Eyelid Thermal Pulsation for the Treatment of Dry Eye Syndrome

Policy Number: 9.03.29                  Last Review: 5/2014

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
The LipiFlow® Thermal Pulsation System (TearScience Inc., Morrisville, NC) is a new treatment option for addressing meibomian gland dysfunction (MGD). MGD is recognized as the major cause of dry eye syndrome. The LipiFlow® System allows heat to be applied 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.

Background
Dry eye syndrome, dry eye disease (DED) 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. (1) DED is considered a significant public health problem and is estimated to affect between 14% and 33% of the population worldwide. (2, 3) The prevalence of DED increases with age, especially in postmenopausal women. (2, 3) It is estimated that DED affects more than 7 million Americans older than 40 years of age, (2) and approximately 1 million to 4 million Americans between 65 to 84 years of age. (1) The prevention and treatment of DED is expected to be of greater importance as the population ages.

DED is often classified into either the aqueous-deficient subtype or the evaporative subtype. (2, 3) Although the initial classification of the DED may be either of these, the classification is not mutually exclusive. (2, 3) 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. (3, 4)

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. (5) 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 DED often improve with treatment, the disease usually is not curable and may lead to substantial patient and physician frustration. (1) Dry
eyes can be a cause of visual morbidity and may compromise results of corneal, cataract, and refractive surgery. Inadequate treatment of DED may result in increased ocular discomfort, blurred vision, reduced quality of life, and decreased productivity. (2) DED is a multi-factorial disease of the ocular surface that may require a combination approach to treatment. (2)

The LipiFlow® Thermal Pulsation System (TearScience Inc., Morrisville, NC) is a new device developed to address the limitations of current treatment options to relieve MGD. (6, 7) This device is designed to safely heat the palpebral surfaces of both the upper and lower eyelids, while simultaneously applying graded pulsatile pressure to the outer eyelid surfaces. The device massages the outer eyelids from the base of the meibomian glands in the direction of the gland orifices, thereby expressing the meibomian glands during heating. The LipiFlow® System is composed of 2 primary components, an ocular component (The Disposable) and a handheld control system. The Disposable has 2 parts, a lid warmer and an eyecup. (6, 7)

Regulatory Status
The LipiFlow® System (assigned the generic name of eyelid thermal pulsation system) was cleared by the Food and Drug Administration (FDA) in June 2011. (8) The FDA classified the LipiFlow® System into class II (special controls) in order to provide a “reasonable assurance of safety and effectiveness” of the device. (8) The LipiFlow® System is identified by the 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.” (8)

Rationale
This policy was created in February 2012 and updated periodically with a search of the MEDLINE database. The most recent update was performed through February 5, 2014. Following is a summary of the key literature to date.

Lane and colleagues reported outcomes out to 1-month from an industry-sponsored prospective, open-label, randomized, crossover multi-center clinical trial undertaken to evaluate the safety and effectiveness of the LipiFlow® System compared to a standardized form of warm compress therapy (iHeat Warm Compress (WC) System, Advanced Vision Research, Woburn, MA) for adults with meibomian gland dysfunction (MGD). (7) Outcomes at 9 and 12 months of follow-up were reported for a sub-cohort composed of patients who had participated at a single site. (8, 9) In the randomized portion of the study, 139 adult patients from 9 participating sites were randomly assigned to either the LipiFlow® System (n=69) or WC control (n=70). These patients had reported dry eye symptoms in the past 3 months, had a Standard Patient Evaluation for Eye Dryness (SPEED) score of 6 or greater, and had evidence of meibomian gland obstruction on ophthalmologic examination. Subjects in the LipiFlow® group received a single 12-minute LipiFlow® treatment and were reexamined at day one, 2 weeks and at 4 weeks of follow-up. Patients in the control group received a single 5-minute iHeat® warm compress (WC) treatment with instructions to perform the same treatment daily for 2 weeks. At 2 weeks, the control patients crossed over (LipiFlow® Crossover) and received the LipiFlow® treatment. The primary outcome measures were MG assessments performed using a hand-held Meibomian Gland Evaluator and tear break-up time (TBUT) in seconds, measured by the Dry Eye Test Method at 2 weeks following treatment. Secondary outcome measures included dry eye symptoms measured by 2 standardized instruments, the SPEED score, and the Ocular Surface Disease Index (OSDI). Device-related adverse events were also reported, primarily treatment-related pain and discomfort. The main analyses were performed on a per-protocol basis, and not by intention to treat.

At 2 weeks, there were significantly greater improvements for the Lipiflow® group on all of the primary and secondary outcome measures. For the MG assessment, there was an improvement of 7.9 points in the Lipiflow® group compared to 0.5 points in the WC group (p<0.0001). The mean change in TBUT was 1.5 seconds in the Lipiflow® group versus 0.1 seconds in the WC group (p=0.0017). For the dry eye symptoms, there was improvement for the Lipiflow® group of 6.2 points on the SPEED scale and 14.7 points on the OSDI scale, compared to changes in the WC group of 3.5 points on the SPEED
scale (p<0.0001) and 8.1 points on the OSDI scale (p=0.0004). The percent of patients with at least a 50% improvement in symptoms was 43% in the Lipiflow® group versus 11% in the WC group (p value NR). There was no difference in patients-reported pain or discomfort between treatments. The improvements in both MG secretion and TBUT were maintained at 9 months in the sub-cohort of 21 out of 30 adult patients who had participated at a single-site. Results for the subset of patients available for 1-year follow-up (n=18) are shown in the following table, which shows some reduction in efficacy as measured by MG score, TBUT, and OSDI, but not SPEED, over the course of a year.

<table>
<thead>
<tr>
<th></th>
<th>Pre-procedure</th>
<th>1-month</th>
<th>1-year</th>
</tr>
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<tbody>
<tr>
<td>MG score¹</td>
<td>4.0</td>
<td>11.3</td>
<td>7.3</td>
</tr>
<tr>
<td>TBUT²</td>
<td>4.9</td>
<td>9.5</td>
<td>6.0</td>
</tr>
<tr>
<td>OSDI³</td>
<td>22.2</td>
<td>8.5</td>
<td>12.4</td>
</tr>
<tr>
<td>SPEED⁴</td>
<td>12.9</td>
<td>6.4</td>
<td>6.3</td>
</tr>
</tbody>
</table>

1. The Meibomian Gland Evaluator is a device developed by TearScience to evaluate gland secretion through gland expression to determine if meibomian glands are blocked.
2. Practice Parameters from the American Academy of Ophthalmology indicate that a tear break-up time (TBUT) of less than 10 seconds is considered abnormal. (10)
3. The minimal clinically important difference for the Ocular Surface Disease Index (OSDI) is 4.5 to 7.3 for mild or moderate disease. The overall OSDI score defined 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. (11)
4. The SPEED questionnaire was developed by TearScience and validated in a study funded by TearScience. (12) In this validation study the mean SPEED score of symptomatic subjects was 21.0 and the mean of asymptomatic subjects was 6.25

Results from this trial indicate that one treatment with Lipiflow® may result in greater short-term improvement in meibomian dysfunction and dry eye symptoms compared to warm compresses. Limitations of the trial include the short-term time period (2 weeks) for the primary comparative outcomes, and the lack of analysis by intention to treat. The clinical significance of the outcome measures is not clear, particularly the minimal important clinical difference on some of the symptom scales. The durability of the treatment effect is suggestive of long-term benefit following a single treatment, but evidence is limited because the follow-up data did not include a control arm.

**Ongoing and Unpublished Clinical Trials**

A search of online site ClinicalTrials.gov in February 2014 identified several recently completed studies on the LipiFlow® system for treatment of MGD.

**NCT01521507: Randomized Controlled Trial of Long-term Treatment Effectiveness for Meibomian Gland Dysfunction (MGD) and Dry Eye**

This is a post-market prospective clinical trial sponsored by the manufacturer (TearScience Inc., Morrisville, NC) of the LipiFlow® System. This trial has the estimated enrollment of 200 adult patients across 8 U.S. sites. This trial is divided into 2 stages. The first stage from enrollment to 3 months is an open-label, randomized controlled design to compare the effectiveness of a single LipiFlow® System treatment to a standardized daily warm compress and eyelid hygiene control therapy with crossover LipiFlow® treatment of the control subjects at 3 months. The second stage, occurring between 3 months and 1 year, is an observational design to evaluate the effectiveness of LipiFlow® alone and in combination with other MGD and dry eye treatments over a follow-up period of 1 year. This study is listed as completed as of November 2013. No results have been posted.

**NCT01769105: Comparison of LipiFlow® Treatment and a Standard Lid Hygiene Regime**

This is a randomized prospective single-blind trial comparing the LipiFlow® System with a standard lid hygiene regimen for treatment of MGD. This trial, with an estimated enrollment of 40 adult patients, is being undertaken at a university center in Germany (study sponsor). The primary outcome measure is
improvement of dry eye symptoms using standardized questionnaires at 3-month follow-up. This study is listed as completed as of October 2013. No results have been posted.

NCT01683318: Thermal Pulsation System for the Treatment of Meibomian Gland Dysfunction

This is an observational study designed to test the efficacy of the LipiFlow® System for treatment of MGD. This study, with an estimated enrolment of 25 adult patients, is being undertaken at the Singapore National Eye Center (study sponsor). Patients will be asked to undergo a one-time treatment with LipiFlow® and the investigators will assess for changes in tear film and lipid composition, as well as changes in the anatomy of meibomian glands up to 3 month follow-up. This study is listed as completed as of November 2013. No results have been posted.

Summary

The LipiFlow® Thermal Pulsation System (TearScience Inc., Morrisville, NC) is a new treatment option for addressing meibomian gland dysfunction (MGD). The evidence to date on the LipiFlow® System includes a randomized controlled trial which has been funded by the manufacturer of this device. This trial was designed with crossover at 2-weeks and has follow-up analysis in a sub-cohort of patients.

This RCT reported short-term benefits for LipiFlow® on measures of MG function and dry eye symptoms. However, this single trial is insufficient to determine the effect of LipiFlow® on health outcomes. Further prospective RCTs are needed to assess the impact on health outcomes of the LipiFlow® System compared to alternative treatment options. These trials will require longer follow-up to assess durability of effect and to accurately predict the optimal frequency of treatment with the LipiFlow® System for individual patients. Based on review of the evidence to date, use of the LipiFlow® Thermal Pulsation System is considered investigational for dry eye disease (DED).

Practice Guidelines and Position Statements

In October 2013, the American Academy of Ophthalmology Cornea/External Disease Panel published their Dry Eye Syndrome Preferred Practice Patterns Guidelines. (10) In the process of developing these guidelines, an updated literature search of articles was conducted in January 2013. A number of treatment options were recommended. The use of thermal pulsation treatment devices is not mentioned.

Medicare National Coverage

No national coverage determination.

References


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

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.

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