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THE SECOND DRY EYE FLARES CONSENSUS STATEMENT:

Clinical Recommendations for Acute Exacerbation of Dry Eye Disease

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Dry Eye Flares Consensus Statement:
Clinical Recommendations for Acute Exacerbation of Dry Eye Disease

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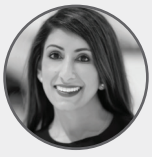

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a roundtable discussion.

ACTIVITY DESCRIPTION

This supplement highlights important points related to the care and treatment of patients with dry eye disease based on the evolving understanding of the disease process. The consensus panel came to an agreement on specific points related to acute versus chronic dry eye to formulate this consensus panel statement with the goal of improving patient outcomes.

TARGET AUDIENCE

This certified CME activity is designed for ophthalmologists who care for patients with dry eye and related disorders.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- **Identify** the prevalence and impact of dry eye flares on visual outcomes and patient satisfaction
- **Improve** understanding of the signs and symptoms associated with episodic flares of ocular surface disease
- **Increase** confidence in making therapeutic decisions for patients who experience acute exacerbations of dry eye disease
- **Describe** the mechanism of mucus-penetrating nanoparticles

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PRETEST QUESTIONS

PLEASE COMPLETE PRIOR TO ACCESSING THE MATERIAL AND SUBMIT WITH POSTTEST/ACTIVITY EVALUATION/SATISFACTION MEASURES FOR CME CREDIT.

1. Please rate your confidence in your ability to identify dry eye flares (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).
a. 1
b. 2
c. 3
d. 4
e. 5

2. Why may ophthalmologists miss dry eye flares in their patients?
a. Immunomodulators mask symptoms
b. Patients self-treat their symptoms
c. Flares primarily occur postoperatively
d. A & B

3. Which of the following can be potential extrinsic trigger/s of dry eye flares?
a. Allergies
b. Air travel
c. Contact lens wear
d. All of the above

4. _____ is a biomarker that has been associated with dry eye flares.
a. Matrix-metalloproteinase-9 (MMP-9)
b. Intraocular pressure
c. Neurofilament light chain
d. Laminin P1

5. Approximately _____ of patients with dry eye disease have flares.
a. 20%
b. 40%
c. 60%
d. 80%

6. The panel reported that the average dry eye patient experiences _____ dry eye flares each year.
a. 2
b. 6
c. 9
d. 15

7. What did panelists recommend as the top three objective tests when evaluating dry eye flares?
a. MMP-9, tear breakup time, and meibography
b. Meibomian gland expression, meibography, and corneal topography
c. MMP-9, corneal staining, and tear osmolarity
d. Conjunctival staining, MMP-9, and corneal topography

8. What is a useful way to identify whether a patient is having periodic dry eye flares?
a. SPEED test
b. Asking patients to compare symptoms with a previous time period
c. Optical coherence tomography
d. Meibography

9. Which of the following is true regarding nanotechnology used for loteprednol 0.25%?
a. It carries the drug into the ocular surface.
b. It increases the side effects of the drug.
c. It is rapidly cleared with tears during blinking.
d. It adheres to mucins.

10. When treating dry eye flares, panelists seek drugs with _____.
a. Long-term action
b. Cholinergic action
c. Rapid action
d. All of the above

11. Panelists stated that _____ can help improve patient compliance with topical immunomodulators when used as an initiation treatment.
a. Loteprednol etabonate nanotechnology suspension 0.25%
b. Oral omega-3 fatty acids
c. Ocular lubricants
d. Blepharoexfoliation

12. _____, which stimulates tearing, is being studied in a preservative-free nasal spray.
a. Oxymetazoline hydrochloride 0.05%
b. Recombinant human lubricin protein
c. Betamethasone
d. A nicotinic acetylcholine receptor agonist

Dry Eye Flares Consensus Statement: Clinical Recommendations for Acute Exacerbation of Dry Eye Disease

ETIOLOGY AND IMPACT OF ACUTE DRY EYE SYMPTOMS

Chronic inflammatory conditions such as asthma, rheumatoid arthritis, and Sjögren syndrome often flare, but eyecare providers may not realize this can occur with dry eye disease (DED). This is particularly true if patients do not complain of their symptoms.

"Flares are a hallmark of all inflammatory diseases, and I am a firm believer that DED is an inflammatory disease," said Richard Lindstrom, MD.

Dry eye flare symptoms are similar to those of chronic DED—eye discomfort and dryness, blurry and fluctuating vision, eye fatigue, and stinging. However, they are acute-onset symptoms that last a shorter period of time, according to Edward J. Holland, MD.

All Dry Eye Flares Consensus panelists strongly agreed that dry eye flares are rapid-onset inflammation-driven responses to environmental and/or intrinsic triggers.

Further refining the definition, Preeya K. Gupta, MD, suggested flare symptoms remain after the noxious stimulus is removed and continue at least 2 or 3 days, but they persist in some cases for days to weeks.

PINPOINTING TRIGGERS

Extrinsic triggers include dry or windy conditions, air travel, allergies, contact lens wear, and additional causes. Intrinsic triggers include stress, hormonal influences, worsening autoimmune diseases, medications, conditions causing dehydration, and other factors.

"Everyone has a different etiology of their dry eye that causes them to become inflamed or flare at certain times during the year," said Eric D. Donnenfeld, MD.

"Many of us are spending a lot more time in front of digital screens, whether that's our laptops, our tablets, our digital phones, and that prolonged screen time certainly can be a trigger for episodic dry eye flares," said Terry Kim, MD.

"I often ask patients who have rheumatoid arthritis or Sjögren syndrome about how their body is feeling, whether they are having flares or more joint pain," Dr. Gupta said. "That can also trigger their dry eye flares."

In addition, cataract and refractive surgical procedures also contribute to ocular surface discomfort, causing a surgery-induced DED flare, Dr. Lindstrom said.

As well as occurring in patients with chronic DED, flares develop in patients who predominantly have no dry eye signs and symptoms.

"I think a lot of patients have primary flare disease," Dr. Gupta said, adding that such patients may have severe cases two or three times a year and may self-medicate, without identifying as having dry eye.

DRY EYE FLARES AND INFLAMMATION

Christopher E. Starr, MD, Stephen C. Pflugfelder, MD, and colleagues, who performed a meta-analysis that has been submitted for publication, explained that little information is available in in the literature about dry eye flares.

"Matrix metalloproteinase-9 was one of the biomarkers that was consistently elevated and could be elevated in as quickly as 2 hours in some of the controlled adverse environment studies," Dr. Starr said. The analysis reported that inflammatory diseases like Sjögren syndrome, rheumatoid arthritis, and asthma generally can be maintained with minimal or no long-term medication and then break through or flare up, often requiring medication such as steroids, Dr. Starr said.

A global consensus by Tsubota and associates defined DED as the presence of an unstable tear film resulting in epitheliopathy, inflammation, and neurosensory abnormalities.[1] "Inflammation is a key aspect of dry eye. It is involved in the pathogenesis of both signs and symptoms," Dr. Pflugfelder said.

"Matrix metalloproteinase-9 is definitely a relevant biomarker, and I've been impressed using that test because many patients with clinical flares test positive," Dr. Pflugfelder said. He explained that controlling inflammation during flares or chronically is necessary to manage patient discomfort in ocular surface disease.

Dr. Pflugfelder and colleagues reviewed the literature on the molecular and cellular basis of dry eye flares.[2] "There are acute or episodic flares of dry eye due to disruption of tear stability and probably acute changes in tear composition like high osmolarity, that can stress the ocular surface. Those are very important inflammatory stressors that can disrupt the corneal barrier, sensitize corneal nerve endings, and make the patient miserable," he said.

In addition, Dr. Pflugfelder said patients with chronic DED have increased levels of inflammatory mediators and cells on the eye.

"Flares are a hallmark of all inflammatory diseases, and I am a firm believer that DED is an inflammatory disease."

— Richard Lindstrom, MD

"Those are the eyes that definitely have a T-cell component and those flares tend to be worse because the inflammatory response is primed. In some cases, they can cause sight-threatening corneal disease," he said.

UNRECOGNIZED CONDITION

Dry eye flares often are underdiagnosed or not fully understood.

"Flares can occur in patients who do not have a chronic DED diagnosis. There is a subset of patients in whom you have a baseline state that is not a diagnosis, and they will have episodes that flip them into a dry eye flare," said Elizabeth Yeu, MD.

"Identification of this entity called dry eye flare is a major advance in our understanding of DED and its pathophysiology," Dr. Kim said. "I liken it to when, decades ago, inflammation was identified as a key component of dry eye pathophysiology, and what resulted from that was the development of immunomodulators, like topical cyclosporine and lifitegrast, based on this understanding."

"This is a new and exciting area, and I think it's something the general ophthalmologist should be aware of and think about when managing DED," Dr. Donnenfeld said. ■

1. Tsubota K, Pflugfelder SC, Liu Z, et al. Defining dry eye from a clinical perspective. *Int J Mol Sci.* 2020;21(23):9271.
2. Perez VL, Stern ME, Pflugfelder SC. Inflammatory basis for dry eye disease flares. *Exp Eye Res.* 2020;201:108294.

PREVALENCE, SEVERITY, AND IMPACT OF DRY EYE FLARES

Approximately 80% of patients with dry eye disease (DED) experience flares, with most having multi-day episodes (2018 Study of Dry Eye Sufferers, Multi-Sponsor Surveys).[1] Nine percent have 25 or more dry eye flares per year.[1]

"This tells us we need to provide treatment for these patients, dependent on the severity of their flares, and baseline therapy is not enough for most of these patients," said Eric D. Donnenfeld, MD.

Panelists reported that, on average, 81% of their patients with DED experience flares on a yearly basis. **Consensus Panel Finding #1** shows the number of dry eye flares the average dry eye patient experiences yearly. On average, a patient with dry eye experiences six flares each year.

"A lot of times, patients will not admit to having dry eye flares and clinicians are not asking these questions," said Terry Kim, MD. "I would guess that if you did inquire, the incidence is higher than we think."

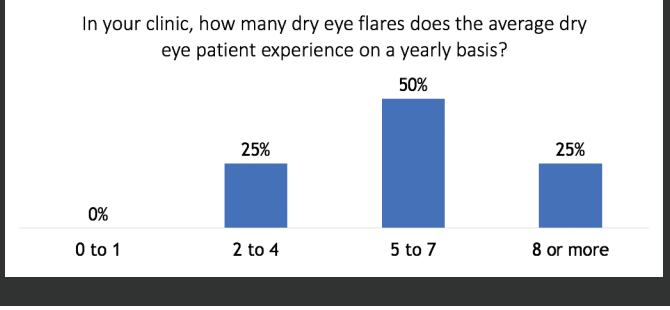
REFRACTIVE AND CATARACT SURGICAL PATIENTS

In **Consensus Panel Finding #2**, panelists stated the percentage of their cataract patients who have dry eye flares before surgery. On average, 70% of cataract patients have dry eye flares preoperatively.

Trattler and colleagues reported that 77% of patients scheduled for cataract surgery had corneal staining and 50% had central corneal staining; however, only 13% had a foreign body

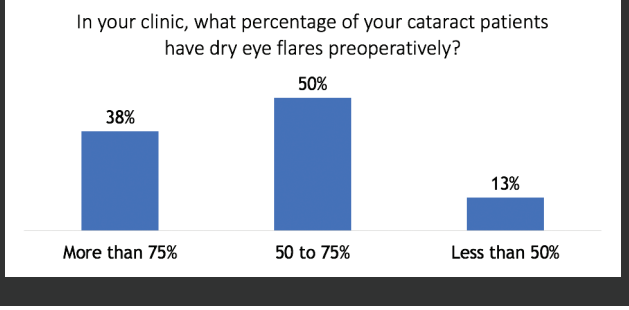
CONSENSUS PANEL FINDING #1:

On average, a dry eye patient experiences 6 dry eye flares each year.



CONSENSUS PANEL FINDING #2:

On average, 70% of cataract patients have dry eye flares preoperatively.



sensation most or half of the time.[2] Undiagnosed and untreated DED can reduce the accuracy of preoperative calculations, impact visual outcomes after surgery, and worsen postoperative dry eye.[3] Preeya K. Gupta, MD, Christopher E. Starr, MD, and colleagues reported that in an asymptomatic cohort of preoperative cataract surgery patients, almost 50% had abnormal tear osmolarity and matrix metalloproteinase-9 testing.[4]

"We want to do everything we can do to preoperatively optimize the ocular surface to prevent patients from having more significant dry eye signs and symptoms after surgery," Dr. Donnenfeld said.

Dr. Starr and his colleagues on the ASCRS Cornea Clinical Committee published recommended consensus guidelines on diagnosing and treating DED and ocular surface diseases before cataract and refractive surgery.[5]

"Dry eye can lead to inaccurate outcomes which will lead to an objective refractive miss and subjectively unhappy patients," said Elizabeth Yeu, MD. "Symptoms with preexisting dry eye are one of the main reasons why you can have worsening and chronic postoperative dry eye with cataract surgery."

Eighty-eight percent of panelists believe unmanaged flares significantly reduce satisfaction after otherwise successful surgery in refractive IOL patients using maintenance therapy for ocular surface disease and 13% reported patients would be mildly dissatisfied.

"These patients have a higher level of expectation, especially if it's an out-of-pocket expense for their cataract procedure," Dr. Kim said. "Anything that interferes with their visual function or their symptomology is going to be seen as a potential problem with the lens. Often it's not the lens. It's the ocular surface."

A significant number of refractive surgery candidates also have dry eye flares, as shown in **Consensus Panel Finding #3**. On average, 63% of refractive surgery patients have dry eye flares preoperatively.

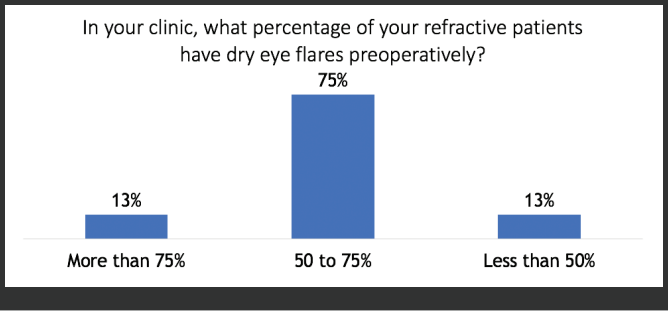
Contact lens intolerance is one of the most common reasons patients consider corneal refractive surgery. "When you look at why patients become contact lens intolerant, often ocular surface disease is right up there, whether it's aqueous deficiency or, much more common, meibomian gland dysfunction," Dr. Gupta said.

"These patients probably have flares prior to their corneal refractive surgery and now we have neurotrophic change after the surgery," said Edward J. Holland, MD. "These patients definitely have dry eye flares in the postoperative period."

All panelists reported that patients using dry eye maintenance therapy can have frequent dry eye flares throughout the year.

CONSENSUS PANEL FINDING #3:

On average, 63% of refractive surgery patients have dry eye flares preoperatively.



QUALITY OF LIFE

DED can significantly impact patients' quality of life.[6] Severe dry eye was rated to be equivalent to angina regarding its impact on a patient's quality of life, said Stephen C. Pflugfelder, MD.[7]

"Dry eye flares are often overlooked as an entity and in terms of their impact on patient satisfaction and quality of life," Dr. Kim said. "Frequently, patients get discouraged that they are having symptoms, especially if they are on maintenance therapy, whether that is an over the counter artificial tear or a prescription antiinflammatory therapy. It's a condition we all need to be more aware of and proactive in treating." ■

"Dry eye flares are often overlooked as an entity and in terms of their impact on patient satisfaction and quality of life."

— Terry Kim, MD

1. Brazzell RK, et al. Prevalence and characteristics of symptomatic dry eye flares: results from patient questionnaire surveys. Presented at: American Academy of Optometry; Oct. 23-27, 2019; Orlando, FL.
2. Trattler WB, Majmudar PA, Donnenfeld ED, et al. The Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) study: the effect of dry eye. *Clin Ophthalmol.* 2017;11:1423-1430.
3. Epitropoulos AT, Matossian C, Berdy GJ, et al. Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning. *J Cataract Refract Surg.* 2015;41(8):1672-1677.
4. Gupta PK, Drinkwater OJ, VanDusen KW, et al. Prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation. *J Cataract Refract Surg.* 2018;44(9):1090-1096.
5. Starr CE, Gupta PK, Farid M, et al. An algorithm for the preoperative diagnosis and treatment of ocular surface disorders: a report by the ASCRS Cornea Clinical Committee. *J Cataract Refract Surg.* 2019;45(5):669-684.
6. McDonnell PJ, Pflugfelder SC, Stern ME, et al. Study design and baseline findings from the progression of ocular findings (PROOF) natural history study of dry eye. *BMC Ophthalmol.* 2017;17(1):265.
7. Schiffman RM, Walt JG, Jacobsen G, et al. Utility assessment among patients with dry eye disease. *Ophthalmology.* 2003;110(7):1412-1419.

DIAGNOSING DRY EYE FLARES

All panelists believe every patient with dry eye should be screened for flares.

Consensus Panel Finding #4 shows panelists' recommendations for objective tests for dry eye flares. The top three objective tests that should be used when evaluating dry eye flares are corneal staining, matrix metalloproteinase-9 (MMP-9), and tear osmolarity testing.

Many clinicians do not have a large range of dry eye tests; however, all clinicians should perform corneal staining and conjunctival staining on their dry eye patients at minimum, said Edward J. Holland, MD. They may consider adding tear osmolarity, MMP-9, meibography, meibomian gland expression, and possibly corneal topography.

"We now know the value of point-of-care tests like tear osmolarity, MMP-9, and meibography that have been extremely helpful in identifying these patients, especially ones that may be asymptomatic at times," said Terry Kim, MD. But he explained that fluorescein staining of the cornea (Figure 1) and conjunctiva, tear breakup time (Figure 2), and lid expression can all be performed quickly at the slit-lamp with minimal cost and time.

QUESTIONNAIRE ASSESSMENT

Panelists discussed whether a more specific dry eye questionnaire would be helpful in diagnosing dry eye flares.

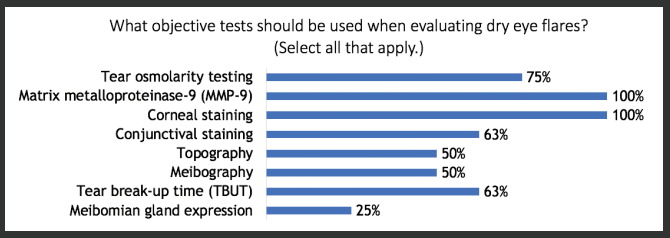
"I like the University of North Carolina dry eye symptom analog scale that has been validated, and it's so quick and easy to use," said Richard Lindstrom, MD.

Dr. Holland explained that the Ocular Surface Disease Index and Standardized Patient Evaluation of Eye Dryness questionnaires do not really identify flares. "I think we should modify and have categories specifically for flares. I would start by defining what a flare is in the questionnaire and then ask the patient if they have a flare." He would ask how often they occur, how long they last, and how they treated them.

Eric D. Donnenfeld, MD, explained that the first Ocular Surface Disease Index box asks how often patients experience symptoms.

CONSENSUS PANEL FINDING #4:

The top three objective tests that should be used when evaluating dry eye flares are corneal staining, MMP-9, and tear osmolarity testing.



He suggested it might be useful to quantitate the question, asking about the number of flares per year within that box.

Stephen C. Pflugfelder, MD, agreed this could be helpful, particularly if it was required to prescribe a medication.

Elizabeth Yeu, MD, said it also would be useful to ask patients questions comparing symptoms during the current visit with a previous time period.

Christopher E. Starr, MD, added that unscheduled phone calls, emails, or office visits related to ocular surface symptoms also would indicate a flare.

DEVELOPING CLASSIFICATION TOOLS

"In my experience, I think flares increase in frequency as time goes on and the severity of DED gets worse when inadequately managed," Dr. Starr said.

To help surgeons identify worsening flares and establish their significance, panelists discussed developing a grading scale comparing the severity of signs and symptoms at maintenance level with flare level.

Dr. Holland recommended asking patients about symptoms and incorporating signs such as conjunctival injection and conjunctival staining and performing meibomian gland expression. "To make it more specific for dry eye flares, we want to add the frequency of flares, duration of flares, and a severity scale of mild, moderate, and severe," he said.

"I would include elevated MMP-9 as an important sign of ocular surface disease, and I would bet that it will be positive in a lot of these patients." Dr. Starr said.

Dr. Lindstrom suggested flares might move patients up one or two levels on the Dry Eye Workshop (DEWS) scale or another scale.

Initiating or increasing tear use should progressively increase the flare grade, Dr. Yeu said.

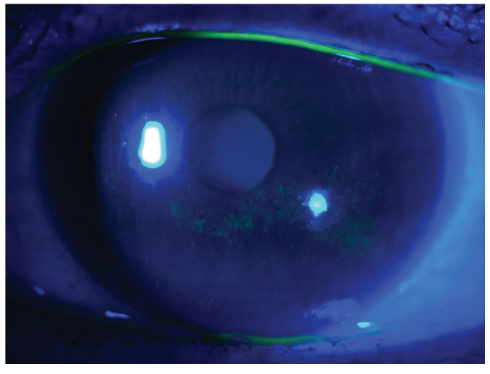


Image courtesy of Stephen Pflugfelder, MD.

Figure 1. Corneal staining with fluorescein.

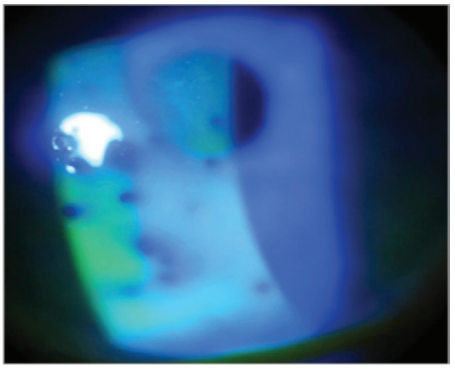


Image courtesy of Christopher E. Starr, MD.

Figure 2. Rapid tear breakup time.

"I would include elevated matrix metalloproteinase-9 as an important sign of ocular surface disease, and I would bet that it will be positive in a lot of these patients."

— Christopher E. Starr, MD

CONCLUSION

"The No. 1 thing we can do is remember to ask our patients about flares and remind ourselves to think about them not only in patients in clinic who have known dry eye, but patients who may not have typical symptoms we consider indicating dry eye," said Preeya K. Gupta, MD. "Even if you pick one or two diagnostic tests and routinely incorporate them into your clinic, that is an easy way to pattern out your clinical process. You do not have think about it on a per-patient basis."

CURRENT AND EMERGING TREATMENT OPTIONS FOR DRY EYE FLARES

Immunomodulators have been effective for chronic dry eye but fall short when treating flares.

"Our immunomodulator therapies can help prevent some level of inflammation, but they are not able to mitigate symptoms and signs on a short-term basis when there are exacerbations of the disease process," said Elizabeth Yeu, MD.

Furthermore, increasing the dosage of immunomodulators does not effectively treat exacerbations, said Richard Lindstrom, MD.

"I think patients get frustrated when they see that over-the-counter therapies have limited effectiveness because you're not actually treating inflammation," said Terry Kim, MD. "You are just providing supportive therapy."

Dr. Lindstrom explained that steroids are often used for flares and to induce remission of acute inflammation.

When clinicians began treating dry eye with cyclosporine, 20% of patients stopped using it because of pain and discomfort, according to Edward J. Holland, MD. He and his colleagues used induction therapy with loteprednol 0.25% for 2 weeks before initiation of cyclosporine treatment, increasing patients' tolerance of cyclosporine and decreasing nonadherence 2 to 3%.[1,2]

Clinicians recognized dry eye flares as patients requested loteprednol refills rather than cyclosporine refills. "That group of patients were having flares, and they realized that loteprednol was treating their flares better than their maintenance therapy cyclosporine," Dr. Holland said.

EMERGING TREATMENTS

New treatments are emerging for dry eye flares.

Loteprednol etabonate ophthalmic nanotechnology suspension 0.25% was approved in October 2020 for short-term treatment of dry eye signs and symptoms. It can be used for initiation therapy before immunomodulators and dry eye flares.

This formulation of loteprednol uses mucous penetrating (nano) particles (MMPs) to allow a lower concentration of loteprednol to be effective, explained Eric D. Donnenfeld, MD.

MMPs more effectively carry loteprednol into the ocular surface compared with loteprednol in its traditional suspension, Dr. Yeu said. "Traditional suspension eyedrops adhere to the mucins and they are rapidly cleared with the tears with blinking versus having these nanoparticles. They freely move through the tear mucins into the membrane-bound mucins, which allows penetration and more even coating of the target tissues, so you can have greater delivery of the loteprednol at lower concentrations."

In the STRIDE 1 and STRIDE 2 phase 3 trials, loteprednol etabonate ophthalmic nanotechnology suspension 0.25% significantly reduced conjunctival hyperemia after 2 weeks.[3,4] "There were more than 450 patients in each of the studies, so the data are robust," said Preeya K. Gupta, MD.

"By day 2, there was already a significant reduction in irritation and discomfort," said Stephen Pflugfelder, MD. "We do not see that with the immunomodulatory agents. It may take weeks or even months."

Most of the panel strongly agreed that nanotechnology increases the efficacy and maintains the safety of loteprednol.

"It is a great technology, and I think it is applicable to a lot of potential medications for the ocular surface in particular," said Christopher E. Starr, MD.

"So far most patients have found it to be comfortable," Dr. Gupta said. "There's the occasional report of some discomfort on instillation, which I find is very common almost universally in dry eye patients who are more sensitive. Patients have found it to work very quickly. To date, I have not seen or had any personal experience with IOP elevations, which speaks to its excellent safety profile."

For initiation therapy before immunomodulator treatment, generally panelists treat patients with loteprednol etabonate ophthalmic nanotechnology suspension 0.25% four times a day for 2 weeks and twice a day for 2 weeks.

"Loteprednol etabonate ophthalmic nanotechnology suspension 0.25% improves the side effect profile we have seen with other immunomodulatory agents," Dr. Kim said.

"Our immunomodulator therapies can help prevent some level of inflammation, but they are not able to mitigate symptoms and signs on a short-term basis…."

— Elizabeth Yeu, MD

OC-01 preservative-free nasal spray, a nicotinic acetylcholine receptor agonist, stimulates tearing. The FDA accepted its new drug application in March 2021.[5] Phase 2 clinical trials demonstrated improvements in Schirmer score and symptom scores at 0.6 mg/mL and 1.2 mg/mL. "There's increased mucin and goblet cell discharge with the application of this stimulant, and if you want to get a meaningful amount of new natural tears immediately, this is a good treatment," Dr. Lindstrom said.

"Nasal neurostimulation increases aqueous production, probably even causes discharge of meibomian glands in the conjunctival goblet cells," Dr. Pflugfelder said.

A recombinant human lubricin protein is being investigated in clinical trials for dry eye. "Lubricin is a lubricating protein found in joints, and it has been found in the tear fluid," Dr. Pflugfelder said. Significant improvements were seen in fluorescein staining, instillations, eyelid and conjunctival erythema, tear film breakup time, and Symptom Assessment in Dry Eye questionnaire.[6]

Betamethasone in Klarity vehicle (SURF-200) has been developed for acute dry eye. Researchers are studying 0.02% and 0.04% concentrations in a phase 2 clinical trial that will assess improvement of symptoms in 120 to 140 patients.[7] It is used short-term to treat dry eye flares. Betamethasone has not been used previously as a topical ophthalmic in the United States. ■

1. Donnenfeld E, Sheppard JD, Holland EJ, et al. Prospective, multi-center, randomized controlled study on the effect of loteprednol etabonate on initiating therapy with cyclosporin A. Presented at: American Academy of Ophthalmology Annual Meeting. Nov. 10-13, 2007; New Orleans.
2. Sheppard JD, Donnenfeld ED, Holland EJ, et al. Effect of loteprednol etabonate 0.5% on initiation of dry eye treatment with topical cyclosporine 0.05%. *Eye Contact Lens.* 2014;40(5):289-296.
3. Holland E, Nichols K, Foulks G, et al. Safety and efficacy of KPI-121 ophthalmic suspension 0.25% for dry eye disease in four randomized controlled trials. Presented at: American Academy of Ophthalmology 2020, Nov. 13-15, 2020; virtual meeting.
4. Data on file. Kala Pharmaceuticals. Watertown, MA.
5. Oyster Point Pharma announces FDA acceptance for filing new drug application for OC-01 (varenicline) nasal spray for the treatment of signs and symptoms of dry eye disease. March 2, 2021. https://investors.oysterpointrx.com/news-releases/news-release-details/oyster-point-pharma-announces-fda-acceptance-filing-new-drug. Accessed March 3, 2021.
6. Lambiase A, Sullivan BD, Schmidt TA, et al. A two-week, randomized, double-masked study to evaluate safety and efficacy of lubricin (150 µg/mL) eye drops versus sodium hyaluronate (HA) 0.18% eye drops (Vismed) in patients with moderate dry eye disease. *Ocul Surf.* 2017;15(1):77-87.
7. Surface Ophthalmics announces first patient dosed in phase II trial for SURF-200 for acute dry eye. February 4, 2021. www.prnewswire.com/news-releases/surface-ophthalmics-announces-first-patient-dosed-in-phase-ii-trial-for-surf-200-for-acute-dry-eye-301222308.html?tc=eml_cleartime. Accessed March 3, 2021.

TREATMENT DECISIONS

All consensus panelists base their treatment decisions on both signs and symptoms. Every panelist takes a different approach to treating patients with chronic dry eye disease versus those experiencing intermittent dry eye flares.

When dry eye is diagnosed, it is important to establish that flares are part of the disease cycle, said Elizabeth Yeu, MD. "Some people may require treatment at baseline and still need an additional therapy to calm down the flare," she said.

Some patients may not require therapy or only need maintenance therapy with artificial tears, and then treatment of flares, said Richard Lindstrom, MD. "After you treat a flare, the remission can last a month or 2 before it wears off. That might reduce the necessity for chronic dry eye therapy immunomodulation if we can do nothing and then treat flare," he said.

Eric D. Donnenfeld, MD, agreed with that approach, based on the number of flares and severity of the disease. "For patients who only have a small number of flares a year, immunomodulation with a corticosteroid is certainly cost effective and very comfortable for the patient," he said.

"For patients who have intermittent flares, we want to use something that is rapid-acting, and we don't need to use it chronically," said Edward J. Holland, MD, who added that a topical steroid would be his treatment of choice.

PREOPERATIVE STRATEGIES

Preoperative treatment of dry eye is critical in cataract patients to improve the accuracy of IOL calculations.

Preeya K. Gupta, MD, and her colleagues reported that 80% of patients presenting for cataract surgery have ocular surface

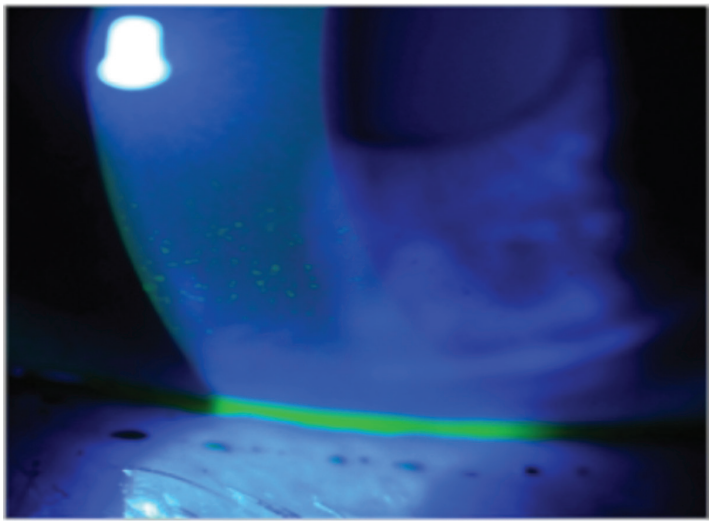


Image courtesy of Christopher E. Starr, MD.

Figure. Corneal staining.

KEYS FOR PATIENT COMMUNICATION

Patient education is an integral part of treating dry eye disease (DED) flares. After treatment, patients need advice on handling future flares.

Following flare treatment with loteprednol etabonate nanotechnology suspension, Stephen C. Pflugfelder, MD, typically prescribes one refill and explains that it can be used for future flares. Similarly, Terry Kim, MD, encourages patients to be proactive and restart the medication when flares begin to recur, rather than waiting.

However, Christopher E. Starr, MD, sees patients in person or via telemedicine before resuming topical steroids.

If treatment controls signs and symptoms well, Drs. Starr, Kim, and Pflugfelder ask patients to return every 6 to 12 months, depending on the patient's condition. However, if vision decreases or they have unusual pain, Dr. Kim recommends an office visit.

"I tell them to contact us if they are still experiencing bothersome symptoms after the 2-week course," Dr. Pflugfelder said. "In some cases, I ask them to return for reevaluation."

"I always let patients know I'm there if they need me, especially when there is an unexpected DED flare," Dr. Starr said. "A sustained worsening in dry eye symptoms, typically from exposure to a known trigger, constitutes a flare and often prompts an 'emergency' visit."

On average, DED flares are adequately addressed for 2 to 3 months after a 2-week course of loteprednol etabonate suspension, Dr. Kim said.

In addition to controlling flares and providing daily DED maintenance, Dr. Starr noted, "by identifying and avoiding particular DED flare triggers, the patient can be comfortably maintained for a long time."

disease.[1] She explained that ocular surface disease can change biometry and keratometry values, which impact IOL selection and can cause refractive misses.[2] "Therefore, it is important that we recognize this but also recognize that we can avoid some of these refractive surprises if we pay attention to the ocular surface preoperatively," she said.

To assist clinicians in treating dry eye before cataract surgery, Christopher E. Starr, MD, and the ASCRS Cornea Clinical Committee published an algorithm delineating the difference between visually significant dry eye and not visually significant dry eye.[3]

"Dry eye flares and signs such as corneal staining (Figure) can affect the quality of preoperative testing as well as the accuracy of my postoperative results, so I'm going to be aggressive about trying to heal the ocular surface," Dr. Holland said. "Postoperatively, patients with flares are frustrated with their outcomes because their eye is uncomfortable, and their vision may be decreased."

"As clinicians, we should not only talk about chronic dry eye, but elicit comments about dry eye flares."

— Edward J. Holland, MD

"For presurgical patients, we all want to optimize the ocular surface as best we can before proceeding with surgery," said Terry Kim, MD. In addition, he said, surgeons need to provide treatment for postoperative patients that has a rapid therapeutic response.

To prepare the ocular surface for any surgical intervention or rapidly improve the corneal surface as quickly as possible in patients with significant dry eye, Dr. Lindstrom prescribes topical steroids for 2 weeks, four times per day. "We also need to protect the ocular surface during surgery and then rehabilitate it and make sure the patient has long-term maintenance therapy as needed," he said.

Dr. Yeu believes it would be helpful to treat patients as they would for induction to remission. "It's a similar therapeutic regimen as a flare, but it also helps to add preservative-free lubrication at a minimum of four times per day, spaced separately from the steroid administration," she said.

"I think treating meibomian gland disease in conjunction with acute inflammation is important because we know that's a chronic condition that is going to contribute to flares," Dr. Gupta said. She added that microblepharoexfoliation is helpful and can be combined with thermal pulsation treatments to remove the biofilm and scar tissue along the orifice of the gland and improve the success of thermal pulsation.

CONCLUSION

"As clinicians, we should not only talk about chronic dry eye, but elicit comments about dry eye flares," Dr. Holland said. "What we will find out is that we have two groups of patients—those who only have dry eye flares and they only want those flares treated, and I would look to a very effective and safe topical corticosteroid to treat those flares. We will have some patients who will need maintenance therapy, and those patients will be very common, too. Patients on maintenance therapy have flares, but increasing the maintenance therapy is not an option. We want to treat flares of those chronic patients as well." ■

1. Gupta PK, Drinkwater OJ, VanDusen KW, et al. Prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation. *J Cataract Refract Surg.* 2018;44(9):1090-1096.
2. Epitropoulos AT, Matossian C, Berdy GJ, et al. Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning. *J Cataract Refract Surg.* 2015;41(8):1672-1677.
3. Starr CE, Gupta PK, Farid M, et al. ASCRS Cornea Clinical Committee. An algorithm for the preoperative diagnosis and treatment of ocular surface disorders. *J Cataract Refract Surg.* 2019;45(5):669-684.

CASE MANAGEMENT

Panelists shared how they would treat the following hypothetical cases.

CASE 1

History

- 66-year-old postmenopausal woman
- Aqueous deficiency dry eye
- Topical lifitegrast twice daily; artificial tears
- Significant breakthrough dry eye flares from air conditioning 10 times throughout the summer, lasting 2 to 3 days

Suggested Diagnostics

Stephen C. Pflugfelder, MD, would check for matrix metalloproteinase-9 (MMP-9) positivity, rapid tear breakup time, and corneal fluorescein staining (Figure 1). "However, if she has symptoms, I would treat her based on those alone," he said.

For women with aqueous-deficient dry eye, regardless of age, Christopher E. Starr, MD, also recommended blood tests for Sjögren syndrome, as well as other autoimmune conditions.

Diagnostic Findings

- Osmolarity: 298/315 mOsm/L
- 1+ lissamine green conjunctival staining
- OSDI: Significant worsening during flares

Suggested Treatment

Based on the patient's history and these findings, Dr. Starr offered the following treatment suggestions. "For this patient, I think loteprednol etabonate ophthalmic nanotechnology suspension 0.25% has a role," he said.

Dr. Starr also recommended managing the air conditioning or using a humidifier: "Education and avoidance are important for people who can identify triggers. That is key here, hand-in-hand with the use of steroids when dry eye flares."

He also recommended oral omega-3 supplements and lid hygiene if the patient has meibomian gland dysfunction (MGD) or blepharitis. "If the MMP-9 was positive and she had a very scant tear lake, I would probably treat it with steroids first and then possibly insert punctal plugs during a subsequent visit if the inflammation was under control," Dr. Starr said.

Image courtesy of Stephen C. Pflugfelder, MD.

Figure 1. Corneal staining with fluorescein.

CASE 2

History

- 33-year-old man
- Daily wear soft contact lens wearer
- Mild seasonal allergies
- Intermittent contact lens intolerance, red eyes

Suggested Diagnostics

Elizabeth Yeu, MD, suspected an allergy component potentially exacerbated by contact lens wear. She recommended a thorough examination and meibography. "Contact lens wear can certainly increase the risk for architectural dropout and MGD," she said. "If he is experiencing an exacerbation of symptoms, I would add MMP-9 testing."

Diagnostic Findings

- 2+ conjunctival hyperemia
- 1+ tarsal papillary changes
- 1+ meibomian gland inspissation

Suggested Treatment

Based on the patient's history and findings, Edward J. Holland, MD, would discontinue contact lens wear and add a topical antihistamine and possibly an oral antihistamine.

Dr. Holland suggested prescribing artificial tears, and since the patient had significant symptoms, a topical steroid for rapid symptom relief.

CASE 3

History

- 71-year-old woman with diffractive presbyopic IOLs in both eyes
- Significant variation in night driving glare and halos when using car heater in winter
- Patient very happy with vision

Suggested Diagnostics

Terry Kim, MD, explained her visual fluctuation signifies an ocular surface component that is probably related to MGD. He recommended fluorescein staining (Figure 2), and if results are negative, he would use lissamine green staining of the conjunctiva and cornea. He also would check the tear breakup time and press on the eyelid with a cotton-tipped applicator to assess the status and quality of the meibum, checking for inspissation or clogging.

He also suggested tear osmolarity, Schirmer test, and especially meibography if available. "Patients don't understand they have evaporative DED coming from moderate to severe MGD. To be able to show them an image of the abnormality of their meibomian gland anatomy provides an extremely important tool for educating our patients on the disease process and for motivating our patients to stay compliant with their medical and mechanical therapies," Dr. Kim said.

Diagnostic Findings

- No refractive error or posterior capsule opacification
- Normal macular optical coherence tomography
- Schirmer scores with anesthesia: 11/13
- Osmolarity: 300 and 310 mOsm/L
- 1+ central fluorescein corneal staining

Suggested Treatment

Based on the examination and diagnostic findings, Dr. Pflugfelder would use loteprednol etabonate ophthalmic nanotechnology suspension 0.25% as first-line treatment. "If it looks like her dry eye is becoming chronic or her dissatisfaction is more frequent, I would probably add cyclosporine or lifitegrast. If she's aqueous deficient, I would consider punctal plugs. I tend to like the dissolvable short-term punctal plugs for the initial trial." He would also add nutritional supplements as needed.

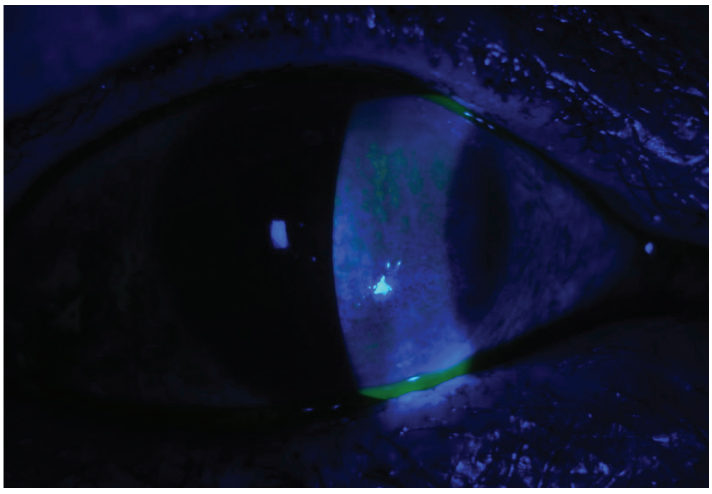


Image courtesy of Stephen Pflugfelder, MD.

Figure 2. Corneal staining with fluorescein.

CONCLUSIONS

"I'm impressed that there's consensus among these experts in the field that dry eye flares are common," Dr. Pflugfelder said. "We have underdiagnosed them. They have an inflammatory basis, and antiinflammatory therapy is the way to go."

"This is an exciting time," Dr. Starr said. He explained that clinicians have been using topical steroids off-label as the conventional treatment for flares. "Now that we have an FDA-approved steroid drop for this exact purpose, I think that's tremendous not only for us, but people who might have been a little trepidatious or reticent to use steroids for these patients," he said. "Now they have a good reason." ■

DRY EYE FLARES CONSENSUS STATEMENT:
Clinical Recommendations for Acute Exacerbation of Dry Eye Disease

Release Date: May 2021
Expiration Date: May 2022

INSTRUCTIONS FOR CME CREDIT

To receive credit, you must complete the attached Pretest/Posttest/Activity Evaluation/Satisfaction Measures Form and mail or fax to Evolve Medical Education LLC; 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please go to http://evolvemeded.com/online-courses/2042-supplement. If you experience problems with the online test, please email us at info@evolvemeded.com. Certificates are issued electronically, therefore, please provide your email address below.

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Full Name_____ ❑ MD/DO participant ❑ OD ❑ non-MD participant

Phone (required) _____ ❑ Email (required) _____

Address/P.O. Box _____

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License Number _____ OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
___ 51+

Region
___ Northeast
___ Northwest
___ Midwest
___ Southeast
___ Southwest

Setting
___ Solo Practice
___ Community Hospital
___ Government or VA
___ Group Practice
___ Other
___ I do not actively practice

Models of Care
___ Fee for Service
___ ACO
___ Patient-Centered Medical Home
___ Capitation
___ Bundled Payments
___ Other

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	Agree	Neutral	Disagree
Identify the prevalence and impact of dry eye flares on visual outcomes and patient satisfaction	_____	_____	_____
Improve understanding of the signs and symptoms associated with episodic flares of ocular surface disease	_____	_____	_____
Increase confidence in making therapeutic decisions for patients who experience acute exacerbations of dry eye disease	_____	_____	_____
Describe the mechanism of mucus-penetrating nanoparticles	_____	_____	_____

PLEASE COMPLETE AT THE CONCLUSION OF THE PROGRAM.

1. **Based on this activity, please rate your confidence in your ability to identify dry eye flares (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).**
   a. 1
   b. 2
   c. 3
   d. 4
   e. 5

2. **Why may ophthalmologists miss dry eye flares in their patients?**
   a. Immunomodulators mask symptoms
   b. Patients self-treat their symptoms
   c. Flares primarily occur postoperatively
   d. A & B

3. **Which of the following can be potential extrinsic trigger(s) of dry eye flares?**
   a. Allergies
   b. Air travel
   c. Contact lens wear
   d. All of the above

4. **_____ is a biomarker that has been associated with dry eye flares.**
   a. Matrix-metalloproteinase-9 (MMP-9)
   b. Intraocular pressure
   c. Neurofilament light chain
   d. Laminin P1

5. **Approximately _____ of patients with dry eye disease have flares.**
   a. 20%
   b. 40%
   c. 60%
   d. 80%

6. **The panel reported that the average dry eye patient experiences _____ dry eye flares each year.**
   a. 2
   b. 6
   c. 9
   d. 15

7. **What did panelists recommend as the top three objective tests when evaluating dry eye flares?**
   a. MMP-9, tear breakup time, and meibography
   b. Meibomian gland expression, meibography, and corneal topography
   c. MMP-9, corneal staining, and tear osmolarity
   d. Conjunctival staining, MMP-9, and corneal topography

8. **What is a useful way to identify whether a patient is having periodic dry eye flares?**
   a. SPEED test
   b. Asking patients to compare symptoms with a previous time period
   c. Optical coherence tomography
   d. Meibography

9. **Which of the following is true regarding nanotechnology used for loteprednol 0.25%?**
   a. It carries the drug into the ocular surface.
   b. It increases the side effects of the drug.
   c. It is rapidly cleared with tears during blinking.
   d. It adheres to mucins.

10. **When treating dry eye flares, panelists seek drugs with _____.**
    a. Long-term action
    b. Cholinergic action
    c. Rapid action
    d. All of the above

11. **Panelists stated that _____ can help improve patient compliance with topical immunomodulators when used as an initiation treatment.**
    a. Loteprednol etabonate nanotechnology suspension 0.25%
    b. Oral omega-3 fatty acids
    c. Ocular lubricants
    d. Blepharoexfoliation

12. **_____, which stimulates tearing, is being studied in a preservative-free nasal spray.**
    a. Oxymetazoline hydrochloride 0.05%
    b. Recombinant human lubricin protein
    c. Betamethasone
    d. A nicotinic acetylcholine receptor agonist

ACTIVITY EVALUATION/SATISFACTION MEASURES

Your responses to the questions below will help us evaluate this CME activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom _____ Yes _____ No

Probability of changing practice behavior based on this activity: _____ Yes _____ No _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

_____ Change in pharmaceutical therapy
_____ Change in diagnostic testing
_____ Change in current practice for referral
_____ My practice has been reinforced
_____ Change in nonpharmaceutical therapy
_____ Choice of treatment/management approach
_____ Change in differential diagnosis
_____ I do not plan to implement any new changes in practice

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____
_____

The design of the program was effective for the content conveyed. ___ Yes ___ No

The content supported the identified learning objectives. ___ Yes ___ No

The content was free of commercial bias. ___ Yes ___ No

The content was relative to your practice. ___ Yes ___ No

The faculty was effective. ___ Yes ___ No

You were satisfied overall with the activity. ___ Yes ___ No

Would you recommend this program to your colleagues? ___ Yes ___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____ I certify that I have participated in this entire activity.

This information will help evaluate this CME activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.

_____