Corneal Collagen Cross-linking

Policy # 00325
Original Effective Date: 12/21/2011
Current Effective Date: 06/08/2020

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.

Note: Implantation of Intrastromal Corneal Ring Segments is addressed separately in medical policy 00164.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider corneal collagen cross-linking (CXL) using riboflavin and ultraviolet A (UVA) as a treatment of progressive keratoconus in patients who have failed conservative treatment (e.g., spectacle correction, rigid contact lens) to be **eligible for coverage.****

Note: The correction of refractive errors of the eye, including but not limited to radial keratotomy and laser surgery, are excluded from coverage under medical benefits on majority of member contracts. In addition, treatment of complications of non-covered services are also excluded from coverage. If it is determined that corneal ectasia was a complications of refractive surgery, request for corneal collagen cross-linking will be denied as not a covered benefit.

When 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 corneal collagen cross-linking (CXL) using riboflavin and ultraviolet A (UVA) for all other indications to be **investigational.***

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Policy Guidelines

Progressive keratoconus is defined as one or more of the following:

- An increase of 1 diopter (D) in the steepest keratometry value
- An increase of 1 D in regular astigmatism evaluated by subjective manifest refraction
- A myopic shift (decrease in the spherical equivalent) of 0.50 D on subjective manifest refraction
- A decrease ≥0.1 mm in the back optical zone radius in rigid contact lens wearers where other information was not available.

Background/Overview

Treatment of Keratoconus and Ectasia

The initial treatment for keratoconus often consists of hard contact lenses. A variety of keratorefractive procedures have also been attempted, broadly divided into subtractive and additive techniques. Subtractive techniques include photorefractive keratectomy or laser in situ keratomileuses, although generally, results of these techniques have been poor. Implantation of intrastromal corneal ring segments (see medical policy 00164) is an additive technique in which the implants are intended to reinforce the cornea, prevent further deterioration, and potentially obviate the need for penetrating keratoplasty. Penetrating keratoplasty (ie, corneal grafting) is the last line of treatment. About 20% of patients with keratoconus will require corneal transplantation. All of these treatments attempt to improve the refractive errors but are not disease-modifying.

Treatment options for ectasia include intraocular pressure-lowering drugs and intracorneal ring segments. Frequently, penetrating keratoplasty is required.

None of the currently available treatment options for keratoconus and corneal ectasia halt the progression of the disease, and corneal transplantation is the only option available when functional vision can no longer be achieved.

Corneal collagen cross-linking has the potential to slow the progression of the disease. It is performed with the photosensitizer riboflavin (vitamin B2) and ultraviolet A irradiation. There are 2 protocols for corneal collagen cross-linking:

1. Epithelium-off corneal collagen cross-linking (also known as "epi-off"): In this method, about 8 mm of the central corneal epithelium is removed under topical anesthesia to allow

better diffusion of the photosensitizer riboflavin into the stroma. Following de-epithelialization, a solution with riboflavin is applied to the cornea (every 1-3 minutes for 30 minutes) until the stroma is completely penetrated. The cornea is then irradiated for 30 minutes with ultraviolet A 370 nm, a maximal wavelength for absorption by riboflavin, while the riboflavin continues to be applied. The interaction of riboflavin and ultraviolet A causes the formation of reactive oxygen species, leading to additional covalent bonds (cross-linking) between collagen molecules, resulting in stiffening of the cornea. Theoretically, by using a homogeneous light source and absorption by riboflavin, the structures beyond a 400-mm thick stroma (endothelium, anterior chamber, iris, lens, retina) are not exposed to an ultraviolet dose that is above the cytotoxic threshold.

2. Epithelium-on corneal collagen cross-linking (also known as "epi-on" or transepithelial): In this method, the corneal epithelial surface is left intact (or may be partially disrupted) and a longer riboflavin loading time is needed.

Currently, the only corneal collagen cross-linking treatment approved by the U.S. Food and Drug Administration (FDA) is the epithelium-off method. There are no FDA approved corneal collagen cross-linking treatments using the epithelium-on method. Corneal collagen cross-linking is being evaluated primarily for corneal stabilization in patients with progressive corneal thinning, such as keratoconus and corneal ectasia following refractive surgery. Corneal collagen cross-linking may also have anti-edematous and antimicrobial properties.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In 2016, riboflavin 5′-phosphate in 20% dextran ophthalmic solution (Photrexa Viscous®‡; Avedro) and riboflavin 5′-phosphate ophthalmic solution (Photrexa®‡; Avedro) were approved by the FDA for use with KXL System in corneal corneal collagen cross-linking for the treatment of progressive keratoconus and corneal ectasia after refractive surgery.

Rationale/Source

Corneal collagen cross-linking is a photochemical procedure approved by the U.S. Food and Drug Administration (FDA) for the treatment of progressive keratoconus and corneal ectasia. Keratoconus is a dystrophy of the cornea characterized by progressive deformation (steepening) of the cornea

while corneal ectasia is keratoconus that occurs after refractive surgery. Both lead to functional loss of vision and need for corneal transplantation.

For individuals who have progressive keratoconus who receive corneal collagen cross-linking using riboflavin and ultraviolet A, the evidence includes multiple randomized controlled trials (RCTs), systematic reviews, and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary endpoint (an intermediate outcome) of reducing maximum corneal curvature by 1 diopter (D) was achieved at month 3 and maintained at months 6 and 12 in corneal collagen cross-linking treated patients compared with sham controls. In both RCTs, the difference in mean change in maximum corneal curvature from baseline to 12 months was 1.9 D and 2.3 D, respectively, favoring the corneal collagen cross-linking treated patients. Several other studies measured visual acuity and found significant and lasting improvements in corrected visual acuity and other measures with corneal collagen cross-linking. Long-term follow-up for visual acuity outcomes is needed. The adverse events associated with corneal collagen cross-linking include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month but continued in a few (1%-6%) patients for 6 to 12 months. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have corneal ectasia after refractive surgery who receive corneal collagen cross-linking using riboflavin and ultraviolet A, the evidence includes multiple RCTs and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary endpoint (an intermediate outcome) of reducing maximum corneal curvature by 1 D was achieved at month 3 and maintained at months 6 and 12 in the corneal collagen cross-linking treated patients compared with sham controls. In both RCTs, the difference in mean change in maximum corneal curvature from baseline to 12 months was 2.0 D and 1.1 D, respectively, favoring corneal collagen cross-linking treated patients. Other trials showed significant improvements not only in maximum corneal curvature but also visual acuity measures in the corneal collagen cross-linking groups compared with the control groups. The first and longest trial followed patients up to 3 years and saw continued improvement in visual acuity with corneal collagen cross-linking. Long-term follow-up for visual acuity outcomes is needed. The adverse events associated with corneal collagen cross-linking were the same for the ectasia trials as for the keratoconus. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 1 academic medical center (2 reviewers) while this policy was under review in 2012. The input was mixed, noting the limited literature and lack of U.S. Food and Drug Administration (FDA) approval for this procedure, although there are ongoing clinical trials regulated by the FDA. Reviewers also commented on the lack of alternatives to slow disease progression, and that data indicated the procedure is safe and effective enough to offer to patients with adequate informed consent under an investigational protocol.

Practice Guidelines and Position Statements

National Institute for Health and Care Excellence

In 2013, the National Institute for Health and Care Excellence (NICE) issued guidance on corneal collagen cross-linking using riboflavin and ultraviolet A, updating its 2009 guidance. The 2013 guidance stratified recommendations for corneal collagen cross-linking as follows:

> "Most of the published evidence on photochemical corneal collagen cross-linkage using riboflavin and ultraviolet A (UVA) for keratoconus and keratectasia relates to the technique known as 'epithelium-off corneal collagen cross-linking'. 'Epithelium-on (transepithelial) corneal collagen cross-linking' is a more recent technique and less evidence is available on its safety and efficacy. Either procedure (epithelium-off or epithelium-on corneal collagen cross-linking) can be combined with other interventions, and the evidence base for these combination procedures (known as 'corneal collagen cross-linking plus') is also limited. Therefore, different recommendations apply to the variants of this procedure, as follows.
>
> 1.1 Current evidence on the safety and efficacy of epithelium-off corneal collagen cross-linking for keratoconus and keratectasia is adequate in quality and quantity. Therefore, this

procedure can be used provided that normal arrangements are in place for clinical governance, consent and audit.

1.2 Current evidence on the safety and efficacy of epithelium-on (transepithelial) corneal collagen cross-linking, and the combination (corneal collagen cross-linking plus) procedures for keratoconus and keratectasia is inadequate in quantity and quality. Therefore, these procedures should only be used with special arrangements for clinical governance, consent and audit or research."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01604135	Collagen Crosslinking for Keratoconus - a Randomized Controlled Clinical Trial	200	May 2019
NCT01708538[a]	Phase III Study of Corneal Collagen Cross-linking Using Two Different Techniques	30	Oct 2020
NCT03531047	A Prospective, Controlled Study of Refractive Corneal Cross-linking for Progressive Keratoconus	52	Nov 2021
NCT01112072	Randomized Study of Safety and Efficacy of Corneal Collagen	160	Dec 2021

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Crosslinking and Intacs for Treatment of Keratoconus and Corneal Ectasia		
NCT03319082[a]	A Phase IV Observational Registry to Assess the Durability of Effect of Corneal Collagen Cross-linking With Photrexa Viscous, Photrexa, and the KXL System in Patients With Corneal Ectasia Following Refractive Surgery	200	Jul 2023
NCT03760432	Clinical Trial of Laser Custom Corneal Collagen Cross-Linking in Keratoconus	100	Dec 2023
NCT00560651	German Corneal Cross-Linking Registry	7500	Nov 2027
Unpublished			
NCT01459679	A Multi-Center, Randomized, Controlled Evaluation of the Safety and Efficacy of the KXL System With VibeX (Riboflavin Ophthalmic Solution) for Corneal Collagen Cross-Linking in Eyes With Keratoconus or Corneal Ectasia After Refractive Surgery	4000	Jan 2016 (terminated; updated 07/05/18)
NCT01344187[a]	A Multi-Center, Randomized, Placebo-Controlled Evaluation of the Safety and Efficacy of the KXL System With VibeX (Riboflavin Ophthalmic Solution) for Corneal Collagen Cross-Linking in Eyes With Keratoconus	236	Jun 2016 (updated 06/13/18)

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT01972854[a]	A Multi-Center, Randomized, Placebo-Controlled Evaluation of the Safety and Efficacy of the KXL System With VibeX (Riboflavin Ophthalmic Solution) for Corneal Collagen Cross-Linking in Eyes With Keratoconus	92	Apr 2017 (terminated; updated 06/13/18)
NCT01189864[a]	Collagen Crosslinking With Ultraviolet-A in Asymmetric Corneas	500	Dec 2018 (terminated; updated 10/12/18)[b]
NCT02721628	Femtosecond Laser Assisted Epi-keratoplasty Versus Collagen Cross-Linking in Progressive Keratoconus	60	Mar 2018 (unknown; updated 03/29/16)

NCT: national clinical trial.
a Denotes industry-sponsored or cosponsored trial.
b Terminated to initiate FDA and IND-cleared study protocol.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Corneal Collagen Cross-linking", 9.03.28, April 2020.
2. Avedro Inc. Photorexa Viscous and Photorexa Prescribing Label. 2016; http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/203324s000lbl.pdf.
3. Davis LJ, Schechtman KB, Wilson BS, et al. Longitudinal changes in visual acuity in keratoconus. Invest Ophthalmol Vis Sci. Feb 2006;47(2):489-500. PMID 16431941
4. McMahon TT, Edrington TB, Szczotka-Flynn L, et al. Longitudinal changes in corneal curvature in keratoconus. Cornea. Apr 2006;25(3):296-305. PMID 16633030
5. Center for Drug Evaluation and Research. Application Number 203324Orig2s000. Summary Review. 2015; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/203324Orig2s000SumR.pdf.
6. U.S. Food and Drug Administration. FDA Briefing Package for Joint Meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee and Ophthalmic Device Panel of the

Medical Devices Advisory Committee NDA 203324: Photrexa Viscous and Photrexa (riboflavin ophthalmic solution) and KXL System (UVA light source) Avedro, Inc. 2015; https://www.pharmamedtechbi.com/~/media/Supporting%20Documents/The%20Pink%20Sheet%20DAILY/2015/February/22015%20DODAC_ODPB101FDA_Backgrounder.pdf.

7. Hersh PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia: One-year results. J Cataract Refract Surg. Jan 2011;37(1):149-160. PMID 21183110
8. Hersh PS, Stulting RD, Muller D, et al. United States multicenter clinical trial of corneal collagen crosslinking for keratoconus treatment. Ophthalmology. Sep 2017;124(9):1259-1270. PMID 28495149
9. Renesto Ada C, Barros Jde N, Campos M. Impression cytologic analysis after corneal collagen cross-linking using riboflavin and ultraviolet-A light in the treatment of keratoconus. Cornea. Oct 2010;29(10):1139-1144. PMID 20622670
10. Sykakis E, Karim R, Evans JR, et al. Corneal collagen cross-linking for treating keratoconus. Cochrane Database Syst Rev. Mar 24 2015;3(3):CD010621. PMID 25803325
11. Meiri Z, Keren S, Rosenblatt A, et al. Efficacy of corneal collagen cross-linking for the treatment of keratoconus: a systematic review and meta-analysis. Cornea. Mar 2016;35(3):417-428. PMID 26751990
12. McAnena L, Doyle F, O'Keefe M. Cross-linking in children with keratoconus: a systematic review and meta-analysis. Acta Ophthalmol. May 2017;95(3):229-239. PMID 27678078
13. Toprak I, Yaylali V, Yildirim C. Visual, topographic, and pachymetric effects of pediatric corneal collagen cross-linking. J Pediatr Ophthalmol Strabismus. Mar 1 2017;54(2):84-89. PMID 27668869
14. Badawi AE. Accelerated corneal collagen cross-linking in pediatric keratoconus: One year study. Saudi J Ophthalmol. Jan-Mar 2017;31(1):11-18. PMID 28337057
15. Knutsson KA, Paganoni G, Matuska S, et al. Corneal collagen cross-linking in paediatric patients affected by keratoconus. Br J Ophthalmol. Feb 2018;102(2):248-252. PMID 28655729
16. Papaioannou L, Miligkos M, Papathanassiou M. Corneal collagen cross-linking for infectious keratitis: a systematic review and meta-analysis. Cornea. Jan 2016;35(1):62-71. PMID 26509768
17. Padmanabhan P, Rachapalle Reddi S, Rajagopal R, et al. Corneal collagen cross-linking for keratoconus in pediatric patients-long-term results. Cornea. Feb 2017;36(2):138-143. PMID 28060058
18. Raiskup-Wolf F, Hoyer A, Spoerl E, et al. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. J Cataract Refract Surg. May 2008;34(5):796-801. PMID 18471635

19. Raiskup F, Theuring A, Pillunat LE, et al. Corneal collagen crosslinking with riboflavin and ultraviolet-A light in progressive keratoconus: ten-year results. J Cataract Refract Surg. Jan 2015;41(1):41-46. PMID 25532633
20. Caporossi A, Mazzotta C, Baiocchi S, et al. Long-term results of riboflavin ultraviolet a corneal collagen cross-linking for keratoconus in Italy: the Siena Eye Cross Study. Am J Ophthalmol. Apr 2010;149(4):585-593. PMID 20138607
21. Hersh PS, Stulting RD, Muller D, et al. U.S. multicenter clinical trial of corneal collagen crosslinking for treatment of corneal ectasia after refractive surgery. Ophthalmology. Oct 2017;124(10):1475-1484. PMID 28655538
22. Wittig-Silva C, Whiting M, Lamoureux E, et al. A randomized controlled trial of corneal collagen cross-linking in progressive keratoconus: preliminary results. J Refract Surg. Sep 2008;24(7):S720-725. PMID 18811118
23. Wittig-Silva C, Chan E, Islam FM, et al. A randomized, controlled trial of corneal collagen cross-linking in progressive keratoconus: three-year results. Ophthalmology. Apr 2014;121(4):812-821. PMID 24393351
24. National Institute for Health and Care Excellence (NICE). Photochemical corneal collagen cross-linkage using riboflavin and ultraviolet A for keratoconus and keratectasia [IPG466]. 2013; https://www.nice.org.uk/guidance/ipg466.

Policy History

Original Effective Date: 12/21/2011
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12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. New policy.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. No change to coverage.
11/07/2013	Medical Policy Committee review
11/20/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Coverage changed from investigational to eligible for coverage. Added that corneal collagen cross-linking using riboflavin and ultraviolet A may be considered eligible for coverage as a treatment of progressive keratoconus and corneal ectasia after refractive surgery, Added that corneal collagen cross-linking using riboflavin and ultraviolet A is considered investigational for all other indications. Added BCBSA Policy Guidelines section.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2019	Coding update
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage changes "or corneal ectasia after refractive surgery" removed from coverage statement and note added for clarity stating "The correction of refractive errors of the eye, including but not limited to radial keratotomy and laser surgery, are excluded from coverage under medical benefits on majority of member contracts. In addition, treatment of complications of non-covered services are also excluded from coverage. If it is determined that corneal ectasia was a complications of refractive surgery, request for corneal collagen cross-linking will be denied as not a covered benefit."
05/07/2020	Medical Policy Committee review
05/13/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 05/2021

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Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

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

Code Type	Code
CPT	0402T, 66999
HCPCS	J2787
ICD-10 Diagnosis	H18.601-H18.609, H18.711-H18.719

*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:
    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.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.