NICE advice

LipiFlow thermal pulsation treatment for dry eyes caused by blocked meibomian glands

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Summary

The LipiFlow system applies heat and gentle pressure to the eyelids to treat dry eyes caused by meibomian gland dysfunction. Two randomised controlled trials showed that the LipiFlow system was at least as effective as warm compresses and reported some improved patient-reported outcomes. The LipiFlow system costs £35,500 with additional costs for consumables and software upgrades.

Product summary and likely place in therapy	Effectiveness and safety
• The LipiFlow system applies heat to the inner eyelid and pressure to the outer eyelid surfaces at the same time. These actions are designed to loosen, liquefy and express hardened meibomian lipids, which have blocked the meibomian glands. • The LipiFlow system is intended to remove blockages to the meibomian glands, thereby relieving both dry eye symptoms and preventing meibomian gland atrophy. • The LipiFlow system could be used in primary care by optometrists, or in ophthalmology departments in secondary or tertiary care.	• Two randomised controlled trials (n=139 and n=31) compared the efficacy and safety of the LipiFlow system with regular, self-administered warm compresses, with or without massage, to the eyelids for people with obstructed meibomian glands. The first study showed that the LipiFlow system was more effective and the second study showed LipiFlow therapy was non-inferior. • In the first trial, there was a statistically significant improvement in meibomian gland secretion and tear break-up time after treatment with the LipiFlow system. Patient-reported symptoms also statistically significantly improved after treatment, with the exception of pain and discomfort scores. • In the second trial, the number of expressible meibomian glands statistically significantly improved after treatment with the LipiFlow system. Patient-reported symptoms statistically significantly improved after treatment. • A clinical feasibility study (n=14) compared the LipiFlow system with heated manual expression of the meibomian glands. Results demonstrated a statistically significant improvement ($p<0.05$) in meibomian gland secretion scores, tear break-up time, corneal staining score and patient-reported symptom scores for people suffering with meibomian gland dysfunction over 3 month follow-up in those who used the LipiFlow system. • Three adverse events were reported in the clinical feasibility study, although they were all resolved without long-term harm.

Technical factors	Cost and resource use
• The system uses a standard AC power supply and is run from a table-top console. • Heat is delivered from the lid warmer to the eyelids at a temperature of 42.5°C. The treatment must be delivered to both the top and bottom eyelids of each eye simultaneously. • Treatment can be given to 1 eye at a time or both eyes simultaneously.	• No publicly available reports were identified about the resource consequences of adopting the LipiFlow system for obstructed meibomian glands. • The LipiFlow system costs £35,500. The single-use, single-eye activators are sold in packs of 10 that cost £2250 each. Annual software upgrades and servicing cost £5000 per year (all prices exclude VAT).

Introduction

A thin film of fluid (the tear film) covers the exposed areas of the open eyes. The tear fluid has 3 layers; the outer lipid layer, the middle aqueous layer and the inner mucin layer (Bron et al. 2002).

The lipids in the outer layer, also known as meibomian lipids, are produced and secreted by the meibomian glands. These glands are in the upper and lower eyelids, and there are as many as 40 glands per lid. The aqueous layer is produced and secreted by a single lacrimal gland, situated above the top outer corner of the eyelid, and multiple accessory glands situated along the upper eyelid. The mucin layer is secreted from specialised goblet cells found in both the eyeball and eyelids (Bron et al. 2002).

The tear film provides a smooth moist surface for light to pass through. If tear fluid production is disrupted this may result in 'dry eye', which causes the eye to feel dry, gritty or sore. In some people, symptoms include red eyes, temporary blurred vision and the eyelids may stick together on waking up. Dry eye affects up to 1 in 3 people over the age of 65 years (NHS Choices 2014a; Lemp et al. 2012).

Dry eye can be classed as either evaporative dry eye or aqueous-deficient dry eye. Evaporative dry eye is the most common type of dry eye and there are a number of types. One type of evaporative dry eye is caused by the tear film evaporating from the surface of the eye too quickly, because of a deficient lipid layer. Aqueous-deficient dry eye is the result of an insufficient aqueous layer (Lemp et al. 2012).

Evaporative dry eye can also be caused by an obstruction or the abnormal functioning of the meibomian glands. This condition is called meibomian gland dysfunction (MGD; Lemp et al. 2012), and is the indication for the technology in this briefing. MGD can be caused by cell debris and meibomian lipids hardening in the terminal ducts of the glands and obstructing the secretion of meibomian lipids. MGD can also refer to the quality of meibomian lipids being secreted, which in turn will affect the quality of the lipid layer in the tear film. The prevalence of MGD is uncertain. In people over the age of 40 years, it has been reported to range from 68% in people of Asian origin to 19.9% in people of white origin. It is important to note that the clinical symptoms of MGD overlap with those of other types of evaporative dry eye, as well as those of aqueous-deficient dry eye. This may account for the high and variable figures reported (Nichols et al. 2011).

Conventional treatment of MGD involves warming and massaging the eyelids to reliquefy the meibomian lipids and force the obstruction out of the glands. There is little consensus within the literature as to the specific frequency and method of application for the treatment of MGD (Finis et al. 2014a). Therefore, a standardised treatment regime for MGD, which relieves symptoms of dry eye, may improve patient outcomes.

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The LipiFlow system was CE-marked under the Medical Devices Directive 2007/47/EC in July 2011 as a Class IIa device.

Description

The LipiFlow system (TearScience) is a thermal pulsation system, which delivers heat at a temperature of 42.5°C to the inner eyelid, and pressure to the outer eyelid surfaces simultaneously. These actions are designed to loosen, liquefy and express hardened meibomian lipids that have blocked the meibomian glands.

The LipiFlow system consists of the control unit (non-disposable component) and the single-use disposable activator.

The control unit, known as the console (model LFTP-1000), enables the user to regulate the application of heat and pressure to the eyelids. The console is a benchtop AC powered device, consisting of a touchscreen display with graphical user interface and patient database, the activator connection points (for either eye), a power cord connection (with a power switch) and 3 USB ports. As an optional extra, the touchscreen display can be mounted onto a pivoting arm, which allows the user to reposition the screen.

The activator is the only component that is in direct contact with the person during treatment. Two models of the activator are available:

- Model LFD-1000 is compatible with LipiFlow consoles operating any software version.
- Model LFD-1100 is compatible with LipiFlow consoles operating software versions 1.1 and above.

The activator is a single-use eyepiece made of biocompatible polycarbonate and silicone. It is inserted around the person's eyelids and consists of 5 parts:

- lid warmer
- eye cup
- handle
- air and electrical tubing
- electronic connection piece.

The lid warmer is a curved plastic cup, approximately 24 mm in diameter. It sits under the eyelids, on the eyeball. The surface of the lid warmer is silicone-lined and this makes it soft and flexible. An electric temperature-controlled heater is embedded in the convex

surface of the lid warmer and transfers heat through the inner eyelids to the meibomian glands. The concave surface is insulated to protect the cornea from heat. The eye cup is connected to the lid warmer. It sits over the closed eyelids once the lid warmer is in place. Two inflatable bladders on the eye cup continually pressurise and depressurise, squeezing the meibomian glands against the lid warmer. Each treatment takes 12 minutes.

The handle aids the user in positioning the activator on the eye. One activator is needed for each eye, and the air and electrical tubing connect to separate ports on the console so that both eyes can be treated at the same time.

TearScience produce 2 other products that work with the LipiFlow system, which are beyond the scope of this briefing. These are:

- LipiView, a Class IIb medical device
- the Meibomian Gland Evaluator.

Intended use

The LipiFlow system is intended for use in adults with obstructive meibomian gland dysfunction, where terminal meibomian gland ducts are blocked and the glandular secretions cannot be drained.

TearScience list a number of contraindications and advise that the LipiFlow system should not be used in people who have, or have had, the following conditions or treatments:

- Ocular surgery within the last 3 months.
- Ocular injury within the last 3 months.
- Ocular herpes within the last 3 months.
- Active ocular infection.
- Active ocular inflammation or history of chronic, recurrent ocular inflammation within the last 3 months.
- Eyelid abnormalities that affect lid function.
- Ocular surface abnormality that may compromise corneal integrity.

Setting and intended user

In current NHS eye care services, opticians, optometrists and ophthalmologists advise on eye care. Treatment at specialist eye departments and hospitals can be provided following a referral from a GP or optician (NHS Choices 2014b).

The LipiFlow system is intended to be used by optometrists in primary care, or by optometrists or ophthalmologists in secondary care ophthalmology departments or in tertiary care at specialist eye hospitals.

Current NHS options

The most likely current treatment for meibomian gland dysfunction (MGD) involves regular self-administration of warm compresses and massage therapy to the eyelids. Commercially available eye pads or flannels can be warmed in water (or a microwave in some cases) and placed over closed eyes for short but regular periods of time. This action is intended to loosen the hardened lipids within the meibomian glands. Eyelid massage, using a finger or cotton wool bud, is then applied to force the lipids out of the meibomian glands, relieving the obstruction. Increased lid hygiene can also be used to aid removal of debris from the eyelids. This can involve washing the eyes in a weak solution of baby shampoo, tea tree shampoo or bicarbonate of soda dissolved in warm water (NHS Choices 2014c).

Generic dry eye treatments may also be prescribed to people with MGD to relieve discomfort. Examples include lubricants, which are intended to increase the aqueous layer in the tear film and keep the surface of the eye moist (NHS Choices 2014d). Oily tear drops and eye ointments, which increase the lipid layer in the tear film, may also provide relief from symptoms (NHS Choices 2014d). In addition, anti-inflammatory medication to reduce pain caused by swelling of the eyelids can be prescribed (NHS Choices 2014d), as can topical or systemic antibiotics to treat infections. Eating a diet high in omega-3 fatty acids may also help to improve dry eye symptoms (NHS Choices 2014c). However, these generic eye treatments do not treat the root cause of MGD as they do not loosen blockages in the meibomian glands.

In very rare circumstances, surgery may be offered to treat severe dry eye symptoms. Punctal occlusion involves the insertion of silicone plugs to block the tear ducts. This prevents the tears draining from the surface of the eye. If the plugs fail the tear ducts can be cauterised, permanently blocking the ducts to stop tears draining from the surface of

the eye (NHS Choices 2014d). The final surgical option is salivary gland auto-transplantation. The transplanted salivary gland produces fluid, which acts as a substitute for tears (NHS Choices 2014d).

NICE is aware of the following CE marked device that appears to fulfil a similar function to the LipiFlow system:

- Blephasteam, Laboratoires Théa.

Costs and use of the technology

The capital component of the LipiFlow system, the console, costs £35,500 (excluding VAT), and has a lifespan of 3 years. The single-use activators are sold in packs of 10 that cost £2250 each. Annual software upgrades, including servicing, cost £5000.

The treatment takes 12 minutes for either a single or bilateral eye treatment. If it is assumed that the procedure would take a total of 20 minutes (including set-up time), then approximately 20 cases can be treated in a day.

Assuming that 20 treatments were done per day for 240 days per year, the overall equipment cost per treatment is estimated to be £228 per eye or £453 for both eyes. This assumes a standard annuity method with an equipment lifespan of 3 years and a discount rate of 3.5% (Drummond et al. 2005). Free on-site user training is provided by the manufacturer.

The alternative treatment options are self-administered warm compresses or lid massage, which incur only minimal equipment costs. Artificial tears used for relieving dry eye symptoms are available over the counter (price range £3–10). However, they are not considered as an alternative treatment to LipiFlow since they do not remove blockages from meibomian glands.

No other practical difficulties have been identified in using or adopting the technology.

Likely place in therapy

The LipiFlow system is not currently being offered within the NHS, although it is available for purchase in the UK. The LipiFlow system is currently only available in private clinics. If

adopted within the NHS, the LipiFlow system would be used to treat people who have not responded to currently available treatments. These people are likely to be referred from their optician or GP to ophthalmologists for treatment with the LipiFlow system.

Specialist commentator comments

Two specialist commentators noted that the LipiFlow system is 1 of many treatment options intended to alleviate symptoms of dry eye in people with meibomian gland dysfunction (MGD). One commentator added that LipiFlow should only be used to treat people who have not responded to conservative treatment options, such as increased lid hygiene or lubricants. These people may benefit from treatment with the LipiFlow system, which could be considered before invasive surgical intervention.

One specialist commentator reflected that the LipiFlow system cannot treat symptoms caused by poor-quality meibomian lipid secretions that tend to solidify at body temperature and so are prone to blocking the meibomian glands. These poor-quality secretions can have underlying causes such as infection with Demodex parasites (eyelash mites), seborrhoeic conditions, or omega-3 fatty acid deficiency. Therefore, the LipiFlow system should always be used in conjunction with other adjuvant therapies. This specialist felt that the LipiFlow system would be more beneficial to people with more acute and transient dry eye rather than those with chronic symptoms. People with chronic symptoms often have meibomian gland 'drop-out', where the meibomian glands are partly or completely lost, so the LipiFlow system would be of little benefit to these people.

One specialist commentator noted that there are currently no published studies comparing use of the LipiFlow system with the standard therapies for MGDs, including omega-3 supplements and systemic or topical antibiotics.

One specialist commentator felt that the LipiFlow system could be used to treat people whose meibomian secretions are cloudy and of poor quality. They speculated that LipiFlow treatment would be probably not be performed in specialist eye hospitals, as it is currently being performed by technicians. This commentator did not consider LipiFlow treatment to be a specialist procedure, and so in the NHS it would be more likely to be performed by trained ophthalmologists or nurses.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act (2010).

TearScience state that the LipiFlow system is intended for use in adults, which therefore excludes children or young people from being treated with the device.

The reportedly high prevalence of meibomian gland dysfunction in people of Asian family origin compared with figures for people of white origin (Nichols et al. 2011) could mean that more people of Asian family origin are eligible for treatment with the LipiFlow System compared with the general population. Dry eye can impact upon all age groups, but it is more common in people aged over 65 years (NHS Choices 2014a). Age and race are protected characteristics defined in the Equality Act 2010.

Evidence review

Clinical and technical evidence

Regulatory bodies

One adverse event report was listed on the US Food and Drug Administration (FDA) Manufacturer and User Device Facility Experience (MAUDE) database.

One person suffered a corneal abrasion 5 days after having treatment with the LipiFlow system. No permanent impairment was sustained. The manufacturer stated the injury could not be attributed to the device given the time delay between the treatment and the injury (MAUDE Adverse Event Report: TearScience LipiFlow thermal pulsation system).

A search of the Medicines and Healthcare Products Regulatory Agency (MHRA) website revealed no manufacturer Field Safety Notices or Medical Device Alerts for this device.

Clinical evidence

The evidence on the use of the LipiFlow system is provided by 2 randomised controlled trials, for which 3 additional follow-up publications have been reported, and 1 clinical feasibility study. These studies are described below.

Randomised controlled trials

Lane et al. (2012) conducted a multicentre study in the USA, comparing the safety and effectiveness of the LipiFlow system with the iHeat warm compress. iHeat warm compresses are single-use, chemically-activated, warm compresses that deliver heat to the outer eyelids and surrounding tissue. In the study 139 people with meibomian gland dysfunction (MGD) were randomised into a LipiFlow therapy group (n=69) and a control group (iHeat, n=70). The LipiFlow intervention was administered in a single, 12-minute session and the iHeat warm compresses were applied in daily 5-minute sessions for 2 weeks. Follow-up was at 1 day (LipiFlow group only), 2 weeks (LipiFlow and control groups) and 4 weeks (LipiFlow group only) post treatment. The control group then crossed over to have LipiFlow therapy, and follow-up data were recorded at 1 day and 2 weeks after this treatment. Statistically significant increases in both meibomian gland secretions and tear break-up time (TBUT), and statistically significant reductions in dry eye symptoms, were observed in the LipiFlow therapy group from baseline to follow-up. The crossover group also showed similar statistically significant improvements in mean meibomian gland secretions and TBUT and significant reductions in dry eye symptoms after they had LipiFlow therapy. Patient-reported pain and discomfort scores during and after treatment were statistically significantly higher in the LipiFlow treatment group compared with the iHeat warm compresses group. A summary of these results is reported in tables 1 and 2.

Two additional publications (Greiner 2012, 2013) report longer-term outcomes from the same group of people treated in the Lane et al. (2012) study, with 9- and 12-month follow-up respectively. Data were collected from people who had had LipiFlow treatment (n=21 at 9 months and n=18 at 12 months). At both additional follow-up points, the statistically significant reductions in dry eye symptoms compared with baseline (originally observed by Lane et al. 2012) were sustained, as were the significant increases in meibomian gland secretions and TBUT. A summary of Greiner (2012 and 2013) is reported

in tables 3 and 4.

Finis et al. (2014a) conducted a randomised controlled trial in Germany, comparing 1 single LipiFlow treatment with twice-daily application of heat and massage to the eyelids for 3 months. People with MGD (n=31) were randomised into a LipiFlow treatment group (n=17) and a control group (n=14). Both groups were studied at baseline and with 1- and 3-month follow-up. The control group then crossed over to LipiFlow therapy and were studied at baseline and 1- and 3-month follow-up. Treatment with LipiFlow demonstrated non-inferiority compared with twice-daily warming and massage of the eyelids, in respect to dry eye symptoms, TBUT, tear osmolarity, lipid layer thickness, tear meniscus height, ocular surface staining, lid margin parallel conjunctival folds and number of expressible meibomian glands. A summary of these results is reported in tables 5 and 6.

An additional publication (Finis et al. 2014b) reported 6-month follow-up data from the original study by Finis et al. (2014a). People who had LipiFlow treatment (n=26), including those from the crossover group (n=9), were included. Subjective dry eye symptoms were statistically significantly improved from baseline as were lipid layer thickness, the number of expressible meibomian glands, lid margin parallel conjunctival folds and bulbar redness. In addition, treatment with LipiFlow demonstrated no effect on meibomian gland atrophy. A summary of Finis et al. (2014b) is reported in table 7.

Clinical feasibility study

Friedland et al. (2011) conducted a multicentre, prospective, clinical feasibility study in the USA comparing LipiFlow with heated manual expression of the meibomian glands. The authors studied 14 people at baseline and at 1 day, 1 week, 1 month and 3 months after the treatment. All 14 people had a single 12-minute session of LipiFlow in both eyes. Immediately after receiving LipiFlow treatment, each person received further treatment in 1 randomly selected eye using an alternative manual heated expression device, which was not named in the study. Results demonstrated LipiFlow statistically significantly improved dry eye symptoms and objective meibomian gland functionality outcomes during the 3-month study period compared with baseline. No statistically significant differences were observed in any outcome measures between eyes that received LipiFlow therapy only versus those that received LipiFlow therapy and additional heated manual expression. Three adverse events were reported during the study and these were resolved without long-term harm. A summary of these results is reported in table 8.

Table 1 Summary of the Lane et al. (2012) randomised controlled

trial

Study component	Description
Objectives/ hypotheses	To evaluate the safety and effectiveness of LipiFlow compared with the iHeat warm compresses for adults with MGD.
Study design	Prospective, open-label, randomised, crossover multicentre clinical trial.
Setting	9 US based centres. People were recruited between March and May 2009. People in the study were followed-up at: • 1 day, 2 and 4 weeks (LipiFlow cohort) • 2 weeks (iHeat warm compresses cohort) • 1 day and 2 weeks (crossover cohort).

Inclusion/ exclusion criteria	Inclusion: • people aged 18 years or over • willingness to comply with the study procedures and follow-up schedule • dry eye symptoms within 3 months of the baseline examination (SPEED score≥6) • evidence of meibomian gland obstruction (based on a total meibomian gland secretion score≤12 for 15 glands of the lower lid) • provided informed consent. Exclusion: • evidence of coexisting ocular conditions (e.g. active ocular infection or inflammation in either eye) • ocular surgery or trauma within 3 months of the baseline examination • ocular surface abnormality potentially compromising corneal integrity • eyelid abnormalities affecting lid function • systemic disease resulting in dry eye • unwillingness to abstain from systemic medications known to cause dryness for the study duration • coexisting conditions that could interfere with the assessment of safety and effectiveness of the treatment (e.g. macular disease; women who were pregnant or nursing).

Outcomes	Primary: • meibomian gland assessment (gland secretions) and TBUT. Secondary: • dry eye symptoms using SPEED and OSDI questionnaires. Safety: • adverse events, ocular health examination, ocular surface staining, intraocular pressure, visual acuity, patient-reported pain and discomfort scores (1–2, slight or transient awareness of pressure without pain; 3–4, moderate discomfort with minimal pain; 5–6, moderate pain; 7–8, severe pain; and 9–10, intolerable pain).
Statistical methods	Descriptive statistics were used to present data in the form of the mean and SD. Paired 2-tailed t-tests were used to compare baseline and post-treatment outcomes for each treatment group. Two sample 2-tailed t-tests were used to compare the mean changes from baseline to 2 weeks between treatment groups. Fischer's exact test was used to compare the incidence of device-related adverse events between treatment groups. All enrolled intention-to-treat patients (139 patients; 278 eyes) were analysed for safety and all eligible per-protocol treated patients (133 patients; 266 eyes) were analysed for efficacy. Significance was set at the 0.05 level.

Participants	All people in the study had to discontinue the use of systemic antihistamines or isotretinoin (Accutane) for at least 1 month, cyclosporine-A (Restasis) for at least 2 months, and other dry eye or MGD-related medication (e.g. antibiotics, non-steroidal and anti-inflammatory drugs, and corticosteroids) for at least 2 weeks, before the beginning of the study. People could not use this medication throughout the study duration. A total of 139 people (278 eyes) were enrolled on the study and randomised into the following groups: Group 1: had a single, 12-minute treatment of LipiFlow; n=69 (138 eyes). Group 2: had a 5-minute iHeat warm compress treatment with instructions to perform the same treatment daily for 2 weeks; n=70 (140 eyes). Group 3: crossed-over to a single, 12-minute treatment of LipiFlow; n=68 (136 eyes).

Results	Mean (±SD) meibomian gland secretion and TBUT significantly increased (p<0.0001) with LipiFlow from baseline to 2 and 4 weeks (meibomian gland secretion: baseline 6.3±3.5; 2 weeks 14.3±8.7; 4 weeks 16.7±8.7 and TBUT: baseline 5.5±2.9; 2 weeks 6.9±5.0; 4 weeks 7.4±5.5). There was no significant difference in mean (±SD) meibomian gland secretion (p=0.3214) and TBUT (p=0.6492) with iHeat warm compresses (meibomian gland secretion: baseline 5.6±3.9; 2 weeks 6.1±5.6 and TBUT: baseline 5.4±3.5; 2 weeks 5.3±3.5). The use of LipiFlow resulted in a reduction in dry eye symptoms, which was higher compared with the reduction in dry eye symptoms attributed to the use of iHeat warm compresses (SPEED, p<0.0001; OSDI, p<0.0004). The crossover group demonstrated similar significant improvement in mean meibomian gland secretion (p<0.0001), TBUT (p=0.0027) and dry eye symptoms (SPEED, p<0.0001; OSDI, p<0.0002) 2 weeks post-treatment with the LipiFlow. There was no significant difference between groups in the incidence of non-serious, device-related adverse events (p=0.4455). Self-reported pain and discomfort scores during and after treatment were significantly higher in the LipiFlow treatment group compared with the iHeat warm compresses group (p<0.0001).
Conclusions	The LipiFlow system was significantly more effective than iHeat warm compresses. Results support its safety and effectiveness in the treatment of MGD and dry eye symptoms. However, people in the study experienced greater pain and discomfort with the use of the LipiFlow system.
Abbreviations: MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Table 2 Summary of the Lane et al. (2012) randomised controlled trial

	LipiFlow	Daily warm compresses	Analysis

Randomised	n=69 (138 eyes)	n=70 (140 eyes)	
Efficacy	n=65 (130 eyes)	n=68 (136 eyes)	
Primary outcome: • MG gland secretion score • TBUT(seconds)	MG secretion (mean score[±SD]) • Baseline 6.3 (3.5) • 2 weeks 14.3 (8.7) • 4 weeks 16.7 (8.7) TBUT (mean time [±SD]) • Baseline 5.5 (2.9) • 2 weeks 6.9 (5.0) • 4 weeks 7.4 (5.5)	MG secretion (mean score[±SD]) • Baseline 5.6 (3.9) • 2 weeks 6.1 (5.6) TBUT (mean time [±SD]) • Baseline 5.4 (3.5) • 2 weeks 5.3 (3.5)	• p<0.0001 • p=0.0017
Secondary outcome: SPEED questionnaire score	Mean score (±SD) • Baseline 14.3 (4.8) • 2 weeks 8.1 (5.5) • 4 weeks 7.6 (5.8)	Mean score (±SD) • Baseline 14.8 (4.8) • 2 weeks 11.2 (5.4)	• p<0.0001
Secondary outcome: OSDI questionnaire score	Mean score (±SD) • Baseline 32.0 (20.0) • 2 weeks 17.3 (17.2) • 4 weeks 16.6 (18.1)	Mean score (±SD) • Baseline 34.7 (19.6) • 2 weeks 26.9 (18.2)	• p=0.0004
Safety	n=69	n=70	
Abbreviations: MG, meibomian gland; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.			

Table 3 Summary of the Greiner (2012) follow-up report to Lane et al. (2012)

Study component	Description
Objectives/ hypotheses	To evaluate the effect of a single treatment with LipiFlow on signs of MGD and dry eye symptoms over a 9-month period.
Study design	Follow-up to the prospective, open-label, randomised, crossover multicentre clinical trial (Lane et al. 2012).
Setting	The original setting from Lane et al. (2012): 9 US centres. Participants were recruited between March and May 2009. Study participants were followed-up at: • 1 day, 2 and 4 weeks (LipiFlow cohort) • 2 weeks (iHeat warm compress cohort) • 1 day and 2 weeks (cross-over cohort).
Inclusion/ exclusion criteria	As stated in Lane et al. (2012) study (see table 1).
Outcomes	Primary: • meibomian gland assessment (gland secretions) and TBUT. Secondary: • dry eye symptoms using SPEED and OSDI questionnaires.

Statistical methods	Descriptive statistics were used to present data in the form of mean and SD. ANOVA and post-hoc analysis using Bonferroni correction was used to assess statistical changes in TBUT, meibomian gland secretions and dry eye symptoms over time (baseline and 1 month follow-up [data from original study by Lane et al. 2012] to 9 month follow-up). Significance was set at the 0.05 level.
Participants	A total of 21 participants (42 eyes) were followed-up to 9 months from the original study (Lane et al. 2012): n=21; 5 men and 16 women, mean (±SD) age=62.2±12.1, all of white origin.
Results	Mean (±SD) meibomian gland secretion scores improved significantly ($p<0.0001$) from baseline (4.4±4.0) to 1 month follow-up (11.3±6.2) and this improvement was maintained, with no significant regression ($p>0.05$), at 9 months (11.7 ± 5.9). Mean (±SD) TBUT significantly increased ($p<0.001$) from baseline (4.8±3.2) to 1 month follow-up (9.6±7.6) and this improvement was maintained with no significant regression ($p>0.05$) at 9 months (7.1±5.6). Mean OSDI score (±SD) significantly improved ($p<0.0005$) from baseline (23.4±14.4) to 1 month follow-up (10.9±13.1) and this improvement was maintained at 9 months (12.4±15.3), with no significant difference observed ($p>0.05$). Mean SPEED scores (±SD) significantly improved ($p<0.0001$) from baseline (12.9±4.0) to 1 month (6.3±5.4) and this improvement was maintained at 9 months (6.2±7.1), with no significant difference observed ($p>0.05$).
Conclusions	A single 12-minute LipiFlow treatment results in up to 9 months of sustained improvement of meibomian gland function, TBUT and dry eye symptoms.
Abbreviations: ANOVA, analysis of variance; MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Table 4 Summary of the Greiner (2013) follow-up report to Lane et al. (2012)

Study component	Description
Objectives/ hypotheses	To determine the 1-year post-treatment dry eye status of participants with MGD and dry eye symptoms after having a single LipiFlow.
Study design	Follow-up to the prospective, open-label, randomised, crossover multicentre clinical trial.
Setting	The original setting from Lane et al. (2012; table 1): 9 US centres. This study recruited participants between March and May 2009. Study participants were followed-up at: • 1 day, 2 and 4 weeks (LipiFlow cohort) • 2 weeks (iHeat WC cohort) • 1 day and 2 weeks (crossover cohort).
Inclusion/ exclusion criteria	As stated in Lane et al. (2012) study (see table 1).
Outcomes	Primary: • meibomian gland assessment (gland secretions) and TBUT. Secondary: • dry eye symptoms using SPEED and OSDI questionnaires.

Statistical methods	Descriptive statistics were used to present data in the form of mean and SD. ANOVA and post-hoc analysis using Bonferroni correction was used to assess statistical changes in TBUT, meibomian gland secretions and dry eye symptoms over time (baseline and 1 month [data from original study by Lane et al. 2012] to 12 months). Significance was set at the 0.05 level.
Participants	A total of 18 participants (36 eyes) were followed-up to 12 months from the original study (Lane et al. 2012): n=18; 2 men and 14 women, mean (±SD) age=63.2±12.1, all of white origin.
Results	Mean (±SD) meibomian gland secretion scores improved significantly ($p<0.0005$) from baseline (4.0±3.4) to 1 month follow-up (11.3±4.7) and this improvement was maintained with no significant regression ($p>0.05$) at 12 months (7.3±4.6). Mean (±SD) TBUT significantly increased ($p<0.001$) from baseline (4.9±3.0) to 1 month follow-up (9.5±6.9). There was a significant decrease ($p>0.05$) in mean TBUT from 1-month (9.5±6.9) to 12 month follow-up (6.0±4.4). Mean OSDI symptoms score (±SD) significantly improved ($p<0.0005$) from baseline (22.2±14.2) to 1 month follow-up (8.5±7.5) and this improvement was maintained at 12 month follow-up (12.4±14.6) with no significant difference observed ($p>0.05$). Mean SPEED scores (±SD) significantly improved ($p<0.0005$) from baseline (12.9±3.8) to 1 month follow-up (6.4±5.5) and this improvement was maintained at 12 month follow-up (6.3±5.5), with no significant difference observed ($p>0.05$).
Conclusions	A single 12-minute treatment with the LipiFlow system offers an effective treatment for evaporative dry eye and MGD resulting in significant and sustained improvement in signs and symptoms for up to 1 year.
Abbreviations: ANOVA, analysis of variance; MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Table 5 Summary of the Finis et al. (2014a) randomised controlled trial

Study component	Description
Objectives/ hypotheses	To compare the effectiveness of a single LipiFlow treatment with lid warming and massage in patients with MGD.
Study design	Single-blinded, prospective, crossover, randomised trial.
Setting	German centre. People were recruited between April 2012 and June 2013. People in the study were followed up at 1 and 3 months.
Inclusion/ exclusion criteria	Inclusion: • 18 years or over • provided informed consent • needed treatment for MGD (defined by SPEED score ≥8, LLT≤61 nm and expressible meibomian glands≤4). Exclusion: • used systemic medication with tetracycline derivatives, antihistamines, isotretinoin or nutritional supplements for MGD (beginning less than 3 months before baseline examination) • used topical cyclosporine-A or steroids (beginning less than 1 month before baseline examination) • ocular surgery or trauma less than 3 months before baseline examination • evidence of any eyelid abnormalities • evidence of systemic diseases resulting in dry eye.

Outcomes	Primary: • subjective dry eye symptoms (OSDI and SPEED questionnaires). Secondary: • TBUT, tear osmolarity, LLT, tear meniscus height, ocular surface staining, lid margin parallel conjunctival folds, number of expressible meibomian glands.
Statistical methods	Descriptive statistics were used to present data in the form of the mean and SD. A power analysis was performed using G*Power 3. ANOVA and Bonferroni post hoc tests were used to compare values between time points (non-significant values were given as exact p values of Fisher's post hoc test). Wilcoxon signed rank tests were used to compare relative changes between treatment groups. Student t-tests were used to compare baseline values between treatment groups. Kolmogorov–Smirnov tests were used for normality; Pearson's linear correlation coefficient was used for normally distributed data and Spearman's linear correlation coefficient was calculated for non-normally distributed values. Significance was set at the 0.05 level.
Participants	A total of 31 people were enrolled on the study and randomised into the following groups: Group 1: single, 12-minute treatment of LipiFlow; n=17, 5 men and 12 women, mean (±SD) age=45±23. Group 2: twice-daily lid warming and massage treatment; n=14, 4 men and 10 women, mean (±SD) age=50±19. Group 3: crossed-over to a single, 12-minute treatment of LipiFlow; n=14, 4 men and 10 women, mean (±SD) age=50±19.

Results	Both mean (±SD) OSDI and SPEED scores were significantly improved (p<0.01 and p<0.05 respectively) at 1 month follow-up (OSDI=30.9±20.8 and SPEED=12.7±7.9) compared to baseline (OSDI=46.2±14.8 and SPEED=16.8±5.6) with LipiFlow treatment. Mean (±SD) OSDI scores were significantly improved (p<0.01) from baseline to 3-month follow-up (34.6±19.6) with the LipiFlow treatment, however there was no difference (p=0.055) in mean (±SD) SPEED score between baseline and 3-month follow-up (14.5±7.2). No significant differences were observed in mean OSDI or SPEED scores with the control treatment group. Mean (±SD) number of expressible glands significantly increased (p<0.01 and p<0.01) from baseline (2.5±1.4) to 1-month (5.9±3.5) and 3-month follow-up (5.5±3.6) with LipiFlow treatment. Mean (±SD) number of expressible glands significantly increased (p<0.05 and p=0.0326) from baseline (2.1±1.3) to 1-month (4.9±4.0) and 3-month follow-up (4.6±3.8) with the control treatment. Mean (±SD) TBUT significantly improved (p<0.05) from baseline (6.7±6.1) to 1-month follow-up (11.6±5.8) with the crossover treatment group, however there was no significant difference observed at 3 months. No other significant differences were observed.
Conclusions	Results show that a single LipiFlow treatment is non-inferior to a 3-month, twice-daily lid warming and massage regime for MGD.
Abbreviations: ANOVA, analysis of variance; LLT, lipid layer thickness; MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Table 6 Summary of the Finis et al. (2014a)

	LipiFlow	Twice-daily warming and massage	Analysis
Randomised	n=17 (34 eyes)	n=14 (28 eyes)	
Efficacy	n=17	n=14	

Primary outcome: OSDI questionnaire score	Mean score (±SD) • Baseline 46.2 (14.8) • 1 month 30.9 (20.8) • 3 months 34.6 (19.6)	Mean score (±SD) • Baseline 40.1 (16.7) • 1 month 35.6 (20.9) • 3 months 40.0 (23.4)	• p>0.05 • p>0.05 • p>0.05
Secondary outcome: LLT (nm)	Mean height (±SD) • Baseline 43.4 (9.9) • 1 month 48.8 (15.5) • 3 months 47.4 (16.7)	Mean height (±SD) • Baseline 44.1 (7.9) • 1 month 46.9 (25.7) • 3 months 46.4 (20.8)	• p>0.05 • p>0.05 • p>0.05
Secondary outcome: Tear film osmolarity (mOsm/l)	Mean osmotic concentration (±SD) • Baseline 301.5 (11.4) • 1 month 301.0 (10.2) • 3 months 307.1 (14.0)	Mean osmotic concentration (±SD) • Baseline 296.7 (10.2) • 1 month 298.3 (12.3) • 3 months 303.7 (8.1)	• p>0.05 • p>0.05 • p>0.05
Safety	n=17	n=17	
Patients reporting serious adverse events	Not reported	Not reported	
Abbreviations: LLT, lipid layer thickness; OSDI, ocular surface disease; SD standard deviation.			

Table 7 Summary of the Finis et al. (2014b) follow-up report to Finis et al. (2014a)

Study component	Description
Objectives/ hypotheses	To evaluate the 6-month effect of a single LipiFlow treatment and implications of meibomian gland atrophy on treatment efficacy 6 months after application.
Study design	Follow-up study to the single-blinded, prospective, crossover, randomised trial (Finis et al. 2014a).
Setting	The original setting from Finis et al. (2014a; table 5): Europe based centre. People were recruited between April 2012 and June 2013. Study patients were followed-up at: • 1 and 3 months (LipiFlow group) • 1 and 3 months (lid warming and massage group) • 1 and 3 months (crossover group).
Inclusion/ exclusion criteria	As stated in Finis et al. (2014a) (see table 5).
Outcomes	Primary: • subjective dry eye symptoms (OSDI and SPEED questionnaires). Secondary: • TBUT, tear osmolarity, LLT, tear meniscus height, meibography, bulbar redness, ocular surface staining, LIPCOF and number of expressible meibomian glands.

Statistical methods	Descriptive statistics were used to present data in the form of the mean and SD. Paired t-tests were used to analyse the changes between time points. Heteroscedastic t-tests were used to analyse the changes between different subgroups. Significance was set at the 0.05 level.
Participants	A total of 26 people (52 eyes) were studied and completed the 6-month follow-up: mean (±SD) age=50±22 years, 7 men and 19 women.
Results	Mean (±SD) OSDI scores significantly improved ($p<0.005$) from baseline (42±19) to 6-month follow-up (33±21). Mean (±SD) SPEED scores significantly improved ($p<0.001$) from baseline (16±7) to 6-month follow-up (12±7). Mean (±SD) LLT significantly improved ($p=0.014$) from baseline (44.0±15.6) to 6-month follow-up (51.3±20.4). Mean (±SD) number of expressible glands significantly improved ($p<0.0001$) from baseline (2.9±1.6) to 6-month follow-up (6.4±4.6). Mean (±SD) LIPCOF significantly improved ($p=0.04$) from baseline (2.3±1.0) to 6-month follow-up (2.0±0.9). Mean (±SD) bulbar redness significantly improved ($p=0.0001$) from baseline (1.4±0.5) to 6-month follow-up (1.2±0.5). No other significant differences were observed.
Conclusions	This study demonstrated that a single LipiFlow treatment reduces subjective symptoms and objective dry eye parameters in people with MGD over 6 months but has no effect on atrophy of meibomian glands.
Abbreviations: ANOVA, analysis of variance; LIPCOF, lid margin parallel conjunctival folds; LLT, lipid layer thickness; MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Table 8 Summary of the Friedland et al. (2011) clinical feasibility study

Study component	Description
Objectives/ hypotheses	To evaluate LipiFlow for obstructive MGD.
Study design	Multicentre, prospective, clinical feasibility study.
Setting	US based centres. This study recruited people in June 2008. People in the study were followed-up at 1 day, 1 week, 1 month and 3 months.

Inclusion/ exclusion criteria	Inclusion: • 18 years or older • provided informed consent • willingness and ability to return for all study follow-ups • dry eye symptoms for more than 3 months (SPEED score≥6) and previous diagnosis of moderate-to-severe dry eye • regular use of artificial tears, lubricants or rewetting drops in both eyes • obstructed meibomian gland (presence or absence of secretions expressed. Exclusion: • individuals who had either changed the dosing of systemic or ophthalmic medication less than 30 days prior to screening • individuals unable or unwilling to remain on a stable dosing regimen for the duration of the study • ocular surgery, trauma or herpetic keratitis less than 3 months before baseline examination • evidence of chronic or recurrent eye inflammation or infection • pregnant women, nursing or not utilising adequate birth control measures • evidence of systemic diseases resulting in dry eye • using topical or systemic medications known to cause eye dryness • using another investigational device or agent within 30 days of study participation.

Outcomes	• Meibomian gland assessment (the meibomian gland secretion score and the number of meibomian glands yielding liquid secretion, lower eyelid) • objective dry eye tests (TBUT and corneal fluorescein staining) • subjective dry eye symptoms (SPEED and OSDI questionnaires) • ocular health examination (anterior segment and retina evaluation and intraocular pressure measurement) • discomfort/pain evaluation (during and after treatment).
Statistical methods	Descriptive statistics were used to present data in the form of the mean and SD. ANOVA with post-hoc Bonferroni corrections were used to determine significant changes due to the treatment between visits (time) and between treatment groups. Significance was set at the 0.05 level.
Participants	A total of 14 people (28 eyes) were enrolled: mean age (±SD)=54.2±9.6 (range=37–72) years, 4 men and 10 women. One eye from each person was randomly selected to undergo additional manual heated expression with another treatment device: Group 1: LipiFlow only, n=14 (14 eyes). Group 2: LipiFlow and heated manual expression, n=14 (14 eyes).

Results	The mean meibomian gland secretion score, TBUT, corneal staining score, number of meibomian glands yielding liquid secretion and symptom scores all improved significantly from baseline to 1 week (all $p<0.05$) for both treatment groups. This was maintained at 3-month follow-up. There was no statistically significant difference in any outcomes measured between the treatment groups (LipiFlow versus LipiFlow + heated manual expression). The mean (SD±) discomfort/pain score reported during the treatment with LipiFlow=2.4±1.6 compared with 3.7±1.5 (LipiFlow + heated manual expression; $p=0.003$). Three adverse events were reported: • One person reported a high discomfort score causing treatment to be stopped. • One person developed a chalazion on the upper lid (not recorded at baseline). It completely resolved within a month of therapy. • One person complained of a gritty sensation and irritation in the right eye and lump on the right lower eyelid, 3 weeks post-therapy. The condition completely resolved within a month of therapy.
Conclusions	A single 12-minute session of LipiFlow per eye was highly effective in treating obstructive MGD and dry eye symptoms for the 3-month study period.
Abbreviations: ANOVA, analysis of variance; MGD, meibomian gland dysfunction; OSDI, ocular surface disease index; SD, standard deviation; SPEED, standard patient evaluation of eye dryness; TBUT, tear break-up time.	

Recent and ongoing studies

Seven ongoing clinical trials involving LipiFlow have been identified. Two of these are described as currently active:

- NCT02102464: Treatment of meibomian gland dysfunction and dry eye in contact lens wearers.

- NCT01808560: Treatment of meibomian gland dysfunction prior to cataract surgery.

The remaining five trials are listed as having been completed:

- NCT01769105: Comparison of LipiFlow-treatment and a standard lid hygiene regime.
- NCT01202747: Evaluation of screening methods for treatment of meibomian gland dysfunction.
- NCT01521507: Randomized controlled trial of long-term treatment effectiveness for meibomian gland dysfunction (MGD) and dry eye.
- NCT01683318: Treatment of meibomian gland dysfunction.
- NCT01787942: Investigating abnormal lipid layer thickness in blepharoplasty patients.

Costs and resource consequences

If the LipiFlow system were to be adopted in the NHS, it could potentially help people with meibomian gland dysfunction (MGD). Marketing of the LipiFlow system to the NHS has only recently begun, and this system is not thought to be currently in use in any NHS centres. The potential NHS use for this system is difficult to estimate from MGD prevalence data as alternative treatment options, such as warm compresses or lid massage, are available at little or no cost to the NHS. Therefore, the LipiFlow system would represent a significant additional cost to current services and this may limit uptake. According to the manufacturer, the device is being used by several private healthcare providers.

There would be no need to change the way in which current services are organised or delivered. No other additional facilities or technologies are needed alongside the technology.

No published evidence on resource consequences for the LipiFlow system was identified in the systematic review of evidence.

Strengths and limitations of the evidence

Neither Lane et al. (2012) nor Finis et al. (2014a) reported their method of randomisation. Therefore it is unclear if the randomisation methods could have influenced the outcomes

in either study. Both studies, however, benefited from crossover trial designs. Two potentially confounding issues arise with crossover study designs: the order in which the person has each intervention can affect the outcomes, and a carry-over effect from the previous intervention can affect the results of the second intervention. The latter can be mitigated by a 'wash-out period' (Louis et al. 1984). In both of these studies the people in the crossover group received LipiFlow therapy after the control therapy, but neither study reported a 'wash-out period'. It is unclear how the crossover design may have influenced the Lane et al. (2012) and Finis et al. (2014a) studies.

The study by Finis et al. (2014a) was the only included study to perform a power calculation and adapt the sample size to reflect its findings. A minimum sample size was calculated as n=7 so the authors increased their sample size to n=15. However, they conceded that they lost people to follow-up and that further increasing their sample size may have increased the number of outcomes that reached significance (particularly at 3 months). In their follow-up publication (Finis et al. 2014b), data were collected for a sample size above the n=7 initially intended.

Neither Lane et al. (2012) nor Friedland et al. (2011) reported a power calculation. However, Lane et al. (2012) studied a much larger sample size (n=139, randomised into 2 cohorts) than Finis et al. (2014a) or Friedland et al. (2011). Consequently, it is unclear whether these studies were adequately powered to detect any differences in the primary and secondary outcomes reported by the authors.

The study by Finis et al. (2014a) was 'single-blinded', meaning that the investigators were blinded from the intervention during the data collection phase. However, people were aware which therapy group they were assigned to and this may have introduced performance bias. The studies by Lane et al. (2012) and Friedland et al. (2011) were 'open-label' studies, meaning that neither the investigators nor the people involved were blinded to the assigned therapy groups. This also may have introduced performance bias. However, this limitation is not specific to these trials because, although blinding of the operator is standard practice for studies involving drugs, it is often not feasible in studies involving medical devices.

In addition, another source of potential performance bias is the mode of treatment. Both Lane et al. (2012) and Finis et al. (2014a) compared LipiFlow with a mode of treatment that required substantial compliance in the home (daily and twice-daily interventions respectively). Neither study reported compliance rates therefore it is unclear if this affected the study outcomes.

All studies included in this briefing compared the same intervention, namely, a single 12-minute session with the LipiFlow system. All studies reported a consistent temperature of the activator and duration of therapy. However, only Finis et al. (2014a) reported which pressure cycle they used in their study. TearScience state that it is possible to modify the pressure cycle but both Lane et al. (2012) and Friedland et al. (2011) fail to report which cycle was used.

In an effort to reduce bias both Lane et al. (2012) and Friedland et al. (2011) performed their studies in multiple centres. The former used 9 different centres across the USA and the latter used 2 separate centres, also across North America. Finis et al. (2014a) failed to report if they incurred additional bias with or without the use of the use of multiple centres. None of the studies included in this briefing took place in the UK, and so the generalisability of the results to the NHS is unclear.

Finally, the studies by Lane et al. (2012) and Friedland et al. (2011) were funded by the manufacturer, TearScience, which has the potential for introducing bias in the reporting of outcomes.

Relevance to NICE guidance programmes

The use of the LipiFlow system is not currently planned into any NICE guidance programme.

NICE guidance on dry eye disease – ciclosporin is in development and is expected to be published in August 2015.

References

Bron AJ, Tiffanya JM, Gouveiaa SM et al. (2002) Functional aspects of the tear film lipid layer. Experimental Eye Research 78(3): 347–360

Drummond M, Sculpher M, Torrance G, et al. (2005) Methods for economic health valuation of health care programmes, 3rd ed. Oxford: Oxford University Press

Finis D, Hayajneh J, Konig C et al. (2014a) Evaluation of an automated thermodynamic treatment (LipiFlow) system for meibomian gland dysfunction: a prospective, randomized, observer-masked trial. The Ocular Surface 12(2):146–154

Finis D, Hayajneh J, Konig C et al. (2014b) Six-month effects of a thermodynamic treatment for MGD and implications of meibomian gland atrophy. Cornea 33:1265–1270

Friedland BR, Fleming CP, Blackie CA et al. (2011) A novel thermodynamic treatment for meibomian gland dysfunction. Current Eye Research 36(2): 79–87

Greiner JV (2012) A single LipiFlow thermal pulsation system treatment improves meibomian gland function and reduces dry eye symptoms for 9 months. Current Eye Research April 37(4): 272–8

Greiner JV (2013) Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. Clinical and Experimental Ophthalmology 41(6): 524–530

Lane SS, DuBiner HB, Epstein RJ et al. (2012) A new system, the LipiFlow, for the treatment of meibomian gland dysfunction. Cornea 31(4): 396–404

Lemp MA, Crews LA, Bron AJ et al. (2012) Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea 31(5): 472–8

Louis TA, Lavori PW, Bailar JC et al. (1984) Crossover and self-controlled designs in clinical research. The New England Journal of Medicine 310: 24–31

NHS Choices (2014a) Dry eye syndrome [Last accessed: 19th January 2015]

NHS Choices (2014b) NHS eye care service [Last accessed: 19th January 2015]

NHS Choices (2014c) Dry eye syndrome – Self-help [Last accessed: 19th January 2015]

NHS Choices (2014d) Dry eye syndrome – Treatment [Last accessed: 27th January 2015]

Nichols KK, Foulks GN, Bron AJ et al. (2011) The International Workshop on Meibomian Gland Dysfunction: Executive summary. Investigative Ophthalmology and Visual Science, Special Issue 52(4): 1922–9

Search strategy and evidence selection

Search strategy

Search strategy

For the clinical evidence:

Embase 1980 to 2014 Week 46, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; searched on Wednesday, 7th January 2015.

1. lipiflow.mp.

2. thermodynamic treatment.mp.

3. thermal pulsation system.mp.

4. 1 or 2 or 3

5. meibomian gland dysfunction.mp. or Dry Eye Syndromes/

6. MGD.mp.

7. Eye Diseases/

8. Eye/

9. meibomian gland/

10. eyelid/

11. Evaporative Dry Eye.mp.

12. 5 or 6 or 7 or 8 or 9 or 10 or 11

13. 4 and 12

The Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of

Reviews of Effect (DARE) were searched on Wednesday, 7th January 2015:

1. LipiFlow OR

2. Thermal pulsation system AND

3. Meibomian gland dysfunction

For the economic evidence:

Embase 1980 to 2015 Week 01, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; Searched on 06 January 2015

1. meibomian gland dysfunction.mp. or Dry Eye Syndromes/

2. MGD.mp.

3. Eye Diseases/

4. Eye/

5. meibomian gland/

6. eyelid/

7. Evaporative Dry Eye.mp.

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. lipiflow.mp.

10. thermodynamic treatment.mp.

11. thermal pulsation system.mp.

12. 9 or 10 or 11

13. cost*.mp.

14. economic*.mp.

15. 13 or 14

16. 8 and 12 and 15

Cochrane Database of Systematic Reviews: Issue 1 of 12, January 2015

Cochrane Central Register of Controlled Trials: Issue 12 of 12, December 2014

Database of Abstracts of Reviews of Effect: Issue 4 of 4, October 2014

Health Technology Assessment Database: Issue 4 of 4, October 2014

NHS Economic Evaluation Database: Issue 4 of 4, October 2014

#1 LipiFlow

#2 Thermal pulsation system

#3 #1 or #2

#4 Meibomian gland dysfunction

#5 #3 and #4

#6 cost*

#7 economic*

#8 #6 or #7

#9 #5 and #8

Evidence selection

For the clinical evidence:

- Total number of publications reviewed: 15
- Total number of publications considered relevant: 9
- Total number of publications selected for inclusion in this briefing: 6

Exclusion Criteria: case studies, editorials, letters, reviews, conference proceedings/ abstracts, animal studies, non-English language studies, not using the LipiFlow system.

For the economic section:

- Total abstracts: 0
- Duplicates: 0
- Abstracts reviewed: 0
- Full papers reviewed: 0

Exclusion Criteria: case studies, editorials, letters, reviews, conference proceedings/ abstracts, animal studies, non-English language studies, not using the LipiFlow system.

Studies for review: 0

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by King's Technology Evaluation Centre (KiTEC). The Interim process & methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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