide (TA) indicated that administration via suprachoroidal injection resulted in more posterior distribution of the pharmacologic agent, with higher exposure to the sclera, choroid, retinal pigment epithelium cells and retina, and lesser exposure to the anterior segment, than observed with IVT administration. Based in part on these findings, clinical trials have examined the safety and efficacy of suprachoroidal administration of pharmacologic therapies in conditions affecting the posterior segment. Data on a proprietary formulation of TA administered by suprachoroidal injection showed improvement in anatomic and visual outcomes in subjects with non-infectious uveitis, with the potential to mitigate the known risks of cataract and increased IOP associated with the use of intra-ocular corticosteroids. The authors concluded that suprachoroidal administration appeared to be a promising treatment modality and is also in the early stages of investigation for other possible applications, such as injection of anti-glaucoma agents into the anterior chamber for long-lasting control of elevated IOP, and as a mode of delivery for gene- or cell-based therapies for retinal disorders.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

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<th>Code</th>
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CPT codes not covered for indications listed in the CPB:
The above policy is based on the following references:


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0777 Suprachoroidal Injection of Pharmacologic Agents

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania updated 01/16/2020

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