MEDICAL POLICY

Capital BLUE

POLICY TITLE	SUPRACHOROIDAL DELIVERY OF PHARMACOLOGIC AGENTS
POLICY NUMBER	MP- 4.032

Original Issue Date (Created):	**October 30, 2012**
Most Recent Review Date (Revised):	**November 26, 2013**
Effective Date:	**February 1, 2014**

I. POLICY

Suprachoroidal delivery of a pharmacologic agent is considered **investigational,** as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-references

MP-2.128 Bevacizumab (Avastin™)
MP-2.028 Eye Care
MP-2.149 Aqueous Shunts and Devices for Glaucoma
MP-2.159 Intravitreal Corticosteroid Implants
MP 2.163 Intravitreal Angiogenesis Inhibitors for Choroidal Vascular Conditions
MP-2.164 Intravitreal Angiogenesis Inhibitors for Retinal Vascular Conditions
MP-4.023 Transpupillary Thermotherapy for Treatment of Choroidal Neovascularization
MP 4.008 Photodynamic Therapy for Choroidal Neovascularization

II. PRODUCT VARIATIONS

[N] = No product variation, policy applies as stated

[Y] = Standard product coverage varies from application of this policy, see below

[N] Capital Cares 4 Kids
[N] PPO
[N] HMO
[N] SeniorBlue HMO
[N] SeniorBlue PPO
[N] Indemnity
[N] SpecialCare
[N] POS
[Y] FEP PPO*

* Refer to FEP Medical Policy Manual MP-9.03.19 Suprachoroidal Delivery of Pharmacologic Agents. The FEP Medical Policy manual can be found at: www.fepblue.org

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III. DESCRIPTION/BACKGROUND

Delivery of pharmacologic agents to the suprachoroidal space is being investigated for treatment of posterior eye segment diseases.

The structure of the eye is classified under two subheadings: 1) anterior segment, and 2) posterior segment. The anterior segment consists of the front one-third of the eye that includes; pupil, cornea, iris, ciliary body, aqueous humor, and lens; the posterior segment consists of the back two-thirds of the eye that includes vitreous humor, retina, choroid, macula, and optic nerve. Posterior segment ocular diseases (e.g., age-related macular degeneration, diabetic neuropathy) are the most prevalent causes of visual impairment. The following is a list of the various routes for ocular drug administration:

- Invasive drug administration to intraocular cavities
  - Suprachoroidal injections
  - Intravitreal surgery
  - Intravitreal injections
  - Intracameral surgery
  - Subretinal injection
  - Intracameral injections

Invasive periocular and scleral modes of drug administration

- Intrascleral surgery
- Episcleral surgery
- Periocular injections
- Subconjuctival injections
- Transscleral diffusion from controlled release systems

Noninvasive methods

- Topical administration on the eye

Systemic administration

- Intravenous infusion and injection
- Oral

Many ocular diseases are treated with either topical or systemic medications. Topical application has remained the most preferred delivery route due to ease of administration. Topical application is useful in the treatment of disorders affecting the anterior segment of the eye. Although topical and systemic routes are convenient, lack of bioavailability and failure to deliver therapeutic levels of drugs to the retina has prompted vision scientists to continue to explore alternative routes of administration.

One potential advantage of suprachoroidal injection would be the ability to minimize systemic adverse effects while delivering higher local tissue levels of drugs. This proposed benefit assumes that high local levels lead to improved outcomes. Weighed against this potential benefit is the risk of localized tissue damage from the microcannula. A microcannula system combines a drug delivery channel with a fiberoptic light source for localization of the cannula tip. This technique is being investigated for the treatment of subchoroidal neovascularization related to diseases of the retina.

Regulatory Status

The iTrack™ (iScience Interventional), which is a flexible microcannula designed to allow atraumatic cannulation of spaces in the eye for infusion and aspiration of fluids during surgery, received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA). The microcannula incorporates an optical fiber to allow transmission of light to the microcannula tip for surgical illumination and guidance. The microcannula "is indicated for fluid infusion and aspiration, as well as illumination, during surgery."

IV. RATIONALE

At the time this policy was created, searches of the MEDLINE database did not identify any clinical studies on the suprachoroidal delivery of pharmacologic agents. One review discussed industry-funded tests of the suprachoroidal injection technique in pig eyes. (1) Triamcinolone (3 mg) was found to remain at detectable levels in the posterior tissues of the pig eye for up to 120 days. Adverse events included infection (2 of 94), scleral ectasia (4 of 94), choroidal blood flow abnormalities (4 of 94), and inflammation (6 of 94). Some cannula tip designs resulted in snag lesions in the pigment epithelium, and the suprachoroidal space was found to separate from the sclera following injection of sodium hyaluronate but returned to a normal position after 1 month. Clinical trials in humans were reported to be ongoing.

Periodic literature updates, the most recent performed for the period of August 2011 through October 2012, have identified 2 small studies from the same group of investigators. One was a prospective case series that used a microcatheter (iTRACK) for suprachoroidal drug delivery for the treatment of advanced, chronic macular edema with large subfoveal hard exudates in 6 eyes of 6 patients. (2) The subfoveal hard exudates were reported to be almost completely resolved at 1-2 months following a single suprachoroidal infusion of bevacizumab and triamcinolone, with no surgical or postoperative complications.

These investigators also published an industry-sponsored retrospective analysis of 21 eyes with choroidal neovascularization (CNV) secondary to age-related macular degeneration that were treated with bevacizumab and triamcinolone using the iTRACK microcatheter. (3) Patients were included in the analysis if they had been unresponsive to at least 3 prior treatments including thermal laser photocoagulation, photodynamic therapy, or intravitreal

injections of pegaptanib, bevacizumab, or ranibizumab. Best corrected visual acuity (BCVA) did not improve significantly from baseline through the 6-month follow-up (0.98 logMAR at baseline, 0.92 logMAR at 1 month and 0.93 logMAR at 6 months). There was a significant decrease in central foveal thickness (407.2 microns at baseline to 333.3 microns at 1 month). There was no visible evidence of retinal or choroidal tissue trauma in this safety and feasibility study.

A 2008 review article by Del Amo and Urtti discussed the emerging methods of ocular drug delivery, which include: polymeric-controlled release injections and implants; nanoparticulates; microencapsulated cells; iontophoresis; and gene therapy. (4) The authors note the biggest drug delivery challenge is to develop effective methods for posterior segment therapies that would also be applicable for outpatient use.

Summary

Evidence to date consists of 2 small case series from the same group of investigators in Europe. Controlled trials are needed to evaluate the safety and efficacy of suprachoroidal drug administration compared to the standard of care. Current evidence is insufficient to determine whether suprachoroidal delivery of pharmacologic agents improves the net health outcome. Thus, this procedure is considered investigational.

V. DEFINITIONS

ANGIOGENESIS refers to the development of blood vessels.

CHOROID is the thin, highly vascular membrane covering the posterior five sixths of the eye between the retina and the sclera.

CHOROIDAL NEOVASCULARIZATION refers to the abnormal formation of new blood vessels usually on or under the retina, usually seen in diabetic retinopathy, blockages of central retinal vision and macular degeneration.

EXUDATION refers to the pathological oozing of fluids, usually the result of inflammation.

MACULAR DEGENERATION refers to loss of pigmentation in the macular region of the retina, usually affecting persons over age fifty (50); a common disease of unknown etiology that produces central visual field loss and is the leading cause of permanent blindness in the United States.

OCULAR refers to the eye or vision.

PHOTODYNAMIC refers to the effects of light on biological, chemical, or physical systems.

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VI. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital for benefit information.

VII. DISCLAIMER

Capital's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. REFERENCES

1. *Olsen T. Drug delivery to the suprachoroidal space shows promise. Retina Today; March/April 2007. 2007. Available online at: http://www.retinatoday.com/Html%20Pages/0307/0307_feature_olsen.pdf. Last accessed October, 2012.*
2. *Rizzo S, Ebert FG, Bartolo ED et al. Suprachoroidal drug infusion for the treatment of severe subfoveal hard exudates. Retina 2012; 32(4):776-84.*
3. *Tetz M, Rizzo S, Augustin AJ. Safety of submacular suprachoroidal drug administration via a microcatheter: retrospective analysis of European treatment results. Ophthalmologica 2012; 227(4):183-9.*
4. *Del Amo EM, Urtti A. Current and future ophthalmic drug delivery systems. A shift to the posterior segment. Drug Discov Today 2008; 13(3-4):135*-43.
5. *Taber's Cyclopedic Medical Dictionary, 19th edition.*

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IX. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore not covered:

CPT Codes®								
0186T								

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X. POLICY HISTORY

MP 4.032	**CAC 10/28/12** Adopting BCBSA**.** • New policy • Extracted information regarding Suprachoroidal Delivery of Pharmacologic Agents from MP 4.008 Ocular Therapy. • No change to policy statement, remains investigational. • Codes reviewed 9/19/2012 klr
	CAC 11/26/13 Consensus review. References updated but no changes to the policy statement. Rationale added. FEP variation revised to refer to the FEP medical policy manual.

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