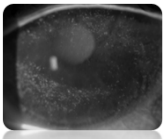


Preservatives & OSDs




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Overview

- Preservatives
 - Types & Toxicities
- Glaucoma
- Dry Eye
- Clinical take home points



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Clinical Setting - Glaucoma

- Long-term Rx
- Multiple Rx
- All preservatives disrupt ocular surface
- All preservatives exacerbate pre-existing OSD
- Preservative sensitivity/toxicity common
- Preservative allergy rare
- BAK in 80% Glc drops


Medication	Preservative
Xalatan	BAK 0.02%
Lumigan	BAK 0.02%
Azopt	BAK 0.01%
Timoptic	BAK 0.01%
Trusopt	BAK 0.0075%
Cosopt	BAK 0.0075%
Combigan	BAK 0.005%
Travatan Z	SofZia
Alphagan P	Purite

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Benzalkonium chloride (BAK)

- Since 1940s
- Effective & cheap, regulatory requirements since '70s
- Detergent - lysing cell membranes & tight junctions



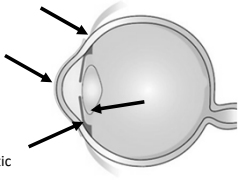
Preservative	Mechanism	Advantages	Disadvantages	Medications
BAK	Detergent	Excellent broad antimicrobial efficacy, weakens corneal epithelial tight junctions to facilitate drug's entry	Corneal epithelial breakdown and tear film instability	Azopt, Lumigan, Timoptic, Xalatan
Purite	Oxidative stress	Less conjunctival inflammation and corneal toxicity than BAK	Mild cytotoxicity still present	Alphagan P

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BAK Toxicity

- Conjunctiva
 - Inflammation & pro-apoptotic effects
- Corneal epith
- Trabecular meshwork
 - Reduced TM cell numbers, growth, pro-apoptotic
- Lens epithelial cells
 - BAK strongly induces inflam' mediators in lens epith cells
 - Higher rates of cataracts in pts on Glc Rx (Blue Mountains Eye Study)



Pellinen, et al. The cytotoxic effects of preserved and preservative-free prostaglandin analogs on human corneal and conjunctival epithelium in vitro and the distribution of benzalkonium chloride homologs in ocular surface tissues in vivo. *Curr Eye Res* 2012;37:545-54.

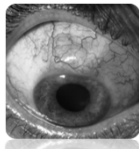
Liang, et al. Toxicological evaluation of preservative containing and preservative-free topical prostaglandin analogues on a three-dimensional reconstituted corneal epithelium system. *Br J Ophthalmol* 2011;95:869-75.

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BAK – Clinical Evidence

- Detergent properties
 - Disrupts lipid layer – evaporative DED
 - Reduced TBUT
 - Reduced goblet cell numbers & mucin production
- No evidence from RTCs that BAK causes OSD in pts with healthy OS
 - Survey of 2500 NZ patients – high level of satisfaction with BAK Glc drops
- Trabeculectomy failure
 - Higher failure rate with long-term multiple BAK Glc drops
 - Helpful to withdraw Glc Rx 4wks preop, and Rx FML




Kerr NM, Patel HV, Chew SS, et al. Patient satisfaction with topical ocular hypotensives. *Clin Exp Ophthalmol* 2013;41:27-35.

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Glaucoma drops – Alternatives to BAK

- Purite in Alphagan-P
- PF Glc drops in NZ
 - Lumigan PF (\$40-60/btl)
 - Ganfort PF (timolol/bimatoprost)
 - Pilocarpine MINIM
 - Many others available overseas...
- No evidence that PF Glc drops any less effective than BAK
- Novel bottle design for multidose PF drops
 - <https://www.eyekarekitch.com/>



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Dry Eye Drops

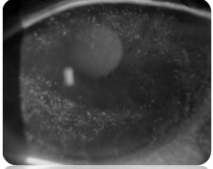
- Polyquad
 - Detergent
 - Large molecule
 - Low toxicity
 - Similar to hydrogen peroxide CL solutions
- Purite
 - Oxidising - light
- Sodium perborate
 - Oxidising – tear catalase
- Preservative Free
 - Unit doses

Supplier	Name	Preservative	Concentration (where stated)
Alcon	Systeme Original	Polyquad	0.001%
	Systeme Ultra	Polyquad	0.001%
	Systeme Ultra Hydration	Polyquad	0.001%
	Systeme Balance	Polyquad	0.001%
	Systeme Complete	Polyquad	0.001%
	Systeme Gel Drops	Polyquad	0.001%
	Systeme Lubricant Eye Gel	Sodium perborate	
	GenTeal	Carbopol/butylam parborate	
	Tears Naturalite II	Polyquad	0.001%
	Tears Naturalite Forte	Polyquad	0.001%
Allergan	Purite (stabilized aerythron complex)		
	Ruthven Opive	Purite (stabilized aerythron complex)	
	Ruthven Opive Gel Drops	Purite (stabilized aerythron complex)	
	Ruthven Opive Advanced	Purite (stabilized aerythron complex)	
	Ruthven Tears	Purite (stabilized aerythron complex)	
Ruthven Contacts			
	Ruthven Lignell	Purite (stabilized aerythron complex)	
Bausch + Lomb	Soothe XR Essential Eye Drops	Polyquad	
	Soothe Hydration Lubricant Eye Drops	Ethicon disodium Sorbic acid	0.1%
			0.1%
Focus Laboratories	FreeKase Lubricant Eye Drops	Polyquaternium-42	
Johnson and Johnson Vision	Blink Tears Lubricating Eye Drops	Octapur (stabilized aerythron complex)	
	Blink Gel Tears Lubricating Eye Drops	Octapur (stabilized aerythron complex)	
Thera Tears	Tears Dry Eye Therapy	Dequert (sodium perborate)	
	Dry Eye Therapy	Dequert (sodium perborate)	

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Clinical Advice - summary

- Listen & Look
- DED symptoms and/or signs?
- Glaucoma
 - Most without OSD cope well with 1-2 BAK drops
 - Consider Alphagan-P (Purite)
 - High cost of PF (27% to 1,600% higher than same preserved drug)
 - Consider non-drop Mx
 - SLT or MIGS
- Dry Eye Disease
 - Treat the cause...!!!
 - MGD, inflammation, ATD, exposure, etc...
 - Don't just supplement



Thank You

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