Management of Meibomian Glands

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers devices for evacuating meibomian glands by means of heat and intermittent pressure for the treatment of meibomian gland dysfunction (e.g., the LipiFlow System) experimental and investigational because of insufficient evidence of their effectiveness.

Aetna considers tear film imaging (e.g., LipiView Ocular Surface Interferometer) experimental and investigational because its clinical value has not been established.

Aetna considers in-vivo confocal microscopy experimental and investigational for evaluation of meibomian glands because its clinical value has not been established.

Aetna considers near-infrared dual imaging (e.g., LipiScan Dynamic Meibomian Imager) for evaluation of meibomian glands experimental and investigational because its clinical value has not been established.

Aetna considers meibomian gland probing experimental and investigational for the treatment of dry eye because the effectiveness of this approach has not been established.

Background
Meibomian glands are large sebaceous glands that are located as separate gland strands in parallel arrangement within the tarsal plates of the eyelids. Their oily product, meibum, is secreted via a holocrine mechanism during which meibocytes are transformed into the meibum. Following production in the gland acini, meibum is transported through the ductal system via the connecting duct and the central duct towards the orifice at the free eyelid margin close to the inner eyelid border. Meibum is a complex mixture of various lipids and minor protein components as well as other components of the meibocytes, which form a clear liquid at body temperature. It is transported within the gland by the force of secretory pressure from continuous secretion and by muscular action of the orbicularis muscle and Riolans muscles during blinking. After it is delivered onto the posterior eyelid margin, meibum moves from the posterior eyelid margin reservoir onto the tear meniscus and is pulled as a thin layer onto the pre-ocular tear film every time the eyelid opens. During closure of the eyelid, it is compressed and a small part is continuously renewed. Meibum also has a barrier function against the spillage of tears over the inner border of the eyelid and against the entry of skin lipids (sebum) from the free eyelid margin (Knop and Knop, 2009a; Knop et al, 2009).

Obstructive meibomian gland dysfunction (MGD) is a common source of complaint among patients with dry eye (DE) syndrome and its prevalence increases with age. The principal clinical consequence of obstructive MGD is evaporative DE syndrome. Moreover, chronic obstruction of the meibomian glands may also result in degeneration of the secretory gland tissue that can lead to a secondary hypo-secretion even if the primary obstruction is later resolved by therapeutic approaches. Risk factors in the pathogenesis of obstructive MGD include age, hormonal disturbances and environmental influences (e.g., contact lenses). Furthermore, qualitative alterations in the composition of the meibum may lead to hyper-keratinization of the ductal epithelium and increased viscosity of the meibum. This can result in obstruction of the duct and orifice leading to a lack of meibum on the eyelid margin and tear film with downstream hyper-evaporative DE syndrome. At the same time, obstruction leads to a stasis of meibum inside the meibomian gland with increased pressure and resulting dilatation of the ducts and in atrophy of the acini with rarefaction of the secretory meibocytes and gland dropout. Stasis can also increase the growth of commensal bacteria, their production of oil degrading enzymes and release of toxic mediators. These factors can act as self-enforcing feedback loops that aggravate the primary hyper-keratinization and compositional disturbance of meibum and can hence lead to a progressive MGD (Knop and Knop, 2009b).

Conventional treatments of obstructive MGD entail eyelid hygiene (e.g., lid washing and use of preservative-free artificial tears), omega-3 dietary supplementation (e.g., eicosapentaenoic acid and docosahexaenoic acid), topical antibiotics (e.g., bacitracin and erythromycin), topical corticosteroids, topical cyclosporine, oral antibiotics (e.g., doxycycline, minocycline, and tetracycline), oral omega-6 fatty acids (e.g., linoleic acid and gamma-linolenic acid), as well as
unclogging of glands that are blocked, which can be achieved by applying warm compresses to the eyelid or gentle lid massaging (Olson et al, 2003; Romero et al, 2004; Yoo et al, 2005; Perry et al, 2006; Pinna et al, 2007; Souchier et al, 2008; and Foster et al, 2009). Moreover, eyelid-warming devices have also been employed in the treatment of patients with MGD. However, the effectiveness of these devices has not been established.

Thermal Pulsation System (e.g., the LipiFlow System)

In a prospective, non-comparative, interventional case series, Goto et al (2002) assessed the short term safety and effectiveness of an infra-red warm compression device as treatment for non-inflamed MGD. In a total of 37 cases, subjective symptom scores and subjective face scores improved significantly, from 12.3 to 8.4, and from 7.0 to 5.3. The results for tear evaporation rates during forced blinking, fluorescein staining, rose bengal staining, tear film break up time (BUT), and meibomian gland orifice obstruction score had also improved significantly at the end of the 2-week period of infra-red thermotherapy. The authors concluded that the infra-red warm compression device was safe and effective for the treatment of MGD. Moreover, they noted that while the results were promising, the small sample size and lack of comparison group limit the generalizability of the findings.

In a prospective, controlled, observer masked, single intervention trial, Mitra et al (2005) measured changes in tear film lipid layer thickness (LLT) and ocular comfort in normal subjects after 10 mins use of a novel device, which delivers meibomian therapy with latent heat. A total of 24 normal subjects were randomized into three groups: Group I underwent 10 mins treatment with the activated device, Group II used the inactivated device for the same duration of time, and Group III had no intervention. The LLT of each subject was measured with a Keeler Tearscope prior and subsequent to the 10-min period. Subjective alteration in ocular comfort was also assessed. Seven of 8 subjects (87.5 %) in Group I exhibited an increase in LLT. The mean LLT in this group showed a statistically significant increase compared to Groups II and III. Six of 8 subjects (75 %) using the activated device experienced subjective improvement in ocular comfort.

In a prospective, interventional clinical trial, Matsumoto et al (2006) evaluated the safety and effectiveness of an original warm moist air device on tear functions and ocular surface of patients with simple MGD. A total of 15 patients with simple MGD and 20 healthy volunteers were enrolled in this study. The device was applied to the eyes of the subjects for 10 mins. Temperatures of the eyelids and corneas were measured with an infra-red thermometer. Symptoms of ocular fatigue were scored using visual analog scales (VAS). Schirmer test, tear film BUT, DR-1 tear film lipid layer interferometry, fluorescein staining, and rose bengal staining were also performed before and after the application of the eye steamer. After the initial study,
another 2-week, prospective, clinical trial was carried out in 10 patients with MGD who received the warm moist air treatment. Ten other patients were also recruited and received warm compress treatment with hot towels for 2 weeks to evaluate the long-term effects of the warm moist air device and the warm compresses on tear film LLT and ocular surface health. The warm moist air device and the warm compresses were applied for 10 mins twice-daily. The changes in VAS scores for symptoms, tear film BUT values, fluorescein, and rose bengal staining scores were examined before and after each treatment during the second trial. VAS scores of ocular fatigue improved significantly with short- and long-term applications of the warm moist air device in both studies. The mean corneal surface and eyelid temperatures showed significant elevation within safe limits 10 mins after the moist air application. The mean tear film BUT prolonged significantly in patients receiving warm moist air applications but did not change significantly in those treated with warm compresses. DR-1 tear film lipid layer interference showed evidence of lipid expression in the patients and controls, with thickening of the tear film lipid layer after 10 mins of warm moist air device use. In the 2-week trial, tear film LLT increased in both warm moist air device and warm compress groups, with a greater extent of increase in the warm moist air device group. The authors concluded that the use of warm moist air device provided symptomatic relief of ocular fatigue and improvement of tear stability in patients with MGD. The new warm moist air device appears to be a safe and promising alternative in the treatment of MGD.

Korb and Blackie (2011) determined (i) the pressure needed to express the first non-liquid material from non-functional lower lid meibomian glands, (ii) the pressure required to evacuate all of the expressible material from the glands (simulating the authors' methodology for therapeutic meibomian gland expression), and (iii) the level of pain associated with these procedures. All patients (n = 28) were recruited from those presenting for ocular examinations at a single practice. Custom instrumentation exerting pressures from 1.0 to 150.0 psi was developed to quantify the pressure applied during expression. The instrument was applied to the inner surface of the lower lid. The lid was then compressed between the thumb and the contact surface of the instrument. The applied pressure was displayed on a digital meter. The first procedure evaluated the pressure required to obtain the first non-liquid material from non-functional glands. The second evaluated the pressure needed for evacuating all expressible gland contents. The pain response was monitored throughout the procedure. The pressure to obtain the first non-liquid material ranged from 5 to 40 psi (mean of 16.1 +/- 8.2 psi) and for the evacuation of expressible contents, from 10 to 40 psi (mean of 25.6 +/- 11.4 psi). Only 7% of the patients could tolerate the pressure necessary to administer complete therapeutic expression along the entire lower eyelid. The authors concluded that forces of significant magnitude are needed for therapeutic expression. Pain is the limiting factor for the conduct of this treatment.
In a prospective, cohort, observational, single-center study, Greiner (2016) examined the long-term (3 years) effects of a single (12 minutes) thermal pulsation system (TPS) treatment on symptomatic patients with evaporative DE disease (DED) secondary to MGD. Signs (meibomian gland secretion [MGS] scores and tear film break-up time [TBUT]) and symptoms (Ocular Surface Disease Index [OSDI] and SPEED questionnaires) were determined in 20 patients (40 eyes) with MGD and dry eye symptoms at baseline (BL), 1 month, and 3 years post-TPS treatment using LipiFlow. Meibomian gland secretion scores increased from BL (4.5 ± 0.8) to 1 month (12.0 ± 1.1, p ≤ 0.001). Improvement persisted at 3 years (18.4 ± 1.4) relative to BL (p ≤ 0.001). Meibomian gland secretion scores in all regions of the lower eyelid were improved over BL at 1 month (nasal [p ≤ 0.001], central [p ≤ 0.001], temporal [p ≤ 0.01]) and 3 years (nasal [p ≤ 0.001], central [p ≤ 0.001], temporal [p ≤ 0.001]). Tear break-up time increased from BL (4.1 ± 0.4) to 1 month (7.9 ± 1.4, p ≤ 0.05) but was not significantly different than BL at 3 years (4.5 ± 0.6, p > 0.05). The OSDI scores decreased from BL (26.0 ± 4.6) to 1 month (14.7 ± 4.3, p ≤ 0.001) but returned to BL levels at 3 years (22.5 ± 5.4, p > 0.05). The SPEED scores decreased from BL (13.4 ± 1.0) to 1 month (6.5 ± 1.3, p ≤ 0.001), and this improvement persisted at 3 years (9.5 ± 1.6, p ≤ 0.001). The authors concluded that thermal pulsation may be an effective treatment option for DED secondary to MGD in that a single 12-min procedure is associated with significant improvement in MGS and SPEED scores for up to 3 years. The findings of this small study (n = 20) need to be validated by well-designed studies.

In summary, there is currently insufficient evidence to support the use of devices for evacuating meibomian glands by means of heat and intermittent pressure for the treatment of MGD.

Tear Film Imaging (Ocular Surface Interferometry)

Interferometry is a non-invasive technique for recording tear film surface irregularities. While this technique has been used to diagnose DE, it is hindered by natural eye movements resulting in measurement noise. Currently, there is insufficient evidence to support the use of interferometry for the diagnosis of DE as a consequence of meibomian gland dysfunction or other cause such as hematopoietic stem cell transplantation (HSCT)

Savini et al (2008) noted that the currently available methods for the diagnosis of DE are still far from being perfect for a variety of reasons. These researchers highlighted the advantages and disadvantages of both traditional tests (e.g., Schirmer's test, break-up time, and ocular surface staining) and innovative non-invasive procedures, including tear meniscus height measurement, corneal topography, functional visual acuity, tear interferometry, tear evaporimetry, as well as tear osmolarity assessment.
Ban and colleagues (2009) examined the changes in the tear film lipid layer in HSCT patients with DE associated with chronic graft-versus-host disease (cGVHD) and compared with HSCT recipients without DE. These researchers performed a prospective study in 10 HSCT patients with DE associated with cGVHD and 11 HSCT recipients without DE. They performed Schirmer's test, tear film break-up time examinations, ocular surface dye staining and meibum expressibility test and DR-1 tear film lipid layer interferometry. DR-1 interferometry images of the tear film surface were assigned a “DR-1 grade” according to the Yokoi severity grading system. The DR-1 grades were analyzed according to the presence or absence of DE, conjunctival fibrosis, as well as systemic cGVHD. The mean DR-1 severity grade in patients with DE related to cGVHD (DE/cGVHD group; 3.9 +/- 0.9) was significantly higher than in patients without DE after HSCT (non-DE/non-cGVHD group; 1.3 +/- 0.6; p < 0.05). The DR-1 grade for HSCT recipients with conjunctival fibrosis was significantly higher than in patients without conjunctival fibrosis (p < 0.05). When DE severity was graded according to the recommendation of the 2007 Dry Eye Workshop Report, these findings showed a correlation between the severity of DE and DR-1 grades (r = 0.8812, p < 0.0001). The authors concluded that DR-1 interferometry may be applicable to diagnosing DE and evaluating its progression subsequent to HSCT.

Blackie and colleagues (2009) examined the relationship between DE symptoms and LLT in patients presenting for routine eye examination. Patients presenting consecutively for routine eye examinations were recruited (n = 137, age range of 18 to 60 years, mean of 41.7 +/- 15.5 years, 102 females and 35 males). Patients were required to complete the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire after which their LLT was evaluated using a new interferometer (Ocular Surface Interferometer). Patients were assigned to 1 of 3 symptom categories: (i) no symptoms (SPEED = 0), (ii) mild-to-moderate symptoms (SPEED = 1 to 9), and (iii) severe symptoms (SPEED greater than or equal to 10). Categorical analysis (contingency table) and linear regression were performed on the data. For patients with severe DE symptoms, 74 % had an LLT less than or equal to 60 nm. Conversely, 72 % of patients with no DE symptoms had an LLT of greater than or equal to 75 nm (contingency table, Chi = 12.63, df = 2, p = 0.0018). Furthermore, a linear regression of LLT and SPEED score reveal a significant linear relationship (as LLT increases, SPEED score decreases; p = 0.0014). The authors concluded that these data indicated that approximately 3 of 4 patients reporting severe symptoms have relatively thin lipid layers of 60 nm or less, whereas approximately 3 of 4 patients without symptoms have relatively thick lipid layers of 75 nm or more. Thus, the presence of DE symptoms significantly increases the likelihood of a relatively thin lipid layer. Lipid layer thickness seems to correlate better to symptoms, especially severe symptoms, than other reported correlations with objective clinical tests for DE disease. Moreover, they stated that interferometry has the potential to be a practical and useful addition to clinical practice.
Lane et al (2012) evaluated the safety and effectiveness of the LipiFlow System compared to the iHeat WC for adults with MGD. This was a non-significant risk, prospective, open-label, randomized, cross-over, multi-center clinical trial. A total of 139 subjects were randomized between LipiFlow (n = 69) and WC control (n = 70). Subjects in the LipiFlow group received a 12-min LipiFlow treatment and were re-examined at 1 day, 2 weeks and 4 weeks. Control subjects received a 5-min iHeat treatment with instructions to perform the same treatment daily for 2 weeks. At 2 weeks, they crossed-over (LipiFlow Cross-over) and received the LipiFlow treatment. Effectiveness parameters included subjective symptoms, lipid layer metrics at 2 weeks, and tear film TBUT in the control group. LipiFlow resulted in a greater significant reduction in dry eye symptoms than the iHeat WC. The cross-over group demonstrated similar significant improvement 2 weeks post-treatment with the LipiFlow. There was no significant difference between groups in the incidence of non-serious, device-related adverse events. The authors concluded that the LipiFlow System was significantly more effective than iHeat WC; they stated that these results supported its safety and effectiveness in the treatment of MGD and dry eye symptoms. This was an industry-sponsored, open-label, single cross-over study with a relatively small sample size and short-term follow-up. This study did not include a group receiving warm compresses only for 4 weeks. It should be noted that although the control group did not show significant increases in MG and tear film metrics at 2 weeks, the control group did have a significant reduction in self-reported dry eye symptom frequency and severity. Also, the control group was limited to 5 mins of warm compression therapy once-daily, while typical treatment for MGD consists of hot packs 3 to 4 times daily along with lid margin scrubs. The findings of this study need to be validated by well-designed studies.

In a prospective, randomized, cross-over, observer-masked clinical trial, Finis and colleagues (2014a) compared the effectiveness of a single LipiFlow® treatment with combined lid warming and massage in patients with MGD. Subjects were randomized to receive either a single 12-min LipiFlow-LipiFlow Thermal Pulsation (LTP) system treatment or to perform combined twice-daily lid warming and massage for 3 months. All subjects were examined before, and 1 and 3 months after initiation of treatments. Investigated parameters included subjective symptoms, lipid layer thickness, meibomian gland assessment, tear BUT, tear osmolarity, corneal and conjunctival staining, Schirmer test values, and tear meniscus height. A total of 31 subjects completed the 3-month follow-up. At 1 and 3 months, patients in the LipiFlow treatment group had a significant reduction in Ocular Surface Disease Index (OSDI) scores compared with those in the lid-margin hygiene group. Both treatments produced a significant improvement in expressible meibomian
glands compared to the baseline parameters, but no significant difference was noted between the 2 groups. The other investigated objective parameters did not show a significant difference. The authors concluded that results of this study showed that a single LipiFlow treatment is as least as effective as a 3-month, twice-daily lid margin hygiene regimen for MGD. Moreover, they stated that the present study was observer-masked only, and therefore a placebo effect may have confounded any improvements in subjective symptoms and other parameters in both groups.

Finis and associates (2014b) stated that the quantitative measurement of the tear film lipid layer thickness is a relatively new and promising method. However, so far it has not been investigated whether there is a diurnal or a day-to-day variability and whether certain factors are confounding the measurement of the lipid layer thickness. In 3 different experimental settings, 10 subjects without known sicca syndrome were examined at 3 different time-points on one day, on 3 different days and before and after therapeutic expression of the Meibomian glands. As a comparison, the parameters tear film BUT, tear meniscus height, diagnostic expression of the Meibomian glands and subjective symptoms, determined using the OSDI questionnaire, were measured. The results of the study showed a smaller variation of the lipid layer thickness measurements during the day and from day to day compared to the tear film BUT. The expression of the Meibomian glands significantly increased the lipid layer thickness. There was a correlation between the baseline values of tear film BUT and the lipid layer thickness. The authors concluded that these findings data showed that the lipid layer thickness as measured with the Lipiview® interferometer appears to be a relatively constant parameter over time. In addition, the expression of the Meibomian glands could be identified as a potential confounding factor. In this study these investigators included only healthy subjects without known sicca syndrome; these findings need to be validated in dry eye patients.

Zhao et al (2015) noted that tear lipid morphology is important for normal tear function. Recently, there have been clinical studies using interferometry to assess LLT. These researchers examined the repeatability of a commercially available interferometer. Two observers measured LLT in 20 Asian subjects (20 eyes) using an interferometer (LipiView ocular surface interferometer, TearScience Inc., Morrisville, NC). Dry eye symptoms, TBUT and corneal fluorescein staining were also prospectively evaluated. Data for 20 participants were presented for either right or left eye (randomly selected). The mean LLT ± standard deviation of these participants was 53.53 ± 14.59 nm. When a single observer repeated the imaging on the same day, the coefficient of repeatability was 16 nm and the 95 % limits of agreement were between -11 nm and 18 nm. When a different observer repeated the scan, the coefficient of repeatability was 13 nm and limits of agreement were -9 nm and 16 nm. Lipid layer thickness was not significantly associated with TBUT, presence of any corneal staining in any corneal zones, or symptomatic status. The
authors concluded that with the repeatability of measurements being known, the significance of LLT changes measured by this interferometer may be better interpreted. In this small Asian study, the LLT was lower than previously reported studies.

Satjawatcharaphong et al (2015) identified patient characteristics at a baseline ocular surface evaluation that correlated with improvement in DE symptoms at a follow-up visit after treatment with the LipiFlow Thermal Pulsation System. A total of 32 patients completed a comprehensive baseline ocular surface evaluation and were treated with the LipiFlow Thermal Pulsation System followed by maintenance home therapy. Lipid layer thickness and blink pattern were determined using the LipiView Interferometer. Non-invasive TBUT was measured using a Medmont E300 Corneal Topographer. Slit lamp biomicroscopy was used to evaluate invasive TBUT and corneal staining after instillation of fluorescein dye. Conjunctival staining, location of the line of Marx, and presence of lid wiper epitheliopathy were evaluated with lissamine green dye. Meibomian gland expressibility was scored using the TearScience Meibomian Gland Evaluator, and meibography was imaged using the Oculus Keratograph. A logistic regression model was used to estimate the odds ratios for having a decreased post-treatment score (reduced symptoms) of SPEED. Baseline SPEED score (p = 0.01) and sex (p = 0.03) had significant odds ratios at the α = 0.05 level. Baseline non-invasive TBUT (p = 0.07), number of grade 0 meibomian glands in the lower lid (p = 0.09), and conjunctival staining grade in the inferior region (p = 0.10) met an α = 0.10 criterion for significant odds ratios, but not the typical α = 0.05 criterion. Higher baseline SPEED score and male sex had greater odds for decreased post-treatment SPEED score. The authors concluded that they identified factors that better select candidates for LipiFlow Thermal Pulsation System.

Dohlman and colleagues (2016) noted that DED is a complex, multi-factorial condition that is challenging to diagnose and monitor clinically. To-date, diagnosis has consisted largely of self-reported symptom questionnaires and a collection of clinical tests including vital dye staining, estimation of TBUT and Schirmer's testing, as no gold standard exists. As the dry eye field has made progress in understanding disease pathogenesis, new methods for assessment of this condition have been developed. Dry eye disease is now known to be characterized by tear hyperosmolality and ocular surface inflammation, and there are now commercially available devices that accurately and reliably measure tear osmolarity and matrix metalloproteinase 9 (MMP9), a marker of inflammation and tissue breakdown. In addition, there are a variety of imaging modalities that have shown promise in their ability to identify patients with DED by assessing tear film dimensions and tear film instability. The authors concluded that there is a significant need for the development of tear film assessments for accurate diagnosis and monitoring of dry eye. There are a number of new devices and techniques that have shown promise in their ability help clinicians manage patients with DED.
In a prospective, case-controlled study, Liang and colleagues (2017) observed the morphology, fibrosis grade and inflammatory infiltration of meibomian glands using in-vivo confocal microscopy (IVCM) in MGD patients. According to the diagnostic criteria of MGD, a total of 20 MGD patients (20 eyes) were included in this study from August to October 2015; 15 normal subjects (15 eyes) were also studied. All subjects completed the questionnaire of the OSDI, lid margin and ocular surface examination by slit lamp microscopy, TBUT test, corneal and conjunctival staining (Oxford scale), Schirmer I test, infra-red meibomian photography and IVCM. Main outcomes in IVCM included meibomian gland acinar longest diameter (MGALD), meibomian gland acinar shortest diameter (MGASD), meibomian gland acinar unit density (MGAUD), meibomian gland acinar unit area (MGAUA), meibomian gland inflammatory cell density and fibrosis degree. The parameters between the MGD group and the control group were compared using the independent samples t-test. The OSDI score [(31.80 ± 22.97) points], lid margin abnormality score [(3.10 ± 0.31) points], loss rate of meibomian glands (38.31 % ± 19.94 %) and corneal and conjunctival staining score [1.00 (2.75) points] in the MGD group were obviously higher than those in the control group [(7.93 ± 6.51) points, (0.33 ± 0.31) points, 21.31 % ± 7.70 %, and 0.00 (1.00) points, p = 0.001, p < 0.001, p = 0.004, and p = 0.037, respectively]. The TBUT was significantly lower in the MGD group [(3.35 ± 2.28) s] than in the control group [(6.67 ± 2.51) s, p < 0.001]. According to Schirmer I test, there was no significant difference in the 2 groups (p = 0.139). The mean values of MGALD [(156.80 ± 46.10) μm], MGASD [(38.75 ± 11.72) μm], MGAUA [(10 113.84 ± 5 531.21) μm(2)], meibomian gland inflammatory cell density [(621.90 ± 405.63) cells/mm(2)] and fibrosis degree 1.50 (1.00) in the MGD patients were larger than those in the control group [(67.47 ± 9.117) μm,(22.00 ± 2.95) μm,(3,102.13 ± 1,111.97) μm(2), (188.80 ± 72.25) cells/mm(2), and 0.00 (0.00), all p < 0.001, respectively]. The mean MGAUD was lower in the MGD patients [(61.10 ± 34.97) glands/mm(2)] than in the control group [(105.07 ± 18.58) glands/mm(2), p < 0.001]. The authors concluded that IVCM was pertinent to examine the meibomian glands by detecting the irregularity of meibomian orifices, the diameter and area, and the inflammation and fibrosis levels in MGD patients. It may have a potential clinical value for the diagnosis of MGD.

Near-Infrared Dual Imaging (e.g., LipiScan Dynamic Meibomian Imager)

Near-infrared dual imaging (e.g., LipiScan Dynamic Meibomian Imaging (DMI) utilizes 2 novel imaging technologies -- adaptive trans-illumination and dynamic illumination. Each technology generates its own independent image of the glands, which is then processed, displayed and combined to provide a more accurate visualization of the structure of the meibomian glands. By means of these images, the optometrist or ophthalmologist can detect structural change in the meibomian glands. As MGD progresses, DMI reveals gland truncation and dilation in moderate
disease followed by gland atrophy and drop-out in the most severe disease. However, there is a lack of evidence regarding the effectiveness of near-infrared dual imaging in the management of patients with MGD.

Nichols and colleagues (2005) evaluated the within- and between-reader reliability and the interrelation between 2 methods of grading meibography images. A video meibography sequence (1,200 frames) was captured from 290 patients using near-infrared light (650 to 700 nm) and a near-infrared CCD camera. One frame was selected for grading by 2 masked readers using 2 scales, where the 1st reader graded the image on 2 occasions and the 2nd reader graded the image on 1 occasion. The 1st grading scale was a gestalt assessment (categorically graded), which was an assessment of partial meibomian glands within the image. The 2nd was a count of individual whole glands. Within- and between-reader reliability and concurrent validity between the scales were examined. Within-reader reliability of the gestalt scale was moderate to high (simple kappa = 0.78, 95 % confidence interval [CI]: 0.71 to 0.85 and weighted kappa = 0.91, 95 % CI: 0.88 to 0.95). Within-reader reliability of individual gland counting was moderate via a 95 % limits of agreement analysis (-2.84-2.76 glands). Between-reader reliability of the gestalt scale was fair (simple kappa = 0.38, 95 % CI: 0.30 to 0.46 and weighted kappa = 0.57, 95 % CI: 0.47 to 0.68). Between-reader reliability of gland counting was fair via a 95 % limits of agreement analysis (-4.46-5.08 glands). There was a strong relation between the gestalt scale and gland counting indicating good concurrent validity (Z = -15.15, p < 0.0001). The authors concluded that these methods of grading meibography images demonstrated good within-reader reliability and fair between-reader reliability. Moreover, they stated that responsiveness to change will need to be addressed in future studies.

Furthermore, an UpToDate review on “Blepharitis” (Shtein, 2018) does not mention near-infrared dual imaging as a management tool.

Meibomian Gland Probing for the Treatment of Dry Eye

Maskin (2010) performed a retrospective evaluation of a new treatment for obstructive meibomian gland dysfunction (O-MGD) using invasive orifice penetration and intra-ductal probing. Medical charts of 25 consecutive patients with O-MGD (based on presence of lid margin or tarsal hyperemia, lid margin telangiectasia, thickening or irregularity, and meiboman gland orifice metaplasia) plus lid tenderness or symptoms of lid margin congestion were reviewed to evaluate the effect of probing on tenderness and congestion; 24 of 25 patients (96 %) had immediate post-probing relief, whereas all 25 patients (100 %) had relief of symptoms by 4 weeks after procedure; 20 patients (80 %) only required 1 treatment and had an average of 11.5-month follow-up; 5 patients (20 %) had re-treatment at an average of 4.6 months. All patients had symptom relief at time of last follow-up. Of 56 symptomatic and treated lids, 42 (75
% were upper lids. Patients frequently reported improvement in newly recognized but previously sub-clinical symptoms. The author concluded that invasive orifice penetration and intra-ductal probing appeared to provide lasting rapid symptom relief for patients with O-MGD. Probing findings in this study frequently included (i) mild resistance upon orifice penetration, (ii) proximal duct gritty tactile and aural sensation suggestive of keratinized cellular debris, and (iii) focal variable resistance deeper within the duct, which may be relieved with the probe, suggestive of fibro-vascular tissue. These researchers stated that these findings may offer probing characteristics that may allow for a grading system for duct obstruction. The post-probing improvement of symptoms not previously appreciated supported the notion that meibomian gland disease exists sub-clinically.

Prozornaia and Brzhevskii (2013) reported the findings of 110 patients (aged from 3 to 42 years) who were examined to estimate the efficacy of chronic blepharitis treatment: 50 patients with chronic blepharitis and dry eye syndrome (DES), 28 with DES due to computer vision syndrome and 32 with isolated chronic blepharitis. All patients received eyelid massage. If the secretion was too thick and difficult to evacuate from meibomian glands then duct probing was performed. In addition a complex of hygienic procedures was performed using phyto-products ("Geltec-Medika", Russia): blepharoshampoo, blepharolotion, blepharogel 1 and 2. Moist warm pads (with blepharolotion and calendula extraction) were applied on the eyelids in 25 patients. Massage and probing of meibomian gland ducts and hygienic procedures were showed to be effective in management of clinical signs of chronic blepharitis including co-existing DES. Moist warm pads improved efficacy of background therapy in patients with meibomian gland hypofunction and had no effect in blepharitis with excessive meibomian gland secretion. Eyelid hygiene was showed to be effective in adults, children and infants.

Wladis (2013) stated that rosacea is a significant cause of ocular surface disease, and the current therapeutic armamentarium is often ineffective. Intra-ductal meibomian gland probing is a novel technique to address DES, although its use has not been described in the management of ocular surface disease from rosacea.

In a retrospective study, Maskin and Testa (2018) examined the impact of meibomian gland probing (MGP) on meibomian gland (MG) area from the upper lids of patients with O-MGD. This trial compared pre-MGP/post-MGP non-contact infrared meibography results in patients with O-MGD, viewing signs of MG growth within total measurement field. Post-MGP meibography of 34 lids (19 patients, greater than or equal to 4.5 to less than or equal to 12 months' follow-up) showed 41.2 % with MG growth; 10 lids had meibographies suitable for analysis, showing significant collective (116 glands) increase in mean individual glandular area (MIGA) of 4.87 % (p = 0.0145); 4 of 10 lids independently showed significant increase in MIGA, ranging from 10.70 %
to 21.13 % (p < 0.0001, p = 0.0277, p = 0.0292, p = 0.0345), while 6 did not. At greater than 12 or less than 25 months’ follow-up, 16 lids (9 additional patients) had follow-up showing 25 % with signs of MG growth. Analysis of 3 lids showed a significant collective (33 glands) increase in MIGA of 11.19 % (p = 0.0004); 2 of 3 lids independently showed significant increase in MIGA of 13.73 % and 20.00 % (p = 0.0097, p = 0.0001). Collectively, for all 13 analyzed lids (149 glands), there was a significant increase of 6.38 % in total glandular area (p = 0.0447) and a significant increase of 6.23 % in MIGA (p = 0.0003). The authors concluded that MGP was associated with increased MG tissue area and growth of atrophied MGs as viewed on meibography; MGP provided unequivocal physical proof of a patent meibum outflow tract through the natural orifice, and may promote glandular growth in part by direct mechanical establishment of a patent duct/orifice system. Moreover, these researchers stated that future research is needed to study these post-MGP meibography changes in a randomized controlled clinical trial (RCT).

Furthermore, UpToDate reviews on “Blepharitis” (Shtein, 2019a), “Dry eyes” (Shtein, 2019b), “Treatment of dry eye in Sjogren’s syndrome: General principles and initial therapy” (Baer and Akpek, 2019a) and “Treatment of moderate to severe dry eye in Sjogren’s syndrome” (Baer and Akpek, 2019b) do not mention meibomian gland probing as a therapeutic option.

CPT Codes / HCPCS Codes / ICD-10 Codes

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":*

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>0207T</td>
<td>Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral</td>
</tr>
<tr>
<td>0330T</td>
<td>Tear film imaging, unilateral or bilateral, with interpretation and report</td>
</tr>
<tr>
<td>0507T</td>
<td>Near-infrared dual imaging (ie, simultaneous reflective and trans-illuminated light) of meibomian glands, unilateral or bilateral, with interpretation and report</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H00.011 - H00.019</td>
<td>Hordeolum externum [meibomian stye]</td>
</tr>
<tr>
<td>H00.021 - H00.029</td>
<td>Hordeolum internum [infected meibomian cyst]</td>
</tr>
<tr>
<td>H00.11 - H00.19</td>
<td>Chalazion [meibomian cyst]</td>
</tr>
<tr>
<td>H01.001 - H01.009</td>
<td>Blepharitis [posterior blepharitis]</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>H01.00A - H01.00B</td>
<td>Unspecified blepharitis</td>
</tr>
<tr>
<td>H01.01A - H01.01B</td>
<td>Ulcerative blepharitis</td>
</tr>
<tr>
<td>H01.02A - H01.02B</td>
<td>Squamous blepharitis</td>
</tr>
<tr>
<td>H01.8</td>
<td>Other specified inflammations of eyelid</td>
</tr>
<tr>
<td>H01.9</td>
<td>Unspecified inflammation of eyelid</td>
</tr>
<tr>
<td>H02.881 - H02.889</td>
<td>Meibomian gland dysfunction of eyelid [meibomian infarct]</td>
</tr>
<tr>
<td>H02.88A - H02.88B</td>
<td>Meibomian gland dysfunction of upper and lower eyelids</td>
</tr>
<tr>
<td>H04.111 - H04.119</td>
<td>Dacryops</td>
</tr>
<tr>
<td>H04.121 - H04.129</td>
<td>Dry eye syndrome</td>
</tr>
<tr>
<td>H04.201 - H04.209</td>
<td>Epiphora, unspecified</td>
</tr>
<tr>
<td>H04.211 - H04.219</td>
<td>Epiphora due to excess lacrimation</td>
</tr>
<tr>
<td>H04.221 - H04.229</td>
<td>Epiphora due to insufficient drainage</td>
</tr>
<tr>
<td>H04.9</td>
<td>Disorder of lacrimal system, unspecified</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


33. Shtein RM. Blepharitis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed June 2019a.

34. Shtein RM. Dry eyes. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed June 2019b.


Amendment to
Aetna Clinical Policy Bulletin Number: 0797
Management of Meibomian Glands

There are no amendments for Medicaid.