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Eyelid Thermal Pulsation for the Treatment of Dry Eye Syndrome

Policy Number: 9.03.29 **Last Review:** 11/2018
Origination: 9/2013 **Next Review:** 5/2019

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for eyelid thermal pulsation. This is considered investigational.

When Policy Topic is covered

Not Applicable

When Policy Topic is not covered

Eyelid thermal pulsation therapy to treat dry eye syndrome is considered **investigational**.

Description of Procedure or Service

Populations	Interventions	Comparators	Outcomes
Individuals w ith: ▪ Dry eye symptoms consistent with meibomian glad dysfunction	Interventions of interest are: ▪ Eyelid thermal pulsation	Comparators of interest are: ▪ Standard treatment with warm compresses and eyelid massage	Relevant outcomes include: ▪ Symptoms ▪ Morbid events ▪ Functional outcomes

The LipiFlow Thermal Pulsation System is a treatment option for meibomian gland dysfunction. Meibomian gland dysfunction is recognized as the major cause of dry eye syndrome. The LipiFlow System applies heat to the palpebral surfaces of the upper and lower eyelids directly over the meibomian glands, while simultaneously applying graded pulsatile pressure to the outer eyelid surfaces, thereby expressing the meibomian glands.

For individuals who have dry eye symptoms consistent with meibomian gland dysfunction who receive eyelid thermal pulsation, the evidence includes 3 randomized controlled trials, a nonrandomized comparison study, and longer term follow-up of patients from randomized controlled trials and observational studies. Relevant outcomes are symptoms, morbid events, and functional outcomes. The trials do not provide strong evidence of long-term efficacy. Two randomized controlled trials have demonstrated positive findings for most outcome measures

over the short term (up to 3 months). Observational studies have shown sustained treatment effects for most outcomes up to 3 years. The nonrandomized study showed similar outcomes for eyelid thermal pulsation and standard treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

Background

Dry eye syndrome, dry eye disease (DES) or dysfunctional tear syndrome, either alone or in combination with other conditions, is a frequent cause of ocular irritation that leads patients to seek ophthalmologic care. DES is considered a significant public health problem and is estimated to affect between 14% and 33% of the population worldwide. (1,2) The prevalence of DES increases with age, especially in postmenopausal women. It is estimated that DES affects more than 7 million Americans older than 40 years of age, (1) and approximately 1 million to 4 million Americans between 65 to 84 years of age. (3) The prevention and treatment of DES is expected to be of greater importance as the population ages.

DES is often classified into either the aqueous-deficient subtype or the evaporative subtype. Although the initial classification of the DES may be either of these, the classification is not mutually exclusive. Meibomian gland dysfunction (MGD), characterized by changes in gland secretion with or without concomitant gland obstruction, is recognized to be the most common cause of evaporative dry eye and may also play a role in aqueous-deficient dry eye.

Current treatment options for MGD include physical expression to relieve the obstruction, administration of heat (warm compresses) to the eyelids to potentially liquefy solidified meibomian gland (MG) contents, eyelid scrubs to relieve external meibomian gland orifice blockage, and medications (e.g., antibiotics, topical corticosteroids) to mitigate infection and inflammation of the eyelids. (4, 5) These treatment options however have shown limited clinical efficacy. Physical expression, for example, can be very painful given the significant amount of force needed to express obstructed glands. Warm compress therapy can be both time-consuming and labor intensive, and there is limited evidence that medications can relieve MGD. (5) While the symptoms of DES often improve with treatment, the disease usually is not curable and may lead to substantial patient and physician frustration. Dry eyes can be a cause of visual morbidity and may compromise results of corneal, cataract, and refractive surgery. Inadequate treatment of DES may result in increased ocular discomfort, blurred vision, reduced quality of life, and decreased productivity.

The LipiFlow Thermal Pulsation System is a device developed to relieve MGD. This device heats the palpebral surfaces of both the upper and lower eyelids, while applying graded pulsatile pressure to the outer eyelid surfaces. The LipiFlow System is composed of a disposable ocular component and a handheld control system. Following application of a topical anesthetic, the heated inner portion of the LipiFlow eyecup is applied to the conjunctival surface of the upper and lower eyelids. The outer portion of the device covers the skin surface of the upper and lower eyelids. The device massages the eyelids with cyclical pressure from the

base of the meibomian glands in the direction of the gland orifices, thereby expressing the glands during heating.

Regulatory Status

In 2011, the LipiFlow® Thermal Pulsation System (TearScience; assigned the generic name of eyelid thermal pulsation system) was cleared by the U.S. Food and Drug Administration (FDA).[6] FDA classified the LipiFlow® System as class II (special controls) to provide a "reasonable assurance of safety and effectiveness" of the device. The LipiFlow® System was identified by FDA "as an electrically powered device intended for use in the application of localized heat and pressure therapy to the eyelids. The device is used in adult patients with chronic cystic conditions of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye or lipid deficiency dry eye."

Rationale

This evidence review was created in February 2013 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through January 8, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Dry Eye Syndrome

Comparative studies of eyelid thermal pulsation for the treatment of dry eye syndrome include 3 RCTs and 1 nonrandomized comparative study of the LipiFlow System (see Table 1). In the multicenter RCT by Lane et al (2012), controls crossed over to treatment after 2 weeks; therefore, only the 2-week follow-up is

available (see Table 2).[7] Results at 2 weeks showed statistically significant improvements in the primary and secondary outcome measures. Trial limitations included the short-term follow-up (2 weeks) for the primary comparative outcomes, lack of masking, and lack of intention-to-treat analysis. In addition, the control intervention did not include massage along with the warm compress, which is a common treatment for meibomian gland dysfunction.

An RCT by Finis et al (2014), which reported on outcomes prior to crossover at 3 months, found a significant effect of treatment compared with controls for the primary outcome measure (Ocular Surface Disease Index [OSDI] score), but not for any other outcome measures.[8] The clinical significance of the 11.6-point improvement in OSDI score is unclear because final OSDI scores at 3 months (34.6 for LipiFlow, 40.0 for control) would still be classified as severe dry eye disease.

In a 2-stage multicenter RCT, Blackie et al (2016) evaluated treatment effects of the LipiFlow System for patients with meibomian gland function and dry eye symptoms.[9] The first stage involved the open-label evaluation of treatment effects over the short term. Trialists compared the single, in-office, LipiFlow treatment with conventional treatments consisting of warm compress and eyelid hygiene control therapy, conducted twice daily for 3 months. Significant treatment effects relative to controls were observed for OSDI scores and meibomian gland secretion score (higher scores reflect less dysfunction) (see Table 2). The second stage involved an observational crossover study to evaluate the long-term effects (from 3 to 12 months) of a single session using the LipiFlow System or in combination with other conventional treatments when considered necessary. Sustained treatment effects for the single LipiFlow treatment compared with the combination treatment subgroups were observed over the long-term for OSDI scores, but not for Meibomian glad secretion score. Trial limitations included lack of masking and lack of massage combined with warm compression, the usual treatment approach. The clinical significance of the 17- to 22-point improvement in OSDI scores observed across treatment and controls may be relatively small because final OSDI scores indicated that patients in both groups improved from severe disease to mild disease (treatment) or moderate disease (controls). The lack of blinding might also have led to an overestimation of the treatment effect of LipiFlow.

The nonrandomized trial by Zhao et al (2016) compared 25 patients undergoing a single LipiFlow treatment with 25 patients using warm compresses and lid massage.[10] At 4 and 12 weeks, between-group outcomes were similar for symptom change, change in meibomian gland force evaluator, and tear break-up time. At 12 weeks, change in Schirmer test scores also did not differ significantly between groups.

Three other studies have evaluated long-term outcomes for some trial subjects who had undergone LipiFlow treatment. The study by Greiner (2013)[11] evaluated 18 of 30 subjects from 1 site of the Lane trial (described above).[7] Several outcomes remained significantly improved from baseline, but the improvements were of lower magnitude at 1 year than at 1 month. Finis et al (2014) evaluated

26 patients at 6 months after LipiFlow treatment.[12] Several outcome measures remained improved 6 months after treatment. Another study of 20 patients conducted by Greiner (2016) found that most outcomes remained significantly improved up to 3 years relative to baseline.[13]

Table 1. Summary of Key Characteristics of Comparative Studies

					Interventions	
Study	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Lane et al (2012)[7]	U.S.	9	Mar-May 2009	• 69 LipiFlow • 70 control	Single LipiFlow treatment	Daily warm compress for 2 wk
Finis et al (2014)[8]	Germany	NR	Apr 2012-Jun 2013	• 20 LipiFlow • 20 control	Single LipiFlow treatment	Twice daily lid warming and massage
Zhao et al (2016)[10]	Singapore	1	Feb 2012-Mar 2013	• 25 LipiFlow • 25 control	Single LipiFlow treatment	Twice daily lid warm compresses and massage
Blackie et al (2016)[9]	U.S.	9	Feb-Oct 2012	• 101 LipiFlow • 99 control	Single LipiFlow treatment	Twice daily warm compress and eyelid hygiene control therapy for 3 mo

Table 2. Summary of Key Results of Comparative Studies

Study	**ΔMGS Score[a]**	**ΔTBUT, s[b]**	**ΔOSDI Score[c]**	**ΔSPEED Score[d]**	**Symptom Score, %**	**ΔSchirmer Test, mm**
Lane et al (2012)[7]						
LipiFlow	7.9	1.5	14.7	6.2		
Controls	0.5	0.1	8.1	3.5		
p	<0.001	<0.001	<0.001	<0.001		
Finis et al (2014)[8]						
LipiFlow	3.0	2.0	11.6	2.3		
Controls	2.5	0.2	0.1	1.2		
p	*NS*	*NS*	0.029	*NS*		
Zhao et al (2016)[10]						
LipiFlow		89.2%			-30.5%	1.0
Controls		63.0%			-15.9%	-3.95
p		0.625				0.55
Blackie et al (2016)[9]						
LipiFlow	11.6		-23.4			
Controls	4.5		-17.8			
p	<0.001		0.007			

MGS: meibomian gland secretion; NR: not reported; OSDI: Ocular Surface Disease Index; SPEED: Standard Patient Evaluation for Eye Dryness; TBUT: tear break-up time.

[a] The Meibomian Gland Evaluator device was developed by TearScience to evaluate gland secretion through gland expression to determine if meibomian glands are blocked.

[b] Practice parameters from the American Academy of Ophthalmology (2013) has indicated that a tear break-up time of <10 s is considered abnormal.[3] Note that Zhao et al (2016) is reported in percent not seconds.

[c] The OSDI assesses the patient's frequency and severity of dry eye symptoms in specific contexts during the week prior to the examination. The minimal clinically important difference for the OSDI ranges from 4.5-7.3 for mild or moderate disease. The overall OSDI score defines the ocular

surface as normal (0-12 points) or as having mild (13-22 points), moderate (23-32 points), or severe (33-100 points) disease.[14]

[d] The SPEED questionnaire is a self-reported measure of the frequency and severity of dryness, grittiness, scratchiness, soreness, irritation, burning, watering, and eye fatigue within 3 months of examination. It was developed by TearScience and validated in a 2013 study funded by TearScience.[15] In this validation study, the mean SPEED score of symptomatic subjects was 21.0 and the mean of asymptomatic subjects was 6.25.

Summary of Evidence

For individuals who have dry eye symptoms consistent with meibomian gland dysfunction who receive eyelid thermal pulsation, the evidence includes 3 RCTs, a nonrandomized comparison study, and longer term follow-up of patients from RCTs and observational studies. Relevant outcomes are symptoms, morbid events, and functional outcomes. The trials do not provide strong evidence of long-term efficacy. Two RCTs have demonstrated positive findings for most outcome measures over the short term (up to 3 months). Observational studies have shown sustained treatment effects for most outcomes up to 3 years. The nonrandomized study showed similar outcomes for eyelid thermal pulsation and standard treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Practice Guidelines and Position Statements

In 2013, the American Academy of Ophthalmology published preferred practice patterns guidelines on dry eye syndrome.[3] A number of treatment options were recommended. The use of thermal pulsation treatment devices was not mentioned.

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 unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02894658	LipiFlow Versus Warm Compresses in Parkinson's Disease	25	Jan 2020 (suspended)

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

References

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Billing Coding/Physician Documentation Information

0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral
0330T	Tear film imaging, unilateral or bilateral, with interpretation and report

ICD-10 Codes

H04.121-H04.129	Dry eye syndrome code range

Additional Policy Key Words

N/A

Policy Implementation/Update Information

9/1/13 New policy; considered investigational.
11/1/13 No policy statement changes.
5/1/14 No policy statement changes.
11/1/14 No policy statement changes.
5/1/15 No policy statement changes.
11/1/15 No policy statement changes.
5/1/16 No policy statement changes.
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