9.03.29	Eyelid Thermal Pulsation for the Treatment of Dry Eye Syndrome		
Original Policy Date:	June 30, 2015	**Effective Date:**	May 1, 2024
Section:	9.0 Other	**Page:**	Page 1 of 19

Policy Statement

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

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Coding
See the **Codes** table for details.

Description

Thermal pulsation is a treatment option for meibomian gland dysfunction. Meibomian gland dysfunction is recognized as the major cause of dry eye syndrome. Thermal pulsation 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.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Eyelid thermal pulsation systems (FDA product code: ORZ) cleared by the U.S. Food and Drug Administration (FDA) are summarized in Table 1.

Table 1. Eyelid Thermal Pulsation Systems Cleared by the FDA

Device	Manufacturer	Location	Original Date Cleared/Approved	Original De Novo or 510(k) No. or PMA	Indication
LipiFlow® Thermal Pulsation System	TearScience	Morrisville, NC	2011*	DEN100017*	'For the application of localized heat and pressure therapy in adult patients with chronic

An independent member of the Blue Shield Association

Reproduction without authorization from Blue Shield of California is prohibited

Device	Manufacturer	Location	Original Date Cleared/Approved	Original De Novo or 510(k) No. or PMA	Indication
					cystic conditions of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye or lipid deficiency dry eye.'
iLux® System	Tear Film Innovations	San Diego, CA	2017	K172645	'For the application of localized heat and pressure therapy in adult patients with chronic diseases of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye.'
Systane® iLux2®	Tear Film Innovations	Carlsbad, CA	2020	K200400	'For the application of localized heat and pressure therapy in adult patients with Meibomian Gland Dysfunction (MGD), which is associated with evaporative dry eye, and to capture/store digital images and video of the meibomian glands'
TearCare® System	Sight Sciences	Menlo Park, CA	2021	K213045	'For the application of localized heat and pressure therapy in adult patients with evaporative dry eye disease due to Meibomian Gland Dysfunction (MGD), when used in conjunction with manual expression of the meibomian glands.'
TearCare® MGX™	Sight Sciences	Menlo Park, CA	2023	K231084	'For the application of localized heat therapy in adult patients with evaporative dry eye disease due to meibomian gland dysfunction (MGD), when used in conjunction with manual expression of the meibomian glands.'

*Other 501(k) numbers are associated with more recent versions of the device.

Rationale

Background

Dry Eye Syndrome

Dry eye syndrome, dry eye disease, 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. It is estimated to affect between 5% and 50% of the population worldwide.[1,] Based on data from 2013, an estimated 16.4 million Americans have dry eye syndrome.[2,] The prevalence of dry eye syndrome increases with age, especially in postmenopausal women. For both sexes, prevalence is more than 3 times higher in individuals 50 years of age or older compared to those 18 to 49 years of age. Meibomian gland dysfunction (MGD) is considered to be the most common cause of dry eye syndrome.[3,] Prevention and treatment of dry eye syndrome are expected to be of greater importance as the population ages.

Reproduction without authorization from Blue Shield of California is prohibited.

Treatment

Current treatment options for MGD include physical expression to relieve the obstruction, administration of heat (warm compresses) to the eyelids to liquefy solidified meibomian gland 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.[3,4,5,6,]These treatment options, however, have shown limited clinical efficacy, and often require a trial-and-error approach. For example, physical expression can be very painful given the amount of force needed to express obstructed glands. Warm compress therapy can be time-consuming and labor intensive, and there is limited evidence that medications relieve MGD.[5,] While the symptoms of dry eye syndrome often improve with treatment, the disease usually is not curable and may lead to substantial patient and physician frustration.[3,6,] Dry eyes can be a cause of visual morbidity and may compromise results of corneal, cataract, and refractive surgery. Inadequate treatment of dry eye syndrome may result in increased ocular discomfort, blurred vision, reduced quality of life, and decreased productivity.

Literature Review

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 1 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. Randomized controlled trials 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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Dry Eye Syndrome

Clinical Context and Therapy Purpose

The purpose of eyelid thermal pulsation in individuals who have dry eye syndrome is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population(s) of interest is individuals with dry eye syndrome. Dry eye syndrome is often classified into the aqueous-deficient subtype or the evaporative subtype, although classification is not mutually exclusive. Dry eye syndrome is a multifactorial disease of the ocular surface that may require a combination approach to treatment. Meibomian gland dysfunction (MGD), characterized

Reproduction without authorization from Blue Shield of California is prohibited.

by changes in gland secretion with or without concomitant gland obstruction, is recognized as the most common cause of evaporative dry eye and may also play a role in aqueous-deficient dry eye.

Interventions
The therapy being considered is eyelid thermal pulsation. The LipiFlow Thermal Pulsation System is one of the devices 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.

Comparators
The following practices are currently being used to treat dry eye syndrome: standard treatment with warm compresses and eyelid massage. Current treatment options for MGD include physical expression to relieve the obstruction, administration of heat (warm compresses) to the eyelids to liquefy solidified meibomian gland 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.

Outcomes
The general outcomes of interest are symptoms, morbid events, and functional outcomes.

Tear break-up time (TBUT) is measured in seconds. Practice parameters from the American Academy of Ophthalmology (2013) have indicated that a tear break-up time of <10 s is considered abnormal.[6,]

The Ocular Surface Disease Index (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.[7,]

The Standard Patient Evaluation for Eye Dryness (SPEED) questionnaire is a self-reported measure of the frequency and severity of dryness, grittiness, scratchiness, soreness, irritation, burning, watering, and eye fatigue. It was developed by TearScience and validated in a 2013 study funded by TearScience.[8,] In this validation study, the mean SPEED score of symptomatic subjects was 21.0 and the mean of asymptomatic subjects was 6.25.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
Tao et al (2023) reported results of a systematic review that informed an 'Ophthalmic Technology Assessment' commissioned by the American Academy of Ophthalmology.[9,] The review was designed

Reproduction without authorization from Blue Shield of California is prohibited.

to assess the efficacy and safety of thermal pulsation in improving signs or symptoms of MGD and dry eye compared with no therapy or conventional (nonthermal pulsation) therapy such as warm compress or eyelid hygiene. The literature search was performed in March 2023. For each study, the quality of study methodology was rated according to the American Academy of Ophthalmology's guidelines. 8 studies were rated as providing level I evidence (well-designed and well-conducted randomized controlled trials and systematic reviews) and 3 studies were rated as providing level II evidence (well-designed cohort studies and nonrandomized controlled cohort or follow-up trials). All included studies evaluated the LipiFlow device. The review did not include a meta-analysis. The authors stated that 9/11 of the studies reported greater efficacy with LipiFlow compared to standard warm compress therapy and eyelid hygiene. In general, improvements were detected in both subjective and objective metrics of MGD within 1 to 12 months of thermal pulsation treatment compared with nontreatment. The authors noted that durability beyond several months is uncertain. The RCTs identified in the Tao (2023) systematic review are described below in Tables 2 through 5.

Randomized Controlled Trials

Ten RCTs of eyelid thermal pulsation (LipiFlow System) for the treatment of dry eye syndrome have been published. Characteristics of RCTs are shown in Table 2. Results of the RCTs are summarized in Table 3. Study limitations are briefly described in Tables 4 and 5. Select studies are described below. Several additional RCTs, including trials evaluating systems other than LipiFlow, have been conducted but not published, see Table 6.

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 (Table 2).[10,] 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 MGD.

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.[11,] 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 MGD and dry eye symptoms.[12,] 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) (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 gland secretion scores. 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.

Tauber reported a single-center RCT (2020) comparing the LipiFlow System to twice-daily administration of lifitegrast ophthalmic solution 5% in patients with inflammatory MGD (N=50; 25 patients per group).[13,] The co-primary outcomes were change in eye discomfort and tear lipid layer

Reproduction without authorization from Blue Shield of California is prohibited.

thickness from baseline to day 42. Results demonstrated that changes in the eye discomfort scores were significantly greater in the group that received lifitegrast, while changes in lipid layer thickness did not reach statistical significance between groups (Table 2). Trial limitations included lack of masking, attrition in the lifitegrast group (3 patients discontinued therapy), and selection of patients that had both MGD and inflammation (results may have differed in populations with MGD without inflammation).

Table 2. Summary of Characteristics of Randomized Controlled Trials of LipiFlow

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
Lane et al (2012)[10]	U.S.	9	Mar-May 2009	Adults with MGD	Single LipiFlow treatment n=69	Daily warm compress for 2 wk n=70
Finis et al (2014)[11]	Germany	NR	Apr 2012-Jun 2013	Adults with MGD requiring treatment	Single LipiFlow treatment n=20	Twice daily lid warming and massage n=20
Blackie et al (2016)[12]	U.S.	9	Feb-Oct 2012	Adults with MGD and evaporative dry eye	Single LipiFlow treatment n=101	Twice daily warm compress and eyelid hygiene control therapy for 3 mo n=99
Blackie et al (2018); NCT02102464 [14]	U.S., Canada	6	May 2014-Feb 2015	Adult contact lens wearers with MGD and dry eye symptoms Mean age, 42 y 86% Female 21% Asian 17% Black/African American 59% White Mean baseline MGS score, 8.1	Single LipiFlow treatment with eyelid margin cleaning prior to treatment n=29	No treatment for 3 mo; crossover to LipiFlow at 3 mo n=26
Tauber (2020)[13]	U.S.	1	Sept 2017-Aug 2018	Adults with inflammatory MGD	Single LipiFlow treatment n=50	Twice daily lifitegrast ophthalmic solution 5% n=50
Kasetsuwan (2020) [15]	Thailand	1	Oct 2015-Nov 2016	Adults using anti-glaucoma medications with MGD Mean age, 68 y 52% Female Mean baseline MGS score, 22	Standard lid hygiene twice daily plus a single LipiFlow treatment n=26	Standard lid hygiene twice daily n=22
Park (2021); NCT04457999[16]	Korea	1	April 2019-Dec 2019	Adults with cataract, eligible for	Single LipiFlow treatment following	No treatment n=62

Reproduction without authorization from Blue Shield of California is prohibited.

Study	Countries	Sites	Dates	Participants	Interventions	
				cataract surgery MGD before cataract surgery was NOT required but was allowed Mean age, 64 to 65 y 56% Female	preoperative evaluations for cataract surgery n=62	
Mencucci (2023); NCT05062564 [17,]	Italy	1	Sep 2021-Feb 2022	Adults with mild to moderate MGD who had been scheduled for unilateral cataract surgery Mean age, 74 y 65% Female	Single LipiFlow treatment 5 weeks before cataract surgery n=23	Warm compresses and eyelid massages twice a day for 1 month before cataract surgery n=23
Matossian (2023); NCT03708367 [18,]	U.S.	5	Oct 2018-Jan 2020	Adults, at least 22 years of age, with mild-to-moderate MGD and cataract with planned cataract surgery Mean age, 65 y 59% Female 77% White 6% Asian 17% Black or African American	Single LipiFlow treatment 2 to 4 weeks prior to cataract surgery n=117 eyes	No treatment prior to surgery, single LipiFlow treatment 3 mo after cataract surgery n=115 eyes
Meng (2023) [19,]	China	1	NR	Adults with MGD Mean age, 58 y 48% Female	Single LipiFlow treatment n=50 eyes	Warm compress n=50 eyes

MGD: meibomian gland dysfunction; MGS: Meibomian gland secretion score (0-45); NR: not reported.

Reproduction without authorization from Blue Shield of California is prohibited.

Table 3. Summary of Key Results of Randomized Controlled Trials of LipiFlow

Study	MGS Score[a]	TBUT, s[b]	OSDI Score[c]	SPEED Score[d]	Symptoms ,	Visual acuity	Schirmer Test, mm	Tear lipid layer thickness[f]
Lane et al (2012)[10],								
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)[11],								
LipiFlow	3.0	2.0	11.6	2.3				
Controls	2.5	0.2	0.1	1.2				
p	NS	NS	0.029	NS				
Blackie et al (2016)[12],								
LipiFlow	11.6		-23.4					
Controls	4.5		-17.8					
p	<0.001		0.007					
Blackie et al (2018)[14],	At 3 mo Mean (SD)	At 3 mo Mean (SD)	At 3 mo Mean (SD)	At 3 mo Mean (SD)				
LipiFlow	20.4 (9.1)	6.5 (4.0)	13.4 (15.5)	6.1 (4.6)				
Controls	9.6 (5.7)	4.3 (1.7)	37.5 (23.8)	14.5 (5.3)				
p	<.01	<.01	<.01	<.01				
Tauber (2020)[13],					Eye discomfort[e] Change fom baseline to day 42, mean (SD)			Change from baseline to day 42, mean (SD)
LipiFlow					-0.48 (0.96)			1.25 (15.69)
Controls					-1.05 (0.79)			-3.67 (21.12)
p					.0340			NR
Kasetsuwan (2020)[15],	At 6 mo Change from baseline, mean (95% CI)	At 6 mo Change from baseline, mean (95% CI)	At 6 mo Change from baseline, mean (95% CI)				At 6 mo Change from baseline, mean (95% CI)	At 6 mo Change from baseline, mean (95% CI)
LipiFlow	4.7 (2.2 to 7.2)	-0.3 (-1.5 to 0.9)	-10.0 (-12.2 to -7.8)				-1.2 (-2.3 to -0.04)	2.7 (0.1 to 5.2)
Controls	3.0 (0.3 to 5.7)	-0.6 (-2.0 to 0.9)	-11.8 (-13.5 to -10.1)				1.3 (-.2 to 2.8)	Unclear
p	.40	.65	.57				NS	.68
Park (2021) [16],	At 3 mo Mean (SD)	At 3 mo Mean (SD)	At 3 mo Mean (SD)					At 3 mo Mean (SD)
LipiFlow	0.87 (0.87)	4.4 (1.8)	22.3 (16.5)					87.4 (21.4)
Controls	1.71 (0.82)	3.6 (1.6)	29.8 (20.8)					86.2 (13.6)
p	<.01	.03	.04					.75
Mencucci (2023) [17],				At 1 mo			At 1 mo	

Reproduction without authorization from Blue Shield of California is prohibited.

Study	MGS Score[a]	TBUT, s[b]	OSDI Score[c]	SPEED Score[d]	Symptoms ,	Visual acuity	Schirmer Test, mm	Tear lipid layer thickness[f]
				Mean (SD)			Mean (SD)	
LipiFlow				4.0 (1.8)			12.6 (5.9)	
Controls				6.0 (1.2)			11.2 (6.1)	
p				<.01			.42	
Matossian (2023)[18]	At 3 mo Mean (SD) change from baseline	At 1 mo Mean (SD) change from baseline		At 3 mo Mean (SD) change from baseline	At 3 mo Bothersome ocular symptoms (PRVSQ)	At 3 mo Mean logMAR (SD) monocular uncorrected distance visual acuity		
LipiFlow	7.3 (9.3)	0.69 (4.6)		-2.1 (5.3)	Halos, 7 days: 59% Multiple/double vision, 7 days: 26%	0.08 (0.15)		
Controls	4.7 (10.1)	0.06 (3.7)		-1.5 (5.6)	Halos, 7 days: 79% Multiple/double vision, 7 days: 9%	0.07 (0.13)		
p	.05	.26		.60	Halos, 7 days:.02 Multiple/double vision, 7 days:.06	.42		
Meng (2023) [19]	At 3 mo Mean (SD)	At 3 mo Mean (SD)		At 3 mo Mean (SD)				At 3 mo Mean (SD)
LipiFlow	12.8 (3.9)	5.6 (2.2)		3.8 (1.5)				81.9 (17.6)
Controls	10.7 (3.1)	4.0 (1.9)		6.6 (2.8)				69.3 (13.8)
p	<.01	.01		<.01				NR

MGS: meibomian gland secretion; NR: not reported; NS: not significant; PRVSQ: Patient-Reported Visual Symptom Questionnaire; OSDI: Ocular Surface Disease Index; SD: standard deviation; SPEED: Standard Patient Evaluation for Eye Dryness; TBUT: tear break-up time; VAS: visual analog scale.

[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) have indicated that a tear break-up time of <10 s is considered abnormal.[6] 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.[7]

[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.[8] In this validation study, the mean SPEED score of symptomatic subjects was 21.0 and the mean of asymptomatic subjects was 6.25.

[e] Eye discomfort was reported using a visual analog scale from 0 to 100 mm. Symptoms were reported on a scale of 0 to 3 (0, none/absent; 1, mild; 2, moderate; and 3, severe) and included burning, stinging, foreign body sensation, dryness, pain/soreness, and photophobia.[13]

[f] Tear lipid layer thickness was measured using the LipiView (Johnson & Johnson Vision/TearScience) device, which uses noise canceling technology to measure the submicron thickness of the lipid layer. Authors did not provide the unit of measure for this outcome.[13]

Reproduction without authorization from Blue Shield of California is prohibited.

Table 4. Study Relevance Limitations of Randomized Controlled Trials of LipiFlow

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Lane et al (2012)[10],			2: control group did not include massage along with the warm compress	5: clinical significant difference not prespecified	1, 2: only 2 weeks of follow-up
Finis et al (2014)[11],				3, 6: clinical significance not supported for the primary outcome	
Blackie et al (2016)[12],			2: control group did not include massage along with the warm compress	3, 6: clinical significance not supported for the primary outcome	
Blackie et al (2018)[14],		3: LipiFlow group received eyelid margin cleaning	2,3: Control group did not receive eyelid margin cleaning	3: unclear how harms data were collected 5: clinically significant difference not specified	
Tauber (2020)[13],	4: patients with MGD with inflammation included			4, 5: unclear if co-primary outcomes were validated measures	
Kasetsuwan (2020) [15],	1: Unclear whether participants had chronic disease or whether they had tried previous treatments 5: Not representative of U.S. population diversity			3: unclear how harms data were collected 5: clinically significant difference not specified	
Park (2021)[16],	1. Included a mix of patients with existing MGD (treatment population) and those without (prevention population) 1: Unclear whether participants had chronic disease or whether they had tried			3: unclear how harms data were collected	

Reproduction without authorization from Blue Shield of California is prohibited.

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
	previous treatments 5: Not representative of U.S. population diversity				
Mencucci (2023) [17]	1: Unclear whether participants had chronic disease or whether they had tried previous treatments 5: Racial/ethnic study characteristics not provided			3: unclear how harms data were collected 5: clinically significant difference not specified	1: Follow-up of 1 mo
Matossian (2023) [18]	1: Unclear whether participants had chronic disease or whether they had tried previous treatments		2. No treatment in control group	3: unclear how harms data were collected	
Meng (2023) [19]	1: Unclear whether participants had chronic disease or whether they had tried previous treatments 5: Not representative of U.S. population diversity			3: unclear how harms data were collected 5: clinically significant difference not specified 7: no clear statement regarding what the primary outcome was or whether it was pre-specified	

MGD: meibomian gland disfunction.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5: Enrolled study populations do not reflect relevant diversity; 6: Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest; 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5: Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No

Reproduction without authorization from Blue Shield of California is prohibited.

CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported; 7: Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 8: Other.

Table 5. Study Design and Conduct Limitations of Randomized Controlled Trials of LipiFlow

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Lane et al (2012)[10],	3	1, 2, 3			1, 2	
Finis et al (2014)[11],	3	1; investigator blinded only		1, 6; reasons for drop out not described		
Blackie et al (2016)[12],	3	1, 2, 3	1	1; reasons for drop out not described	1, 2	
Blackie et al (2018)[14],		1,2,3: Open-label			1,3: Assumptions for power calculations not given	
Tauber (2020)[13],	3	1; investigator blinded only	1	1; attrition in the control group	3; the sample size was not based on formal statistical calculations or clinical assumptions	
Kasetsuwan (2020)[15],		1: Participants not blinded; outcome assessors were masked		1: 12/60 originally randomized were lost to follow-up due to: 'inconvenience or health problems unrelated to the ocular disease' 2: No sensitivity analyses for missing data 6: No ITT analyses	3: Justification for powered difference not given	
Park (2021)[16],		1,2,3: Open-label		1: 23% of control participants lost to follow-up (did not have surgery or did not complete study visits) 2: No sensitivity analyses for missing data 6: No ITT analysis	3: Justification for powered difference not given	
Mencucci (2023)[17],		1,2,3: Open-label		2: No description of study flow or missing data	3: Justification for powered difference not given	
Matossian (2023)[18],		1,2,3: Open-label				

Reproduction without authorization from Blue Shield of California is prohibited.

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Meng (2023)[19,]		1: Participants not blinded; outcome assessors were masked	1. No report of registration		1,2,3: No description of sample size/power calculations	2: Unclear whether analyses accounted for multiple eyes per participant

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5: Other.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4: Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4: Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7: Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4: Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5: Other.

Nonrandomized Comparative Trials and Observational Studies

Nonrandomized trials have been conducted but do not provide longer follow-up or inclusion of populations or outcomes of interest beyond what is available from RCTs and will not be discussed further.

Four other studies have evaluated long-term outcomes for some trial subjects who had undergone LipiFlow treatment. The study by Greiner (2013)[20,] evaluated 18 of 30 subjects from 1 site of the Lane trial (described above).[10,] 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.[21,] 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.[22,] Lastly, a retrospective cohort study by Hura et al (2020) compared dry eye disease markers and meibomian gland imaging between patients who had undergone LipiFlow treatment (n=30) versus those who declined LipiFlow treatment (n=13).[23,] At 1 year, visible meibomian gland structure, tear break-up time, corneal staining, and meibomian gland evaluation scores all showed sustained improvements in the treatment group over the control. On the other hand, Standard Patient Evaluation for Eye Dryness scores and tear osmolarity did not show a sustained improvement 1-year post-therapy.

Summary of Evidence

For individuals who have dry eye symptoms consistent with meibomian gland dysfunction (MGD) who receive eyelid thermal pulsation, the evidence includes 10 randomized controlled trials (RCTs), nonrandomized comparison studies, and longer term follow-up of patients from RCTs and observational studies. Relevant outcomes are symptoms, morbid events, and functional outcomes. The RCTs have evaluated only the LipiFlow system. Study populations have been predominately White or Asian. The duration of MGD and previous treatments for MGD were unclear in the study populations. The majority of the RCTs have reported greater efficacy with LipiFlow compared to standard warm compress therapy and eyelid hygiene and improvements were generally seen in both objective metrics of MGD and in patient-reported symptoms for up to 3 months. Limited longer-term follow-up is available. The method for collecting adverse events in the studies was unclear but no

Reproduction without authorization from Blue Shield of California is prohibited.

serious adverse events were reported in any studies. Several additional RCTs have been conducted but have not been published. Observational studies have shown sustained treatment effects for most outcomes up to 3 years. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Ophthalmology

In 2018, the American Academy of Ophthalmology updated preferred practice patterns guidelines on dry eye syndrome.[6,] These guidelines list "In-office, physical heating and expression of the meibomian glands (including device-assisted therapies, such as LipiFlow, or intense pulse light treatment)" as 1 of several step-up treatments for patients who do not respond to conventional management, including the elimination of environmental factors and offending medications, dietary modifications, ocular lubricants, and lid hygiene and warm compresses.

In 2018, the American Academy of Ophthalmology updated preferred practice patterns guidelines on blepharitis.[3,] These guidelines cover the 3 clinical subcategories of blepharitis: staphylococcal, seborrheic, and meibomian gland dysfunction (posterior blepharitis specifically affects the meibomian glands). The following statements are made relevant to thermal pulsation treatment:

"There are also several in-office procedural treatments available that may theoretically unclog the inspissated meibomian gland orifices using intense pulsed light (IPL) or mechanical means (e.g., microblepharoexfoliation of the eyelid margin, meibomian gland probing, and/or devices using thermal pulsation). Although there have been industry-sponsored studies, independent, randomized, masked clinical trials have yet to be performed to assess efficacy of these costly, primarily fee-for-service treatments."

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 or unpublished trials that might influence this review are listed in Table 6.

Table 6. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04795752	Prospective, Randomized, Masked, Controlled Trial To Evaluate The Safety And Effectiveness Of The TearCare® System In The Treatment Of The Signs And Symptoms Of Dry Eye Disease (SAHARA)	350	May 2024

Reproduction without authorization from Blue Shield of California is prohibited.

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT05162261	A Randomized, Masked (Evaluator), Controlled, Prospective Study Evaluating the Effectiveness and Safety of the Tixel® Medical Device, Versus LipiFlow® in the Treatment of Meibomian Gland Dysfunction	110	Sep 2024
Unpublished			
NCT03055832	Randomized Comparison Between iLux™ and LipiFlow® in the Treatment of Meibomian Gland Dysfunction	142	Jul 2017
NCT03502447	Randomized, Controlled Trial to Evaluate the Safety and Effectiveness of the TearCare® System in the Treatment of the Signs and Symptoms of Dry Eye Disease	17	Jan 2019
NCT03857919	Randomized, Controlled Trial to Evaluate the Safety and Effectiveness of the TearCare® System in the Treatment of the Signs and Symptoms of Dry Eye Disease (OLYMPIA)	138	Oct 2019
NCT03956225	Comparison Between iLux and LipiFlow in the Treatment of Meibomian Gland Dysfunction (MGD): A 12-month, Multicenter Study	299	Oct 2020

References

1. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. Jul 2017; 15(3): 334-365. PMID 28736337
2. Farrand KF, Fridman M, Stillman IÖ, et al. Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. Am J Ophthalmol. Oct 2017; 182: 90-98. PMID 28705660
3. Blepharitis. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. San Francisco, CA: American Academy of Ophthalmology; 2018.
4. Nichols KK, Foulks GN, Bron AJ, et al. The international workshop on meibomian gland dysfunction: executive summary. Invest Ophthalmol Vis Sci. Mar 30 2011; 52(4): 1922-9. PMID 21450913
5. Blackie CA, Korb DR, Knop E, et al. Nonobvious obstructive meibomian gland dysfunction. Cornea. Dec 2010; 29(12): 1333-45. PMID 20847669
6. Dry Eye Syndrome. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. San Francisco, CA: American Academy of Ophthalmology; 2018.
7. Miller KL, Walt JG, Mink DR, et al. Minimal clinically important difference for the ocular surface disease index. Arch Ophthalmol. Jan 2010; 128(1): 94-101. PMID 20065224
8. Ngo W, Situ P, Keir N, et al. Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire. Cornea. Sep 2013; 32(9): 1204-10. PMID 23846405
9. Tao JP, Shen JF, Aakalu VK, et al. Thermal Pulsation in the Management of Meibomian Gland Dysfunction and Dry Eye: A Report by the American Academy of Ophthalmology. Ophthalmology. Dec 2023; 130(12): 1336-1341. PMID 37642619
10. Lane SS, DuBiner HB, Epstein RJ, et al. A new system, the LipiFlow, for the treatment of meibomian gland dysfunction. Cornea. Apr 2012; 31(4): 396-404. PMID 22222996
11. Finis D, Hayajneh J, König C, et al. Evaluation of an automated thermodynamic treatment (LipiFlow®) system for meibomian gland dysfunction: a prospective, randomized, observer-masked trial. Ocul Surf. Apr 2014; 12(2): 146-54. PMID 24725326
12. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. Clin Ophthalmol. 2016; 10: 1385-96. PMID 27555745
13. Tauber J. A 6-Week, Prospective, Randomized, Single-Masked Study of Lifitegrast Ophthalmic Solution 5% Versus Thermal Pulsation Procedure for Treatment of Inflammatory Meibomian Gland Dysfunction. Cornea. Apr 2020; 39(4): 403-407. PMID 31895884
14. Blackie CA, Coleman CA, Nichols KK, et al. A single vectored thermal pulsation treatment for meibomian gland dysfunction increases mean comfortable contact lens wearing time by approximately 4 hours per day. Clin Ophthalmol. 2018; 12: 169-183. PMID 29398904

Reproduction without authorization from Blue Shield of California is prohibited.

15. Kasetsuwan N, Suwajanakorn D, Tantipat C, et al. The Efficacy Between Conventional Lid Hygiene and Additional Thermal Pulsatile System in Meibomian Gland Dysfunction Patients Treated with Long-Term Anti-Glaucoma Medications in a Randomized Controlled Trial. Clin Ophthalmol. 2020; 14: 2891-2902. PMID 33061275
16. Park J, Yoo YS, Shin K, et al. Effects of Lipiflow Treatment Prior to Cataract Surgery: A Prospective, Randomized, Controlled Study. Am J Ophthalmol. Oct 2021; 230: 264-275. PMID 33992615
17. Mencucci R, Mercuri S, Cennamo M, et al. Efficacy of vector thermal pulsation treatment in reducing postcataract surgery dry eye disease in patients affected by meibomian gland dysfunction. J Cataract Refract Surg. Apr 01 2023; 49(4): 423-429. PMID 36729441
18. Matossian C, Chang DH, Whitman J, et al. Preoperative Treatment of Meibomian Gland Dysfunction with a Vectored Thermal Pulsation System Prior to Extended Depth of Focus IOL Implantation. Ophthalmol Ther. Oct 2023; 12(5): 2427-2439. PMID 37318707
19. Meng Z, Chu X, Zhang C, et al. Efficacy and Safety evaluation of a single thermal pulsation system treatment (Lipiflow®) on meibomian gland dysfunction: a randomized controlled clinical trial. Int Ophthalmol. Apr 2023; 43(4): 1175-1184. PMID 36112256
20. Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. Clin Exp Ophthalmol. Aug 2013; 41(6): 524-30. PMID 23145471
21. Finis D, König C, Hayajneh J, et al. Six-month effects of a thermodynamic treatment for MGD and implications of meibomian gland atrophy. Cornea. Dec 2014; 33(12): 1265-70. PMID 25321941
22. Greiner JV. Long-Term (3 Year) Effects of a Single Thermal Pulsation System Treatment on Meibomian Gland Function and Dry Eye Symptoms. Eye Contact Lens. Mar 2016; 42(2): 99-107. PMID 26222095
23. Hura AS, Epitropoulos AT, Czyz CN, et al. Visible Meibomian Gland Structure Increases After Vectored Thermal Pulsation Treatment in Dry Eye Disease Patients with Meibomian Gland Dysfunction. Clin Ophthalmol. 2020; 14: 4287-4296. PMID 33324034

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral
	0330T	Tear film imaging, unilateral or bilateral, with interpretation and report
	0507T	Near-infrared dual imaging (i.e., simultaneous reflective and trans-illuminated light) of meibomian glands, unilateral or bilateral, with interpretation and report

Reproduction without authorization from Blue Shield of California is prohibited.

Type	Code	Description
	0563T	Evacuation of meibomian glands, using heat delivered through wearable, open-eye eyelid treatment devices and manual gland expression, bilateral
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
06/30/2015	BCBSA Medical Policy adoption
06/01/2016	Policy revision without position change
04/01/2017	Policy revision without position change
05/01/2018	Policy revision without position change Coding update
05/01/2019	Policy revision without position change
05/01/2020	Annual review. No change to policy statement. Literature review updated.
05/01/2021	Annual review. No change to policy statement. Literature review updated.
05/01/2022	Annual review. No change to policy statement. Literature review updated.
05/01/2023	Annual review. No change to policy statement. Literature review updated.
05/01/2024	Annual review. No change to policy statement. Policy guidelines and literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) 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 the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an

Reproduction without authorization from Blue Shield of California is prohibited.

authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Reproduction without authorization from Blue Shield of California is prohibited.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Eyelid Thermal Pulsation for the Treatment of Dry Eye Syndrome 9.03.29 **Policy Statement:** I. Eyelid thermal pulsation therapy to treat dry eye syndrome is considered **investigational**.	**Eyelid Thermal Pulsation for the Treatment of Dry Eye Syndrome 9.03.29** **Policy Statement:** I. Eyelid thermal pulsation therapy to treat dry eye syndrome is considered **investigational**.

Reproduction without authorization from Blue Shield of California is prohibited