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Global Consensus Statement on the Impact of Ophthalmic Preservatives


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Content Source

This continuing medical education (CME) activity captures content from a panel of expert glaucoma physicians who provided insight in a series of interviews and responded to an online consensus questionnaire.

Activity Description

This supplement summarizes a discussion on the impact of ophthalmic preservatives on the ocular surface in patients with glaucoma.

Target Audience

This certified CME activity is designed for ophthalmologists.

Learning Objectives

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

- **Define** the impact of therapy containing BAK on the ocular surface in patients with glaucoma
- **Identify** the prevalence of BAK-related adverse events among glaucoma patients
- **Examine** how preservative-associated adverse effects can affect surgical or medical outcomes in disease management
- **Consider** the influence of preservatives on patient satisfaction and adherence to medication over time
- **Review** the perceptions of preservatives on a global scale and discuss the challenges and benefits in implementing preservative-free therapies in glaucoma

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PRETEST QUESTIONS

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1. Please rate your confidence in your ability to discuss the impact of ophthalmic preservatives on the ocular surface in patients with glaucoma (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. Which preservative is commonly used in topical glaucoma medications due to its antimicrobial properties and cost-effectiveness?

A. Chlorhexidine
B. Ethanol
C. Benzalkonium chloride (BAK)
D. Sorbic acid

3. What long-term impact has been most associated with the use of BAK in glaucoma medications?

A. Improvement in visual acuity
B. Reduction in intraocular pressure
C. Development of ocular surface disease
D. Decrease in dry eye symptoms

4. Which of the following is NOT a potential benefit of using preservative-free glaucoma medications?

A. Reduced patient compliance
B. Lower risk of ocular surface disease
C. Fewer allergic reactions
D. Decreased discomfort

5. What is the primary function of the trabecular meshwork?

A. Produces the aqueous humor
B. Drains the aqueous humor
C. Focuses light onto the retina
D. Protects the eye from UV light

6. What aspect of ocular surgery does the use of BAK potentially complicate according to the expert panel?

A. The surgical incision healing
B. The postoperative medication regimen
C. The effectiveness of anesthesia
D. Recovery from surgery

7. According to the discussions, why might younger glaucoma patients benefit more from preservative-free medications?

A. They experience faster progression of glaucoma
B. They are less likely to comply with treatment
C. They require treatment over a longer period
D. They have fewer symptoms of glaucoma

8. What clinical strategy is recommended for managing patients with ocular surface disease exacerbated by preservatives?

A. Increase the concentration of BAK in medications
B. Switch to preservative-free medications
C. Use medications with higher viscosity
D. Reduce the frequency of medication application

9. Which of the following is a noted effect of BAK on the ocular surface?

A. Enhancement of tear film stability
B. Reduction of tear evaporation
C. Induction of inflammatory response
D. Improvement of visual acuity

10. A 68-year-old woman with chronic open-angle glaucoma has been on a BAK-preserved IOP-lowering medication for several years. She presents with complaints of persistent eye redness, burning sensation, and fluctuating vision. She has a history of dry eye syndrome, exacerbated since starting her glaucoma medication. Considering her symptoms and medical history, which of the following actions is most appropriate to manage her condition?

A. Increase the dosage of her current BAK-preserved medication
B. Switch to a higher potency BAK-preserved medication
C. Replace her current medication with a preservative-free formulation
D. Advise the patient to use over-the-counter eye drops more frequently

11. A 72-year-old patient undergoing evaluation for glaucoma surgery has been using a BAK-preserved medication regimen. The presurgical assessment indicates significant ocular surface disease, which could compromise surgical outcomes. What preoperative adjustment should be considered to optimize the patient's ocular surface condition before undergoing surgery?

A. Temporarily increase the use of BAK-preserved eye drops to maximize IOP control before surgery
B. Introduce a short course of topical steroids to reduce inflammation
C. Transition to a preservative-free eye drop regimen and use artificial tears
D. No changes are necessary; proceed with the planned surgery

Global Consensus Statement on the Impact of Ophthalmic Preservatives

Topical medication, used to lower intraocular pressure (IOP), is the cornerstone of glaucoma treatment. Traditionally, these medications have incorporated a preservative, typically benzalkonium chloride (BAK), to help keep the bottles of eye drops sterile and suitable for multiple uses over an extended period. Increasingly, physicians are becoming concerned with the toxicity of BAK, and the potential harm it can cause to the patient's ocular surface—which may be uncomfortable and can lead to impaired treatment outcomes. The availability of preservative-free medications may offer ocular surface health benefits to patients on long-term glaucoma treatment. The following is a summary from a panel of expert glaucoma physicians who provided insight into this topic in a series of interviews and an online consensus questionnaire. The expert panel's objectives were to:

- Define the impact of therapy containing BAK on the ocular surface in patients with glaucoma
- Identify the prevalence of BAK-related adverse events among glaucoma patients
- Examine how preservative-associated adverse effects can affect surgical or medical outcomes in disease management
- Consider the influence of preservatives on patient satisfaction and adherence to medication over time
- Review the perceptions of preservatives on a global scale and discuss the challenges and benefits in implementing preservative-free therapies in glaucoma

THE ROLE OF PRESERVATIVES IN TOPICAL GLAUCOMA MEDICATION

Topical medication (eye drops), prescribed to lower IOP, forms the cornerstone of glaucoma management and plays an essential role in slowing disease progression. The inclusion of a preserving agent to inhibit bacterial growth, improve sterility, and lengthen shelf life has been both a practical (see *How Can Preservative-Containing Medications Benefit Patients?* sidebar) and a regulatory requirement in multiuse bottles of medication.

How Necessary are Preservatives in Today's Glaucoma Practice?

The expert panel explained that this can be answered with both a long-term view and with respect to day-to-day routine practice. As developments in preservative-free formulations or lower-toxicity preserving agents continue, preservatives may become progressively less essential to glaucoma medication. However, in current routine practice there is a need to use preservative-containing medication to have access to the full range of available drug classes and pharmaceutical molecules. Currently, only a small subset of IOP-lowering molecules are available without preservatives, and the availability of preservative-free medication varies by region (Table 1). Certain active molecules are yet to be offered without a preservative, including nitric oxide donating agents and Rho-kinase inhibitors.

Why is BAK Used, and What Advantages Does It Offer?

BAK has been used in ophthalmic medication for more than 80 years to preserve solutions and prevent bacterial contamination. It was also historically associated with facilitation of efficacy by increasing drug penetrance (See *Updates in Understanding the Role of BAK in Drug Efficacy* sidebar).[1-3]

HOW CAN PRESERVATIVE-CONTAINING MEDICATIONS BENEFIT PATIENTS?

Preservative-containing medications are typically found in multidose containers that can remain open and in use over a longer period of time, compared with preservative-free formulations that are often supplied as single-use vials.

Patients may prefer the day-to-day convenience of multiuse bottles of medication. Monique M. Barbour, MD, and Joseph F. Panarelli, MD, said they have patients who prefer multiuse formulations for ease of storage and rapid instillation, and when traveling so they don't need to estimate how many single-use vials they may need.

For older patients, or those with impaired dexterity, large multidose bottles also provide a physical advantage: they are easier to grip and manipulate than small bottles and single-use vials. "I think we don't spend enough time talking about it, but a lot of our patients have dexterity challenges," observed Sarah H. Van Tassel, MD. "A bigger bottle is easier to use than a vial. Many, though not all, preservative-free eye drops come in vials, which can be frustrating for elderly patients. Additionally, for those with poor dexterity, when the end is snapped off a single-use vial the opening can be quite sharp, and is uncomfortable if it touches the eye or eyelid."

TABLE 1. PRESERVATIVE-CONTAINING (BAK AND ALTERNATIVES) AND PRESERVATIVE-FREE MEDICATION CURRENTLY AVAILABLE FOR GLAUCOMA[1,2]

USA			Europe		
Preservative-containing (BAK) glaucoma eye drops					
Active ingredient	**Brand name**	**Preservative**	**Active ingredient**	**Brand name**	**Preservative**
Apraclonidine 0.5%	Iopidine	BAK 0.01%	Apraclonidine 0.5%	Iopidine	BAK 0.01%
Apraclonidine 1.0%	Iopidine	BAK 0.01%	Apraclonidine 1.0%	Iopidine	BAK 0.01%
Betaxolol 0.25%	Betoptic S	BAK 0.01%	Betaxolol 0.25%	Betoptic	BAK 0.01%
Betaxolol 0.5%	Betoptic	BAK 0.01%	Betaxolol 0.5%	Betoptic	BAK 0.01%
Bimatoprost 0.01%	Lumigan	BAK 0.02%	Bimatoprost 0.01%	Lumigan	BAK 0.02%
Bimatoprost 0.03%	Lumigan	BAK 0.005%	Bimatoprost 0.03%	Lumigan	BAK 0.02%
-	-	-	Bimatoprost 0.03%/timolol 0.5%	Ganfort	BAK 0.005%
Brimonidine 0.2%	Alphagan	BAK 0.005%	Brimonidine 0.2%	Alphagan	BAK 0.005%
Brimonidine 0.2%/timolol 0.5%	Combigan	BAK 0.005%	Brimonidine 0.2%/timolol 0.5%	Combigan	BAK 0.005%
Brinzolamide 1.0%	Azopt	BAK 0.01%	Brinzolamide 1.0%	Azopt	BAK 0.01%
Brinzolamide 1.0%/brimonidine 0.2%	Simbrinza	BAK 0.003%	Brinzolamide 1.0%/brimonidine 0.2%	Simbrinza	BAK 0.003%
-	-	-	Brinzolamide 1.0%/timolol 0.5%	Azarga	BAK 0.01%
Dorzolamide 2.0%	Trusopt	BAK 0.0075%	Dorzolamide 2.0%	Trusopt	BAK 0.0075%
Dorzolamide 2.0%/timolol 0.5%	Cosopt	BAK 0.0075%	Dorzolamide 2.0%/timolol 0.5%	Cosopt	BAK 0.0075%
Latanoprost 0.005%	Xalatan	BAK 0.02%	Latanoprost 0.005%	Xalatan	BAK 0.02%
Latanoprost 0.005%/netarsudil 0.02%	Rocklatan	BAK 0.02%	Latanoprost 0.005%/netarsudil 0.02%	Roclanda	BAK 0.02%
-	-	-	Latanoprost 0.005%/timolol 0.5%	Xalacom	BAK 0.02%
Latanoprostene bunod 0.024%	Vyzulta	BAK 0.02%			
Levobunolol 0.25%	Betagan	BAK 0.004%			
Levobunolol 0.5%	Betagan	BAK 0.004%	Levobunolol 0.5%	Betagan	BAK 0.004%
Netarsudil 0.02%	Rhopressa	BAK 0.015%			
Pilocarpine 1.0%	Isopto Carpine	BAK 0.01%	Pilocarpine 1.0%	-	BAK 0.01%
Pilocarpine 2.0%	Isopto Carpine	BAK 0.01%	Pilocarpine 2.0%	-	BAK 0.01%
Pilocarpine 4.0%	Isopto Carpine	BAK 0.01%	Pilocarpine 4.0%	-	BAK 0.01%
Timolol 0.25%	Timoptic	BAK 0.01%	Timolol 0.25%	Timolol	BAK 0.01%
Timolol 0.5%	Timoptic	BAK 0.01%	Timolol 0.5%	Timolol LA	BAK 0.01%
Preservative-containing (alternative to BAK) glaucoma eye drops					
Brimonidine 0.1%	Alphagan P	Stabilized oxychloro complex 0.005%			
Brimonidine 0.15%	Alphagan P	Stabilized oxychloro complex 0.005%			
Latanoprost 0.005%	Xelpros	Potassium sorbate			
Timolol-XE 0.25%, 0.5%	Timoptic-XE	Benzododecinium bromide 0.012%			
Travoprost 0.004%	Travatan Z	SofZia	Travoprost 0.004%	Travatan Z	SofZia
-	-	-	Travoprost 0.004%/timolol 0.5%	DuoTrav	SofZia
Preservative-free glaucoma eye drops					
-	-	-	Bimatoprost 0.03%	Lumigan UD	PF
-	-	-	Bimatoprost 0.03%/timolol 0.5%	Ganfort UD	PF
-	-	-	Dorzolamide 2.0%	Trusopt PF	PF
Dorzolamide 2.0%/timolol 0.5%	Cosopt PF	PF	Dorzolamide 2.0%/timolol 0.5%	Cosopt PF	PF
Latanoprost 0.005%	Iyuzeh	PF	Latanoprost 0.005%	Monopost	PF
Tafluprost 0.0015%	Zioptan	PF	Tafluprost 0.0015%	Saflutan	PF
-	-	-	Tafluprost 0.0015%/timolol 0.5%	Taptiqom	PF
-	-	-	Timolol 0.1%	Tiopex Timoptol	PF
Timolol 0.25%	Timoptic in Ocudose	PF	Timolol 0.25%	Tiopex Timoptol	PF
Timolol 0.5%	Timoptic in Ocudose	PF	Timolol 0.5%	Tiopex Timoptol	PF

BAK, Benzalkonium chloride; PF, preservative-free

1. Steven DW, Alaghband P, Lim KS. Preservatives in glaucoma medication. *Br J Ophthalmol*. 2018;102(11):1497-1503.
2. Autry JC, Fingret M, Schmidt E, Bloomenstein MR, O'Dell L. Preserving the ocular surface: When and why should we go preservative-free? Evolve Medical Education LLC. https://d4wgqzyt29bpb.cloudfront.net/documents/me/0523MOD_Evolve%202304_PF_Drops_White_Paper.pdf

UPDATES IN UNDERSTANDING THE ROLE OF BAK IN DRUG EFFICACY

BAK has been promoted as having efficacy-enhancing properties–it was associated with "loosening" tight junctions between corneal epithelial cells and consequently increasing permeability for larger pharmaceutical molecules.[2,5]

Most of the expert panel had been trained with this understanding of the mechanism of action of BAK; however, an expanding evidence base demonstrates that BAK is not required for effective drug action nor translate into greater clinical efficacy.

IOP-lowering efficacy has also been observed in several studies that have compared the same active molecule in combination with, or in the absence of, BAK.[6-15]

BAK is a quaternary ammonium cationic surfactant that has excellent solution stability, limited ocular penetration, and has demonstrated broad-spectrum, highly efficacious antimicrobial action.[4] It is currently found in approximately 70% of available eye drops, and is used in concentrations ranging from 0.004% to 0.02%.[1]

"BAK is effective," Jason Bacharach, MD, summarized. "It has been included in multidose bottles for decades, demonstrating excellent antibacterial properties, and it is accepted by the FDA in both branded and generic formulations. It is inexpensive to place in a plastic or polypropylene bottle, allowing for the formulation of relatively cost-effective glaucoma medication. There's also the potential benefit that it enhances the effectiveness of the drug. Many of us were trained that BAK weakens tight junctions in the cornea, and it allows the active pharmaceutical ingredient to enter the anterior chamber more effectively."

Evaluating the Impact of Preservatives in Glaucoma Treatment

For the past 50 years, it has been recognized that BAK has a deleterious effect on the ocular surface. This was initially observed with the disruption of the tear film and, subsequently, BAK has been associated with apoptosis, neurotoxicity, degeneration of the trabecular network, decreases in cellular viability, and damage to DNA.[16] A recent review succinctly stated: "the antimicrobial activity of the preservative is inversely proportional to its compatibility with the ocular surface."[1]

As physicians consider the optimal approach to managing their patients with glaucoma, there is increasing interest in understanding the balance of preservative-associated effects "in the bottle" versus "in the eye." Nathan M. Radcliffe, MD, explained, "I would start by saying that, ideally, we don't want anything being introduced to the eye. The eye is not like the stomach, which has evolved to absorb things peacefully. The eye was meant to never really have anything in it and, in fact, has mechanisms to keep things out. Anytime we put something on the surface of the eye, be it a molecule to treat glaucoma, or be it the preservative that helps keeps that bottle sterile… we're making a trade-off." Although this trade-off typically focuses on the use of BAK, the expert panel explained that the active drug and other excipients (see *Are Preservatives the Sole Cause of Toxicity and Tolerability Issues?* sidebar) and generic chemicals should also be considered as sources of potential toxicity or patient intolerance.

Miriam Kolko, MD, PhD, noted that preservatives can be of value in short-duration antibacterial treatment, but in the context of chronic medication, any discussion should start with justifying why a toxic agent should be required. This is particularly important when cumulative toxicity is considered—many patients with glaucoma will need to take eye drops for the remainder of their lives, and likely will use multiple eye drops at the same time.

Dr. Panarelli suggested there is a need for greater education on how IOP-lowering pharmaceuticals, excipients, and preservatives interact with the eye: "Education does not place the emphasis on mechanisms of action to the same degree as it did in the past. Without a solid grounding in the functional anatomy of the eye, and how medication interacts with it, there can't be a full understanding of how treatment choice can affect the health of the ocular surface."

"We're not ready to abandon preservatives. But I think that we should pave the way toward ultimately using preservative-free medications."

– Miriam Kolko, MD, PhD

THE IMPACT OF BAK ON THE OCULAR SURFACE

Over the past decade, the benefit of including preservatives in eye drops has been interrogated following the seminal publications on the "vicious cycles" of inflammation in ocular surface disease (OSD) and dry eye disease (DED).[17,18] While there are many drivers of the cycle, attention has been drawn to the clinical wisdom of using BAK in the treatment of OSD because of the overlap between:

- cyclical goblet cell loss, tear film instability, inflammation, apoptosis at the conjunctiva and cornea, and nerve cell stimulation in OSD progression and
- a preservative —BAK—that is associated with introducing or worsening the same factors

Recently, the "vicious cycle" of inflammation in glaucoma has been published,[19] and this has accelerated discussion around the suitability of using preservatives in IOP-lowering eye drops.

Definition and Background of OSD in Glaucoma

The term OSD encompasses several components, each contributing to overall ocular dysfunction and associated sources of discomfort:[20-23]

Tear film instability: OSD often involves abnormalities in the tear film, which is critical for maintaining eye health and providing clear vision. Tear film instability leads to dry eye symptoms due to insufficient lubrication and hydration of the ocular surface.

Meibomian gland dysfunction (MGD): This condition affects the glands responsible for secreting the oil layer of the tear film, crucial for preventing rapid tear evaporation. Dysfunction of these glands is a primary cause of evaporative dry eye, a common form of OSD.

Inflammation: Inflammatory processes play a significant role in OSD, affecting various structures of the eye including the eyelids, conjunctiva, and cornea, leading to symptoms such as redness, burning, and irritation. Inflammatory cytokines and other mediators contribute to this chronic inflammation, which can perpetuate the cycle of tear film instability and epithelial damage.

Neurotrophic conditions: The health of the ocular surface is also closely linked to corneal nerves. Damage to, or reduced function of, these nerves can lead to decreased sensitivity and impaired healing, a condition known as neurotrophic keratopathy.

"We have to consider: what's the value we get out of a chemical that is introduced into the eye, and what's the 'price' we pay for using it?"

– Nathan M. Radcliffe, MD

ARE PRESERVATIVES THE SOLE CAUSE OF TOXICITY AND TOLERABILITY ISSUES?

Several components of an eye drop can potentially contribute to toxicity or tolerability issues. According to Drs. Radcliffe and Van Tassel, they include:

- The pH of the solution can be a source of irritation
- Excipients (alcohols, phosphates, parabens, and EDTA) used to thicken or stabilize the solution may be toxic to the ocular surface
- The active molecule can also be a source of adverse events in the eye and adnexa

The whole formulation of the medication needs to be considered and understood to help select appropriate therapy and to minimize intolerance to treatment. Drs. Radcliffe and Van Tassel added that while alternative preservatives to BAK may be relatively less toxic, they are supported by only a small, short-term evidence base. BAK is currently the most well-understood source of toxicity.

TABLE 2. THE SIGNS AND SYMPTOMS OF OSD IN PATIENTS WITH GLAUCOMA[1]

Signs	Symptoms
Abnormal Schirmer test	Visual disturbances
Abnormal tear osmolarity	Dry eyes sensation
Abnormal TBUT test	Tearing
Meibomian gland dysfunction	Burning
Turbid meibomian gland secretions	Foreign-body sensation
Lid margin vascularization	Stinging or burning sensation
Lid margin laxity and/or irregularity	Eyelid itching
Corneal and/or conjunctival staining	Photophobia
Limbal and/or bulbar hyperemia	Grittiness
	Frequent/repeated blinking

OSD, ocular surface disease; TBUT, tear break-up time

1. Kastelan S, Tomic M, Metez Soldo K, Salopek-Rabatic J. How ocular surface disease impacts the glaucoma treatment outcome. *Biomed Res Int*. 2013;2013:696328.

Allergic reactions: Allergies affecting the eyes, or allergy to components of eye drops can exacerbate OSD symptoms (see *Allergy and Intolerance to BAK* sidebar). The allergic response can cause additional inflammation and discomfort, further destabilizing the tear film and irritating the ocular surface.

The key signs and symptoms of OSD are captured in Table 2. The most common manifestation and presentation of OSD is DED, which is defined as "a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[24]

The Causative Role of BAK in OSD

BAK, when used at the concentrations in the current range of preserved eye drops for glaucoma,[28] can cause OSD via several mechanisms:

Increased inflammatory response: BAK can induce an inflammatory response in the ocular surface tissues. It promotes the release of proinflammatory cytokines and can increase the infiltration of inflammatory cells into the cornea and conjunctiva. BAK-associated inflammation appears to correlate with dose.[29] Unmanaged ocular inflammation is a key driver of the OSD vicious cycle.[17]

Damage to epithelial cells: The detergent properties of BAK can damage the corneal and conjunctival epithelial cells,[30] compromising the barrier function of the ocular surface and leading to increased cell death and turnover; this can exacerbate OSD symptoms such as irritation and redness. Lens epithelial cells, which should be considered ahead of refractive surgery,[1] may also be affected by exposure to BAK.31

Disruption of the tear film: BAK can destabilize the tear film by affecting its lipid layer, leading to increased tear evaporation and tear film instability, and shortened tear breakup time (TBUT);[1,32] this disruption can cause dry eye symptoms. An impaired tear film contributes to the vicious cycle of OSD.[17]

Goblet cell dysfunction: BAK has been shown to decrease the density of goblet cells in the conjunctiva, which are crucial for maintaining a healthy and stable tear film through mucin production. BAK concentration correlates with the degree of change in goblet cell survival.[33,34]

ALLERGY AND INTOLERANCE TO BAK

The prevalence of true allergy to BAK is not clearly established; however, BAK has been recognized as an "allergen of increasing importance," and its role as an irritant is well documented.[25] The allergenic properties of BAK are currently under increased scrutiny following its increased use as an antibacterial agent during the COVID-19 pandemic.[26,27]

In practice, whether BAK results in allergy or intolerance didn't matter to the expert panel—a suspicion of either should result in the patient being offered a BAK-free alternative.

Dr. Bacharach noted how allergy and intolerance can present differently, and that physicians should be aware of both. "Maybe only 1% of patients will have true allergy to BAK, which can manifest quickly and will be very apparent," he explained. "Toxicity leading to intolerance can be slower and easily misdiagnosed or missed."

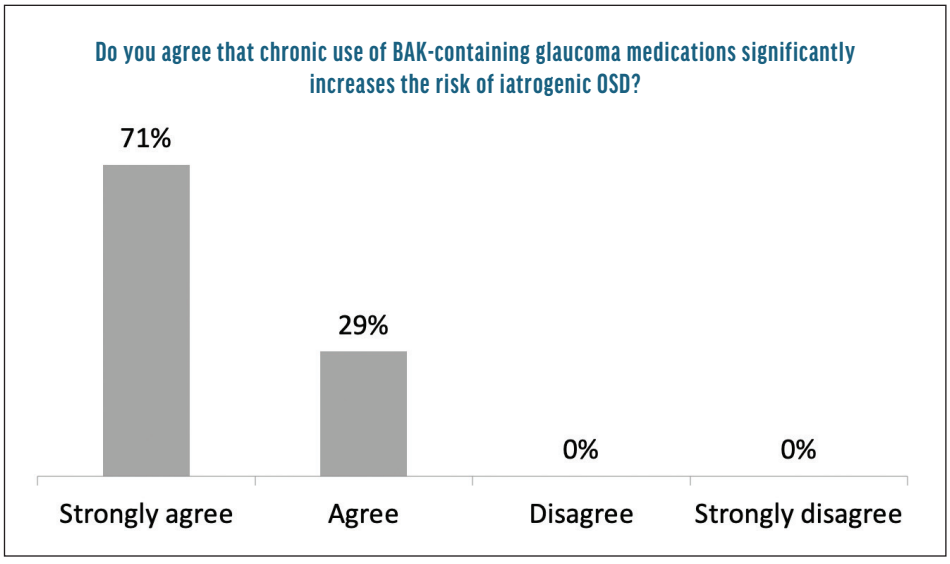

Figure 1. There was unanimous agreement that BAK-associated toxicity increases the risk of OSD.

BAK, benzalkonium chloride; OSD, ocular surface disease

"The higher the concentration, the more toxic the preservative will be; the evidence for this is most prominent when we speak about BAK."

– Miriam Kolko, MD, PhD

Modification of the trabecular meshwork: BAK has been associated with a deleterious and altering effect on the trabecular meshwork and has been shown to accumulate in the meshwork in the course of chronic treatment with preserved eye drops.[1,35]

There exists a strong base of laboratory and clinical evidence demonstrating that

"A lot of the data on the deleterious effects of preservatives come from studies of BAK, but there are alternatively preserved medicines with less toxic effect on the surface of the eye and possibly other beneficial ramifications."

– Jason Bacharach, MD

the prolonged use of, and total exposure to, BAK are risk factors to develop OSD in patients with glaucoma.[3,6]

The expert panel described the need to manage BAK exposure: the deleterious properties of BAK will be enhanced with greater concentration of preservative, and this is driven by the cumulative effects of multiple eye drops given over the course of many years, as is common in glaucoma treatment. There was a full consensus that the use of BAK in eye drops for glaucoma increases the risk of a patient developing OSD (Figure 1).

Are All Preservatives Equal? Are There Other Relevant Preservatives That We Should Be Considering With Glaucoma Medications?

The ongoing need for a preservative option in medical glaucoma treatment—to provide sterile multiuse bottles, and to make available agents that are not in a preservative-free formulation—has led to the development of alternative classes of preservation agents (Table 3). Available evidence suggests that these alternatives to BAK provide lower exposure to toxicity with no significant compromise in efficacy.[28]

The expert panel all noted that the evidence base for these agents is relatively small, despite their availability for several years. Dr. Radcliffe noted, "these agents are the ones we really

TABLE 3. CURRENT ALTERNATIVE PRESERVATIVE OPTIONS FOR TOPICAL GLAUCOMA MEDICATION[1]

Compound	Brand name	Mechanism of action	Support for potential benefits over BAK
Borate, sorbitol, propylene glycol and zinc	SofZia	Ionic buffer system	• Significantly greater survival of conjunctival and corneal cells [in vitro][2] • Maintained IOP-lowering efficacy in combination with a PGA, with a favorable tolerability profile[3] • Favorable findings for TBUT and OSDI[4]
Polyquartenium 1	Polyquad	Acts on cell membranes	• Significantly greater survival of conjunctival and corneal cells [in vitro][2] • Favorable findings for TBUT and OSDI with maintained IOP control[5] • Improved tolerability in conjunction with a PGA versus BAK-containing or preservative-free formulations[6] • Reduced cytotoxicity to goblet cells versus BAK [in vitro][7]
Stabilized oxychloro complex	Purite	Oxidation of intracellular lipids and glutathione via free radicals	• Comparable IOP-lowering efficacy in combination with an a_2 agonist with favorable safety and tolerability profile versus BAK-containing formulation[8] • Improved patient comfort and preference versus BAK[9]
Sodium perborate	Dequest GenAqua	Oxidation (forms hydrogen peroxide)	• Significantly lower toxicity to corneal and conjunctival cells versus BAK [in vitro][10]
Reference: BAK			
Benzalkonium chloride		Detergent action dissolves cell walls and membranes	

BAK, Benzalkonium chloride; IOP, intraocular pressure; OSDI, ocular surface disease index; PGA, prostaglandin analogue; TBUT, tear break-up time

1. Steven DW, Alaghband P, Lim KS. Preservatives in glaucoma medication. *Br J Ophthalmol*. 2018;102(11):1497-1503.
2. Ammar DA, Noecker RJ, Kahook MY. Effects of benzalkonium chloride-preserved, polyquad-preserved, and sofZia-preserved topical glaucoma medications on human ocular epithelial cells. *Adv Ther*. 2010;27(11):837-845.
3. Mizoue S, Nakano T, Fuse N, Iwase A, Matsumoto S, Yoshikawa K. Travoprost with sofZia(R) preservative system lowered intraocular pressure of Japanese normal tension glaucoma with minimal side effects. *Clin Ophthalmol*. 2014;8:347-354.
4. Aihara M, Oshima H, Araie M, group EXs. Effects of SofZia-preserved travoprost and benzalkonium chloride-preserved latanoprost on the ocular surface -- a multicentre randomized single-masked study. *Acta Ophthalmol*. 2013;91(1):e7-e14.
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8. Katz LJ. Twelve-month evaluation of brimonidine-purite versus brimonidine in patients with glaucoma or ocular hypertension. *J Glaucoma*. 2002;11(2):119-126.
9. Mundorf T, Wilcox KA, Ousler GW, 3rd, Welch D, Abelson MB. Evaluation of the comfort of Alphagan P compared with Alphagan in irritated eyes. *Adv Ther*. 2003;20(6):329-336.
10. Epstein SP, Ahdoot M, Marcus E, Asbell PA. Comparative toxicity of preservatives on immortalized corneal and conjunctival epithelial cells. *J Ocul Pharmacol Ther*. 2009;25(2):113-119.

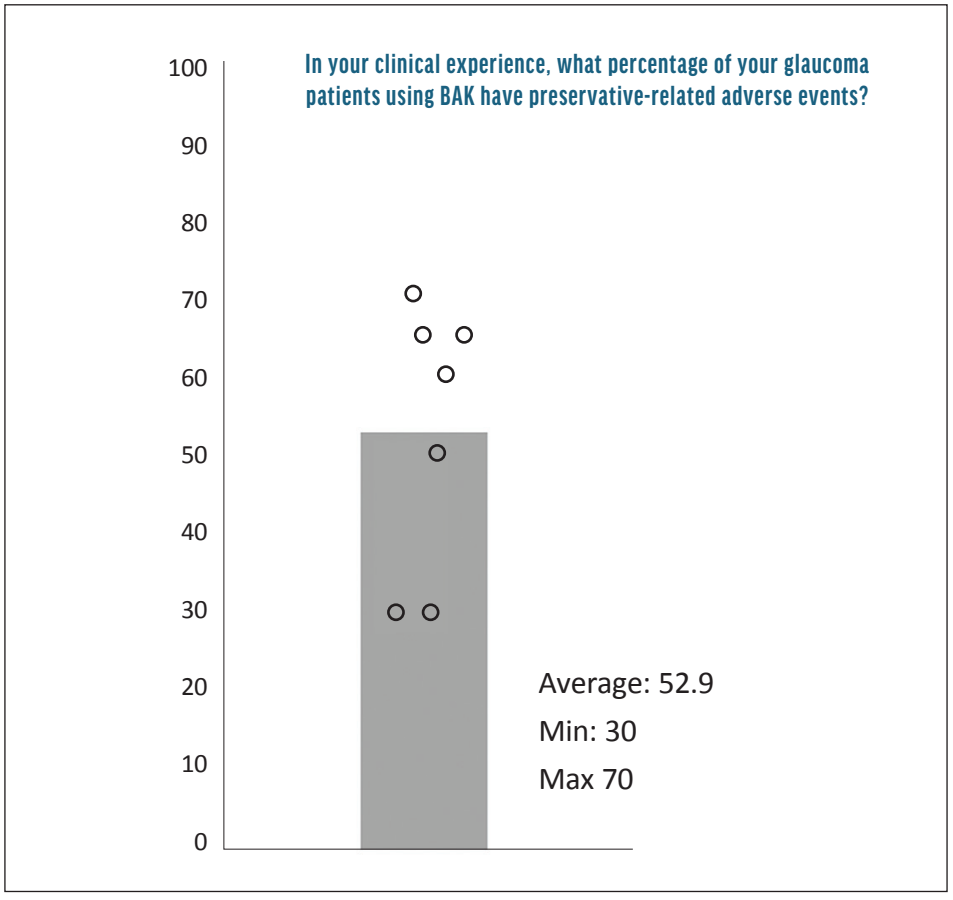


Figure 2. Approximately half of glaucoma patients seen by the expert panel had preservative-related adverse events.

BAK, benzalkonium chloride

know least about." A lack of long-term data in large patient cohorts could limit familiarity and comfort with the alternatives for both the prescribing physicians and for the payors responsible for adding these preservatives to the formulary. Anton Hommer, MD, noted, "In my experience, there is not a significant difference between the description of the different preservatives. In the patient information leaflets, the wording is very similar."

Another barrier to using alternative preservatives centers on cost: if the alternative options are more expensive than a BAK-containing formulation, physicians will need to provide justification for the switch. Dr. Bacharach illustrated how difficult this can be in practice; in his experience "Travatan Z, even when prescribed, commonly is substituted for a less expensive, generic BAK-containing alternative at the pharmacy level. Cost is a major driver for the pharmacy when dispensing glaucoma medication."

"Ultimately, treatment decisions are about doing the best for the individual, the human being in front of us. So it's not always just choosing what you think is the ideal treatment—that means choosing what is most likely the best for that person."

– Miriam Kolko, MD, PhD

PREVALENCE AND IMPACT OF PRESERVATIVE-RELATED ADVERSE EVENTS AMONG GLAUCOMA PATIENTS

In 2013, the global prevalence of glaucoma was estimated to be approximately 3.5%, affecting more than 60 million people who are 40 to 80 years old; this figure is projected to increase to more than 110 million people by 2040.[37] OSD is common in the general population, affecting approximately 15% of people over 65.[38] OSD is reported in more than half of glaucoma patients;[39] this comorbidity is driven by increases in prevalence of both diseases with advancing age, and the use of BAK-containing IOP-lowering medication.[40]

The use of BAK can exacerbate the signs and symptoms of OSD and lead to adverse effects at the conjunctiva and cornea.[39] The expert panel reported that approximately half of their patients with glaucoma had experienced preservative-related adverse events (Figure 2).

What Types of Patients are Most Affected by Preservative-Related OSD Symptoms, and How Does This Influence Management Decisions?

Dr. Hommer framed management decisions in terms of the likely duration of treatment: "Glaucoma is a rest-of-life disease, with many patients needing eye drops for more than 20 years; you have to consider the long-term implications of treatment, including cumulative toxicity." The expert panel explained that there are numerous clinical situations in which a preservative-containing medication would ideally

"A well-treated ocular surface typically gets the best surgical results."

– Sarah H. Van Tassel, MD

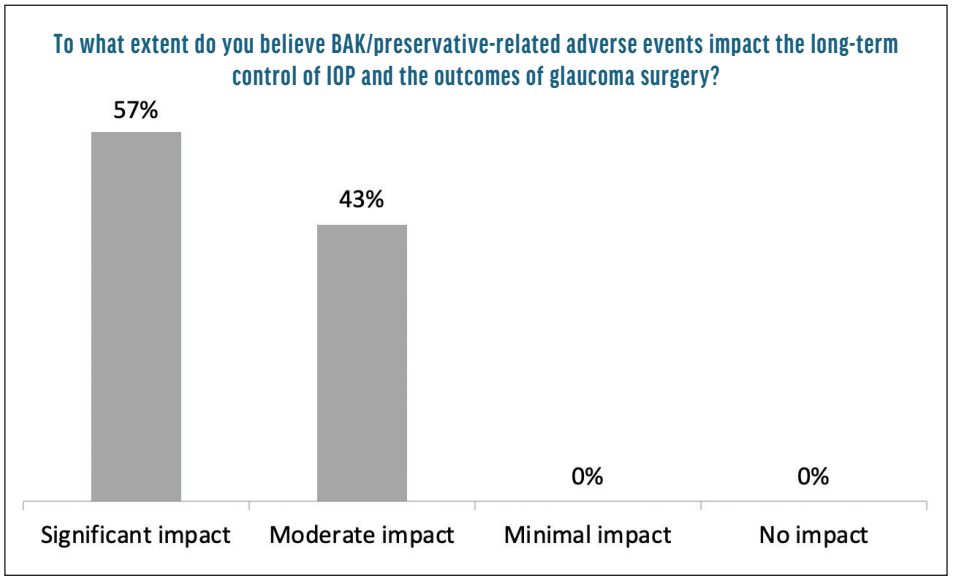


Figure 3. The expert panel agreed that preservative-related toxicity and adverse events have at least a moderate impact on glaucoma treatment outcomes.

BAK, benzalkonium chloride

not be used. Dr. Barbour takes caution in patients who have had LASIK or are on medications that are associated with a risk of developing or worsening DED; Dr. Hommer noted the need for caution in patients with skin diseases, especially around the eyes; Drs. Bacharach and Panarelli both added that patients with upcoming ocular surgery should be spared BAK-containing eye drops when possible. The panel were unanimous is declaring that patients with existing DED or OSD should not be initiated on BAK-containing therapy.

Beyond individual cases, Prof. Kolko recommended stratifying patients by age. There was consensus that younger glaucoma patients will require treatment for the longest period and, consequently, are most vulnerable to cumulative toxicity. By using preservative-free medication in this younger cohort, the ocular surface can be preserved for as long as possible. This has a further benefit in leaving the most treatment options—both medical and surgical—open to the patient, and should help their physician manage glaucoma, rather than glaucoma and OSD, as effectively as possible.

Drs. Radcliffe and Bacharach and Prof. Kolko noted the need for caution in prescribing preserved medication for older patients. These patients may have been exposed to BAK for many years and, even where this has been tolerated, the addition of a new preservative-containing medication could cause adverse events. The risk of OSD is inherently higher in older patients, as it is associated with advancing age, and they may also be receiving polypharmacy for other chronic conditions. It is important not to reach a "tipping point" at the ocular surface and trigger OSD, where this can be avoided. Dr. Radcliffe summarized, "Physicians need to be proactive when introducing a new medication for a patient, and ensure they minimize the risk of developing or worsening OSD."

There was agreement that there is no need for a medication switch for elderly people who are tolerating a BAK-containing monotherapy, especially when the handling benefits of a multidose bottle could provide relatively greater benefit to that patient.

Impact of OSD on IOP Control and Glaucoma Surgery Outcomes

The expert panel reached consensus agreement (Figure 3) on the position that BAK toxicity can impair outcomes with surgical trabeculectomy,[41,42] and that underlying, unmanaged OSD can complicate recovery from surgery.[23,43] Prof. Kolko added, "Among more damaging effects, BAK harms the goblet cells and may damage the meibomian glands, so the lipid content of the tear film is compromised and contributes to poor outcomes. These changes have been indicated to decrease the success of filtration surgeries." While there is ambiguity in the literature

"This is a good time to move toward earlier intervention with MIGS and SLT, along with shifting to preservative-free formulations."

– Jason Bacharach, MD

as to the extent of effect on surgical outcomes in patients who are receiving BAK-containing medication,[1,44] the faculty all advocated minimizing preoperative preservative exposure as much as possible.

Dr. Van Tassel observed that the type of upcoming surgery should guide the preparation of the ocular surface. "True filtration surgery has the best results when performed on a pristine ocular surface. But could they safely just be washed out, or take an oral carbonic anhydrous inhibitor for a few weeks?" This point was raised by several members of the expert panel: in an ideal world, a patient would have their ocular surface optimized ahead of surgery, but in routine practice this approach is a luxury. Dr. Panarelli added, "It is accepted that surgical outcomes may be better with a preservative-free regimen but, in day-to-day practice, is this enough to change a patient's medication, especially for those who cannot afford to switch?" Dr. Barbour agreed, explaining that in many cases "a patient may need to continue on preservative-containing medication into the surgical window…and they may find it more cost-effective to add a medication to try lower their level of inflammation."

Strategies to help prepare the ocular surface prior to filtration surgery must be determined on an individual basis. They include:[45]

- Optimally, switching to a fully preservative-free glaucoma medication regimen
- Reducing the overall toxicity burden by substituting some medication for a preservative-free formulation
- Taking a "time out" from topical medication and using preservative-free artificial tears in the days prior to surgery
- Using steroids to acutely reduce preoperative inflammation
- Prescribing cyclosporine in the postoperative setting for patients with a damaged ocular surface

Dr. Radcliffe presented an additional complication: many patients wish to avoid surgery and request additional medical treatment to prolong the period before surgical intervention is required. This can result in adding to the cumulative preservative-associated toxicity at the ocular surface and make future interventions more prone to failure. Ongoing exposure to preservative-containing medication has been associated with an increased risk of requiring surgical intervention.[46]

Preservative-related adverse effects can also impair the efficacy of medical control of IOP. "When the surface of the eye is inflamed or irritated, the patient may have trouble absorbing the drops," Dr. Radcliffe explained. "Situations may arise where there's so much inflammation that the IOP actually increases. In conjunction with laboratory data that show that BAK harms the trabecular meshwork, which is the eye's natural drainage system, you can reach a point where your glaucoma patients on treatment gradually get worse." Dr. Hommer added, "If patients are experiencing discomfort with their eye drops and rub their eyes, they are mechanically removing a lot of the drop and reducing the effective dose; this results in undertreatment of IOP."

Dr. Bacharach suggested considering minimally invasive glaucoma surgery (MIGS) and selective laser trabeculoplasty (SLT) earlier in the glaucoma treatment strategy. Drs. Bacharach, Panarelli, and Van Tassel all advocated for earlier minimally invasive procedures to achieve IOP lowering combined with a BAK-sparing effect, with post-procedure patients being free of eye drops, or on a reduced regimen. Prof. Kolko summarized, "Of course, there are other ways to spare the ocular surface. These include treatment with SLT, MIGS, and potentially slow-release implants. However, preservative-free eye drops are still a great choice when it comes to protecting the ocular surface."

PATIENT SATISFACTION AND COMPLIANCE IN RELATION TO PRESERVATIVE USE

The long-term effectiveness of glaucoma treatment relies on patient adherence to prescribed medication. It is estimated that 23% to 59% of patients on topical glaucoma therapy are nonadherent to their prescribed treatment.[45]

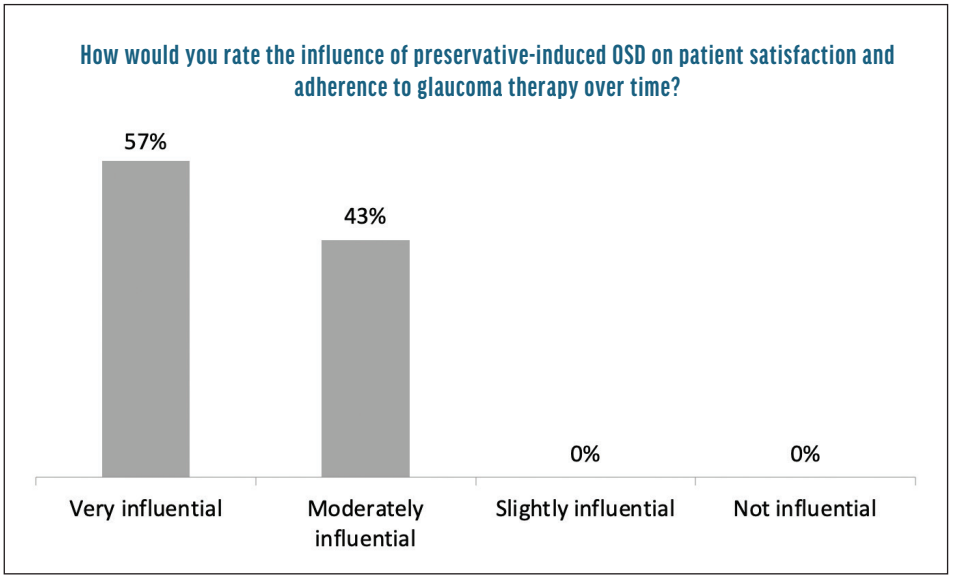


Figure 4. Preservative-associated OSD can negatively affect treatment satisfaction and adherence.

OSD, ocular surface disease

"The types of adverse events common with BAK-containing glaucoma medication—red and itchy eyes or droopy eyelids—can be very uncomfortable socially for patients, especially if they feel they need to explain these effects to friends, family, or colleagues."

– Monique M. Barbour, MD

How Can BAK-Containing Medications Affect Patient Satisfaction?

The expert panel agreed that the patient's experience with their medication is important in encouraging adherence, and over half felt that this aspect of management was "very influential" in determining patient behavior (Figure 4).

Ocular discomfort and hyperemia are most commonly reported as the causes of poor satisfaction with topical glaucoma therapy.[1] A recent study has associated a wider range of signs and symptoms of OSD as potential causes of dissatisfaction; however, this study observed a contradiction that showed high overall satisfaction with treatment, alongside common signs and symptoms of OSD.[47] The study authors concluded that the use of additional artificial tears and a mindset that some discomfort must be the "price to pay" for lowering of IOP were the reasons for this contradiction.[47] This highlights that physicians need to approach monitoring of OSD from several angles to ensure that signs of discomfort or damage are not being "normalized" by the patient.

The faculty identified complaints of redness, itchiness, and burning sensation as the most common complaints in routine practice. Dr. Barbour stressed that these symptoms may lead to a significant burden. "Patients can have serious social concerns when BAK-containing medications cause red and itchy eyes, or exacerbate OSD," he explained. "People who feel self-conscious are less likely to adhere to their treatment plan."

Worsening of OSD symptoms has been linked to anxiety and depression, and this change in patient outlook can also reduce adherence to treatment.[45]

Patients for whom BAK-containing medication is the only offered or affordable option for managing their glaucoma face a difficult journey (Figure 5). By persevering with BAK-containing treatment over a long period of time, the ocular surface becomes damaged, medical therapy loses some efficacy with inflammation, and surgery is both more likely to be needed and more likely to fail. By discontinuing treatment, IOP becomes unmanaged and may progress to the point of a requiring surgery—likely what the patient is often trying to avoid by using eye drops.

How Can Preservative-Free Medications Affect Patient Satisfaction?

There is an emerging evidence base showing that improving the signs and symptoms of OSD can encourage better adherence to treatment, and switching to preservative-free formulations can drive this improvement.[23,44,48,49]

The expert panel reached consensus on the positive effect offering BAK-free or preservative-free glaucoma medication has on both patient satisfaction (Figure 6) and treatment adherence (Figure 7). Dr. Van Tassel noted, "There isn't always an 'ah-ha!' moment when moving to preservative-free medication—it can take time for patients to notice the increase in comfort, but it is almost always beneficial to the patient." This is often the case when a patient is prescribed multiple eye drops, and one of these is being changed to a preservative-free formulation to help reduce overall toxicity burden.

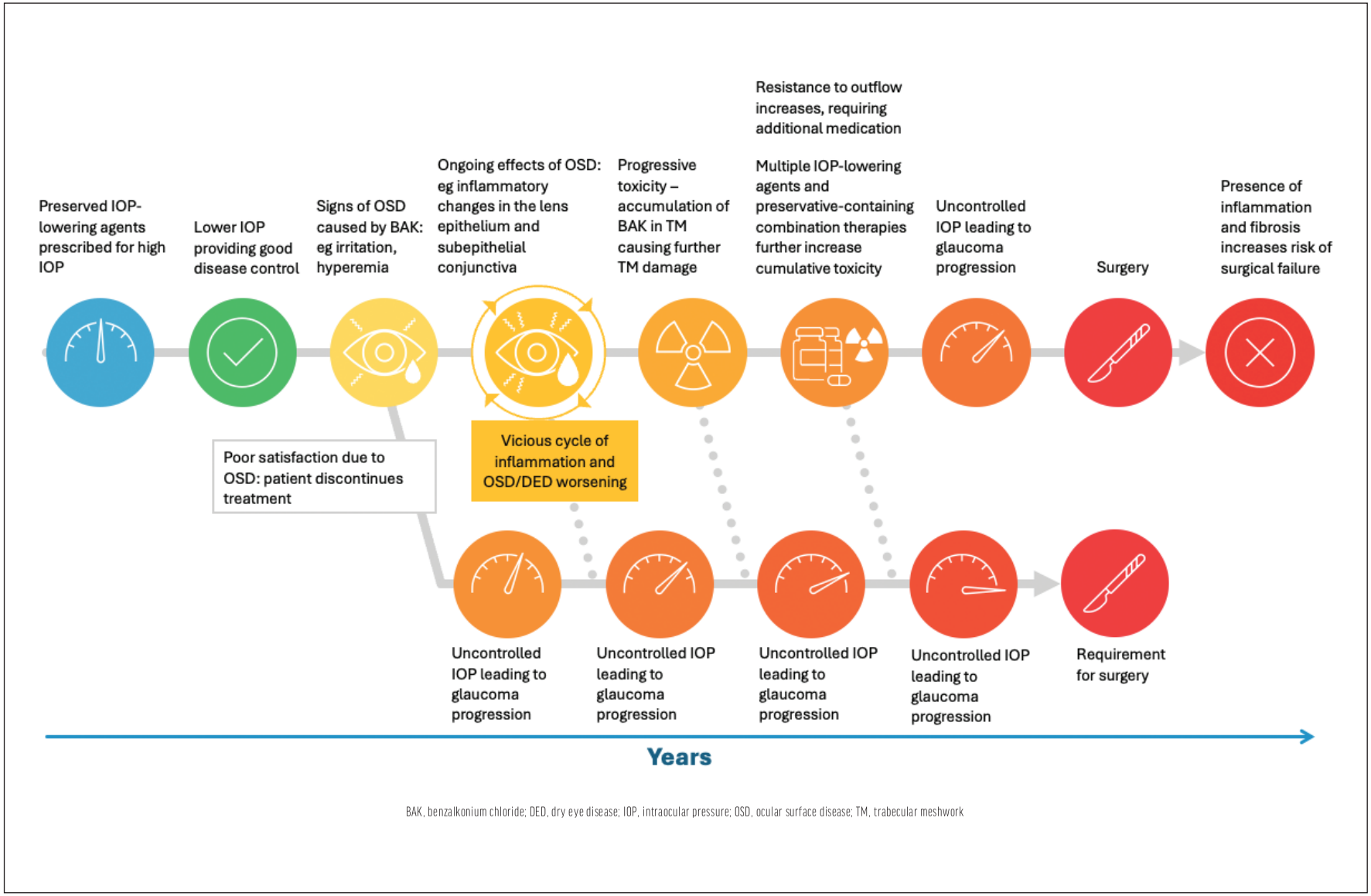
Prof. Kolko added, "In my clinical experience, patients are more satisfied when they receive preservative-free medicines. Although there is a lack of research to systematically confirm that preservatives are toxic to the ocular surface, I think we should ask ourselves why potentially toxic substances are added to eye drops for chronic use when they are not necessary."

Dr. Radcliffe agreed, "In my experience, moving patients to preservative-free formulations does help with compliance and has the benefit of helping the 'long game' by reducing OSD damage over time. Increased satisfaction also helps improve the patient–physician relationship."

Patient satisfaction can affect the physician. "Physicians are trying to meet patient expectations," said Dr. Panarelli. "And these expectations are very high in ophthalmology. Dissatisfaction is a cause of concern for the physician—they are falling short of patient expectations—and a dissatisfied patient will have more frequent clinic visits, which is suboptimal for both parties. Increasing satisfaction is important for the patient and physician."

Preparing the Patient for Preservative-Free Glaucoma Medication

The expert panel agreed unanimously on the key aspect of successfully introducing preservative-free medication into a glaucoma treatment regimen: communication.



BAK, benzalkonium chloride; DED, dry eye disease; IOP, intraocular pressure; OSD, ocular surface disease; TM, trabecular meshwork

Figure 5. Patients who are dissatisfied with their treatment may discontinue it, leaving IOP unmanaged; however, if they remain on BAK-containing treatment their OSD may become progressively damaged and lead to long-term loss of efficacy or surgical failure.

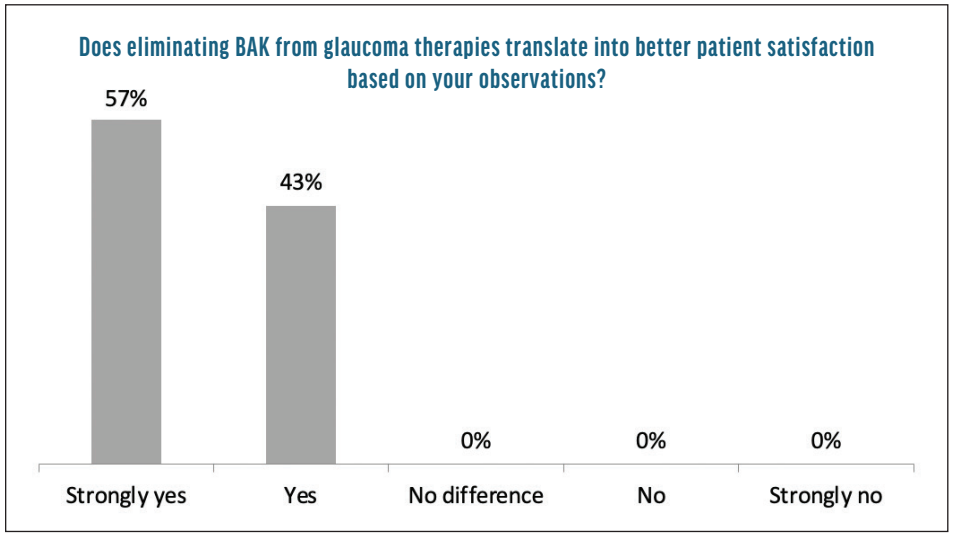


Figure 6. The faculty unanimously agreed that preservative-free medication is associated with greater patient satisfaction than BAK-containing options.
BAK, benzalkonium chloride

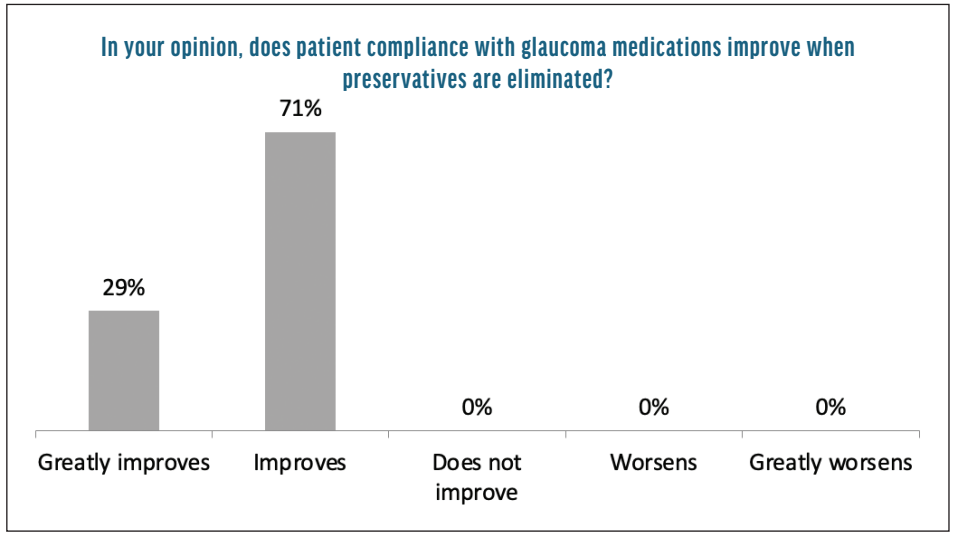


Figure 7. The expert panel judged that increases in satisfaction and tolerability with preservative-free glaucoma medication translate into increased adherence to treatment.

Discussions with the patient should focus on:

- Glaucoma is a lifetime condition so treatment needs to be tailored to provide benefit over the long-term.
- Preservative-free medication is used to keep the ocular surface as healthy as possible for as long as possible, helping glaucoma medication be effective and leaving other treatment options open, as needed.
- Because glaucoma is symptom-free in the earlier stages, patients should be provided with a clear explanation as to why medication with noticeable side effects is being prescribed. It is important that patients don't think the eye drops are "making things worse." Preservative-free options are being prescribed to make treatment for glaucoma as tolerable as possible.

Drs. Radcliffe and Barbour noted that occasionally patients won't believe that their OSD symptoms are related to a BAK-containing medication, especially if they have been taking that therapy for a long time. Education around the progression of OSD and the rationale for moving to preservative-free medication can be especially valuable for these patients.

The faculty found that the most common points of resistance to changing to a preservative-free glaucoma medication from a patient's perspective, besides cost (where applicable), related to handling characteristics and convenience. For those patients who are used to a large and easy-to-handle bottle, or who relied on multidose bottles, the change to individual vials or short-life bottles could be inconvenient or unwelcome. Some patients may also be concerned with the increase of single-use plastics associated with preservative-free treatment. The final decision on suitability of a treatment should be reached following an informed discussion with the patient.

GLOBAL PERCEPTIONS AND SHIFTS TOWARD USING PRESERVATIVE-FREE THERAPIES

There has been an increasing volume of literature on this topic in recent years, exemplified by a +50% peak in PubMed returns in 2021 and 2022 over the average for the term "preservative-free glaucoma." Currently, there is meaningful and frequent advocacy of the benefits of a transition toward preservative-free glaucoma treatment.[1,16,44,50]

How Can Preservatives Be Eliminated From Glaucoma Medication?

The expert panel considered the ideal route to preservative elimination in glaucoma medication, and provided three options: removal by compounding pharmacy, by filtration in the bottle, and during the manufacturing process.

Only the US-based physicians were familiar with compounding pharmacy—effectively "formulations to order" that are prepared in the pharmacy. With concerns over safety, standardization of

"In my experience, adherence to preservative-free medication is many times higher than patients report with BAK-containing eye drops."

– Monique M. Barbour, MD

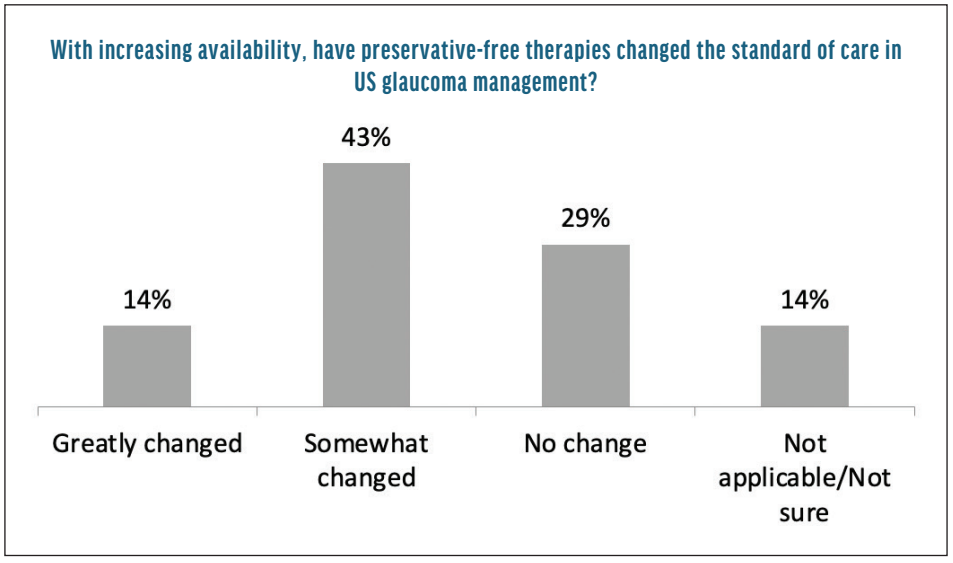


Figure 8. The US-based faculty observed a mixed impact on practice with the availability of preservative-free glaucoma medication.

compounds and process, and a lack of any supportive data, the consensus was that this should not be the sole method for preservative elimination. The faculty believed that in-bottle filtration of BAK, so that the solution could be preserved in a multidose bottle but with the preservative removed at the point of instillation,[51,52] could offer advantages to patients who preferred or required a large bottle. There was also collective interest in the concept of "nano drops" that limit the overall volume of medication being absorbed at the ocular surface; however, there was a preference to wait until more clinical data are available. The faculty also noted that intracameral, sustained-release bimatoprost could be a promising option for some patients,[53] but that it would be suitable for a much smaller population than preservative-free eye drops, and they expressed some concerns with implant procedure risks and resource requirements.

The expert panel reached consensus agreement that preservatives should be eliminated from topical medications during the production process by the pharmaceutical companies, and that the formulations should be supported by robust clinical trial data and real-world evidence.

Changes in Practice With Preservative-Containing Glaucoma Medication: Europe

European health care systems have integrated preservative-free glaucoma medications into routine practice. Although there remains a degree of intercountry variability, published data on prescribing trends support a persistently increasing uptake. For example, in the UK, preservative-free glaucoma eye drops made up 13.6% of total prescription spend in 2018, up from 1.7% of total prescription spend in 2009;[54] in Spain "preservative-free eye drops have displaced preservative-containing topical treatments in all pharmacological groups."[55]

Prof. Kolko and Dr. Hommer, the European members of the faculty, observed that the prescription of preservative-free medication was time-consuming for the physician, with several justification barriers to overcome. "If a drug is in a green box [in the prescription system], the doctor can prescribe it without any limitation… very easy and with no controls," Dr. Hommer, who practices in Austria, explained. "If it's in the yellow box, there are two options: in the bright yellow one, the doctor has to simply document why he's prescribing the brand; in the dark yellow one, he has to send internet-based documentation to

"I don't think any physician would be adverse to using preservative-free glaucoma medication if access was not time-consuming for their practices, and costs were reasonable for their patients."

– Jason Bacharach, MD

support his decision and an authority at the insurance provider has to agree with it. This is time-consuming. Preservative-containing medication sits in the bright yellow box, preservative-free in the dark yellow." It was also noted that receiving authorization for the preservative-free option can take hours or sometimes days, making it inconvenient for the patient.

The process to prescribe preservative-free medication should be simplified. "Make it easy to access preservative-free eye drops," said Prof. Kolko. "If you have to fill in a lot of paperwork to actually get the eye drops, that's a hassle, and we are already under time pressure as physicians."

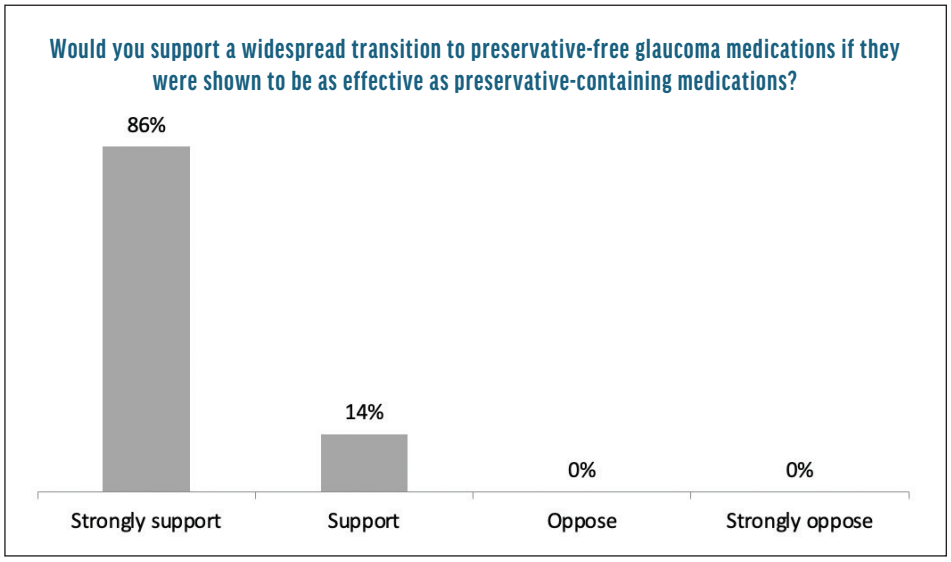


Figure 9. The faculty strongly supported a shift to using preservative-free medication when there was no compromise on clinical efficacy.

Changes in Practice With Preservative-Containing Glaucoma Medication: USA

The US-based faculty noted that the availability of preservative-free glaucoma medication has had a mixed and relatively limited impact on routine prescribing as standard of care (Figure 8). Several barriers to prescription of preservative-free eye drops were identified:

- A lack of preservative-free choices (molecules)
- A lack of supply for preservative-free options
- A significant cost barrier versus BAK-containing medication
- Insurance requiring that preservative-free medication be the "last resort;" patients must be prescribed other, less expensive medications first (and demonstrate this to payors)
- The complexities of knowing which preservative-free options are available to which patient, based on different insurance plans with differing qualification criteria

"Among the options that exist, there are cost and access issues and logistical issues," summarized Dr. Van Tassel. "There are certainly more patients in my practice who could be on preservative-free regimens, but it is extremely labor intensive for my staff to figure out what molecules they need to try first, and who needs prior authorization, and who needs additional documentation…you would need multiple full-time equivalent staff to make it work. So even where there is an interest in using preservative-free medication, it's harder to do than to prescribe a generic."

SUMMARY

The faculty reached consensus on all questions related to the benefits of using preservative-free medication to optimize glaucoma treatment. The toxicities of BAK and its contribution to a deteriorating OSD over a period of long-term treatment were reiterated, and the expert panel agreed that patient satisfaction and adherence can both be improved with a switch to preservative-free medication. These advantages can be gained incrementally by reducing the cumulative toxicity of BAK in a polypharmacy regimen by selecting a preservative-free alternative for at least one of the medications; the advantages can be maximized by initiating patients on preservative-free options from the start of their glaucoma management journey.

The expert panel recognized that this switch is not simple for physicians in routine practice to make, with cost and access barriers being the most difficult to overcome. "It would be ideal if the default was the use of preservative-free rather than preservative-containing," Dr. Barbour noted. To make this possible, Prof. Kolko concluded that health care systems need to "make it easy for the physician to help the patient."

In summary comments, the faculty were strongly supportive of a transition to the use of preservative-free glaucoma medication (Figure 9). ■

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Global Consensus Statement on the Impact of Ophthalmic Preservatives

Release Date: June 2024
Expiration Date: July 2025

INSTRUCTIONS FOR 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, go to https://evolvemeded.com/course/2339-supp. If you experience problems with the online test, email us at info@evolvemeded.com. *NOTE: Certificates are issued electronically.*

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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 educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
____ >50

Region
___ Midwest
___ Northeast
___ Northwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	**Agree**	**Neutral**	**Disagree**
Define the impact of therapy containing BAK on the ocular surface in patients with glaucoma	_____	_____	_____
Identify the prevalence of BAK-related adverse events among glaucoma patients	_____	_____	_____
Examine how preservative-associated adverse effects can affect surgical or medical outcomes in disease management	_____	_____	_____
Consider the influence of preservatives on patient satisfaction and adherence to medication over time	_____	_____	_____
Review the perceptions of preservatives on a global scale and discuss the challenges and benefits in implementing preservative-free therapies in glaucoma	_____	_____	_____

POSTTEST QUESTIONS

Please complete at the conclusion of the program.

1. Based on this activity, please rate your confidence in your ability to discuss the impact of ophthalmic preservatives on the ocular surface in patients with glaucoma (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. Which preservative is commonly used in topical glaucoma medications due to its antimicrobial properties and cost-effectiveness?

A. Chlorhexidine
B. Ethanol
C. Benzalkonium chloride (BAK)
D. Sorbic acid

3. What long-term impact has been most associated with the use of BAK in glaucoma medications

A. Improvement in visual acuity
B. Reduction in intraocular pressure
C. Development of ocular surface disease
D. Decrease in dry eye symptoms

4. Which of the following is NOT a potential benefit of using preservative-free glaucoma medications?

A. Reduced patient compliance
B. Lower risk of ocular surface disease
C. Fewer allergic reactions
D. Decreased discomfort

5. What is the primary function of the trabecular meshwork?

A. Produces the aqueous humor
B. Drains the aqueous humor
C. Focuses light onto the retina
D. Protects the eye from UV light

6. What aspect of ocular surgery does the use of BAK potentially complicate according to the expert panel?

A. The surgical incision healing
B. The postoperative medication regimen
C. The effectiveness of anesthesia
D. Recovery from surgery

7. According to the discussions, why might younger glaucoma patients benefit more from preservative-free medications?

A. They experience faster progression of glaucoma
B. They are less likely to comply with treatment
C. They require treatment over a longer period
D. They have fewer symptoms of glaucoma

8. What clinical strategy is recommended for managing patients with ocular surface disease exacerbated by preservatives?

A. Increase the concentration of BAK in medications
B. Switch to preservative-free medications
C. Use medications with higher viscosity
D. Reduce the frequency of medication application

9. Which of the following is a noted effect of BAK on the ocular surface?

A. Enhancement of tear film stability
B. Reduction of tear evaporation
C. Induction of inflammatory response
D. Improvement of visual acuity

10. A 68-year-old woman with chronic open-angle glaucoma has been on a BAK-preserved IOP-lowering medication for several years. She presents with complaints of persistent eye redness, burning sensation, and fluctuating vision. She has a history of dry eye syndrome, exacerbated since starting her glaucoma medication. Considering her symptoms and medical history, which of the following actions is most appropriate to manage her condition?

A. Increase the dosage of her current BAK-preserved medication
B. Switch to a higher potency BAK-preserved medication
C. Replace her current medication with a preservative-free formulation
D. Advise the patient to use over-the-counter eye drops more frequently

11. A 72-year-old patient undergoing evaluation for glaucoma surgery has been using a BAK-preserved medication regimen. The presurgical assessment indicates significant ocular surface disease, which could compromise surgical outcomes. What preoperative adjustment should be considered to optimize the patient's ocular surface condition before undergoing surgery?

A. Temporarily increase the use of BAK-preserved eye drops to maximize IOP control before surgery
B. Introduce a short course of topical steroids to reduce inflammation
C. Transition to a preservative-free eye drop regimen and use artificial tears
D. No changes are necessary; proceed with the planned surgery

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this 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: _____High _____ Low _____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 nonpharmaceutical therapy _____
Change in diagnostic testing _____
Choice of treatment/management approach _____
Change in current practice for referral _____
Change in differential diagnosis _____
My practice has been reinforced _____
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
You would 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:

_____

_____

This information will help evaluate this activity; may we contact you by email in 3 months to inquire if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____

_____


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