Conjunctival Incision with Posterior Juxtascleral Placement of Anecortave Acetate Depot Suspension

Archived Medical Policy

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Policy # 00192
Original Effective Date: 02/23/2009
Archived Date: 04/25/2012

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers conjunctival incision with posterior juxtascleral placement of anecortave acetate depot suspension to be investigational.*

Background/Overview
Many new pharmacologic agents promoting angiostasis for the treatment of age-related macular degeneration are in development including anecortave acetate (Retaane®) for depot suspension. Anecortave acetate is a synthetic cortisone that has been chemically modified into an angiostatic cortisone that inhibits the proteolysis required for vascular endothelial cell migration, thereby inhibiting ocular neovascularization. Anecortave acetate is a slow-release depot suspension that may be delivered at 6-month intervals and allows for sustained delivery to the affected area near the macula when administered by the novel procedure of posterior juxtascleral placement.

In the conjunctival incision with posterior juxtascleral placement of the depot suspension procedure, after topical anesthesia, a 1.0 –1.5-mm to 2–3 mm incision into the superotemporal quadrant of the orbit is made 8mm posterior to the limbus between the superior and lateral rectus muscle insertions. The incision is made down through the conjunctiva and Tenon’s capsule to reveal bare white sclera but the sclera is not incised. A specially designed, blunt-tipped, curved, 56° cannula is then carefully inserted into the juxtascleral (episcleral) plane between the outer surface of the sclera and Tenon’s capsule and fed forward until the cannula tip is near the macula. Gentle pressure is applied around the inserted cannula during administration of the depot suspension and removal of the cannula to prevent reflux and a semi-pressure patch is applied.

Advantages to the posterior juxtascleral placement of a pharmacologic agent may include reduced risk for retinal detachment, endophthalmitis and other safety issues associated with repeated intravitreal injections (a common route of administration for pharmaceutical agents in the treatment of ocular disorders).

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
Retaane (Alcon Research, Ltd.) received an approvable letter from the FDA in May 2005 for treatment of age-related macular degeneration but has not yet received final FDA approval.
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Centers for Medicare and Medicaid Services (CMS)
Centers for Medicare and Medicaid Services do not have a national coverage policy addressing the use of conjunctival incision with posterior juxtascleral placement of anecortave acetate depot suspension.

Rationale/Source
The procedure of conjunctival incision with posterior juxtascleral placement of anecortave acetate depot suspension has been performed over 350 times in 128 patients with subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (ARMD) in the Anecortave Acetate Clinical Study Group. The Anecortave Acetate Clinical Study, a blinded, randomized controlled trial, was conducted at 18 clinical sites in the United States and the European Union, followed up patients for 2 years, and was completed in June 2003. Some patients in the study had this procedure performed several times in the same superotemporal quadrant, including 4 times in 48 patients and at least 2 times in 81 patients. No serious clinically relevant treatment-related safety issues were reported from either the study medication (anecortave acetate) or the procedure for administration. The 2 most observed adverse events were cataracts and decreased visual acuity (> =; 4logMAR lines or > =; 20logMAR letters), which occurred in both study and placebo groups at similar rates. Cataracts were found in 27% and 30% and decreased visual acuity was noted in 25% and 30% in the treatment and placebo groups, respectively. These occurrences included study eyes, untreated eyes, or both eyes and are commonly experienced in patients with ARMD. Other adverse events that were reported as mild and transient included ptosis, ocular pain, visual abnormalities (e.g., hazy vision, black spots, light flashes), subconjunctival hemorrhage and ocular pruritis.

In summary, conjunctival incision with posterior juxtascleral placement of anecortave acetate depot suspension or placebo appears to be technically feasible and clinically safe in this study of 128 patients. The adverse events reported were mostly mild and transient and were commonly experienced with ocular procedures. However, anecortave acetate has not yet received FDA approval, and further studies on long-term health outcomes are needed.

An October 2005 TEC Special Report on the treatment of age-related macular degeneration supports the conclusions given above. The Special Report noted, although suggestive, the results of the Anecortave Acetate Clinical Study Group lack robustness. The trial was only partially blinded and censoring was substantial. No dose-effect was evident with 15 mg being superior to placebo and 30 mg being the least efficacious. The analytical approach to missing data was suboptimal, and whether assumptions of repeated measures (analysis of variance [ANOVA]) were met (correlations equal over time) was unstated. Finally, adverse events, even transient, were frequent among both treated and placebo groups.

The Anecortave Acetate Clinical Study Group published results of a phase III noninferiority trial of anecortave acetate compared with photodynamic therapy. Patients (n = 530) were randomized to treatment with anecortave acetate and sham photodynamic therapy (n = 263) or photodynamic therapy and placebo...
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(n = 267). Eighty-two percent of the subjects were available for the 12-month evaluation, with similar drop-out rates in the 2 groups. The percentage of patients who lost more than 3 lines of letters was similar in the 2 groups (51% for photodynamic therapy and 55% for anecortave acetate). However, the confidence interval was greater than the 7 percentage points specified by the regulatory agencies and this treatment did not meet statistical criteria for noninferiority. Clinical safety data from 313 patients enrolled in the anecortave acetate studies were also reported. With the exception of nearly 10% retinal detachment with juxtascleral depot injections (either anecortave acetate or vehicle), this was reported to be a safe and well-tolerated procedure. Clinical trials are in progress to evaluate the dose (15 or 30 mg) and administration frequency (every 3 or 6 months), and to determine if administration of anecortave acetate in patients with dry age-related macular degeneration reduces the risk of developing choroidal neovascularization. This procedure has not been demonstrated to be at least as safe and effective as currently available treatments, and is therefore considered investigational.

A Cochrane review of the Anecortave Acetate Clinical Study (AACS) described above concluded that, “anecortave acetate 15 mg may have a slight benefit in treating subfoveal CNV related to AMD. However, the data presented in the AACS are of low quality given the high attrition rate, inadequate sample size, lack of adjustment for multiple comparisons and potential bias in the non-randomized re-treatment schedule.” The author’s overall conclusion was that “given the small size and quality of the trials reported, there is little evidence to support the use of steroids in the treatment of neovascular AMD.” Clinical studies of anecortave acetate are in progress for the treatment of other conditions. The available scientific evidence does not permit conclusions concerning the effect of this treatment on health outcomes. Therefore, the coverage statement remains unchanged.

2009 Update

In July 2008, Alcon Inc. announced that it has terminated the development program designed to evaluate the benefit of anecortave acetate treatment on the risk for developing sight-threatening choroidal neovascularization secondary to AMD. The press releases stated: “The decision followed a planned interim analysis of studies C-02-60 A and B that was performed after 2,546 patients had completed the 24 month time point. In this analysis, anecortave acetate showed no effect on the primary or secondary endpoints. In addition to terminating studies C-02-60 A and B, the company also terminated 2 smaller studies with an identical design that were being conducted in Asia, C-04-30 and C-05-34.”

In July 2009, Alcon officials also announced anecortave acetate would be withdrawn as a potential glaucoma therapy. While this application is not discussed previously in this policy, the announcement appears to indicate an end to development work on this agent. Alcon officials noted that “…the amount of IOP [intraocular pressure] reduction and the responder rate provided by even the highest dose were not sufficient to support this novel approach…”
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Since no anecortave acetate depot products have been approved by the FDA as of August 2009, the coverage statement remains unchanged. This treatment is considered investigational.

References

Coding
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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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Policy History

Original Effective Date: 02/23/2009
01/04/2006 Medical Director review
01/17/2006 Medical Policy Committee review
02/23/2006 Quality Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
01/10/2007 Medical Director review
01/17/2007 Medical Policy Committee approval
01/07/2009 Medical Director review
01/14/2009 Medical Policy Committee approval
01/07/2010 Medical Policy Committee approval
01/20/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/06/2011 Medical Policy Committee review
01/19/2011 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/12/2012 Medical Policy Committee review. Recommend archiving.
04/25/2012 Medical Policy Implementation Committee approval. Archived.

Next Scheduled Review Date: Archived medical policy.

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
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1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

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