Let's talk about...

PROSTAGLANDIN-ASSOCIATED PERIORBITOPATHY SYNDROME

A practical guidebook for you

Click on the buttons to the right to learn more about PAPS

HCP Patient

Select the HCP or patient button to toggle between information that is relevant to you and patient-directed information

Prostaglandin analogues (PGAs) are a common choice for glaucoma control because of their effective and convenient nature. However, they may be associated with some side effects – defined under the constellation of PAPS. Most of the time, these side effects are well tolerated or not noticed, but it remains important to be aware of them in order to weigh up the benefits and risks of any treatment for glaucoma.
This guidebook will explore PAPS in more detail and provide expert insights to facilitate doctor-patient discussions and provide optimal care.

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Santen
APGS Asia-Pacific Glaucoma Society

PAPS refers to a constellation of adverse events occurring around the eye, typically associated with topical PGAs[1–3]

HCP Patient

- PAPS is common in PGA-treated patients with glaucoma and is markedly more frequent and severe in patients treated with bimatoprost compared with latanoprost and travoprost.[4]
- PGAs have been reported to induce periocular changes and cause PAPS in >40% of patients treated for ≥3 months. This increases over time to >60% of patients after just 6 months.[5,6]
- The development of PAPS has even been identified as early as within 1 month of PGA initiation.[4]
- Older patients (>60 years of age) are up to three times more likely to develop signs of PAPS.[6*]

The 10 signs of PAPS[1–3,7–10]

1. Pigmentation of the periorbital skin or the eyelids
2. Ciliary hypertrichosis
3. Deepening of the upper eyelid sulcus (DUES)
4. Flattening of the lower eyelid bags (FLEB)
5. Ptosis
6. Mild enophthalmos
7. Orbital fat atrophy
8. Tight orbit and eyelids
9. Inferior scleral show
10. Involution of dermatochalasis

What do these look like?

It is estimated that less than one-third of patients remain on their initial treatment after 12 months. Non-adherence can lead to disease progression and increased economic burden.[11]
It is important to follow up with your patients receiving PGAs as one of the factors that impacts treatment adherence is actual or perceived side effects to medications.[11,12]

PAPS is a collection of side effects that occur around the eye, typically following the use of glaucoma eye drops called prostaglandin analogues (PGAs)[1–3]

HCP Patient

The 10 signs of PAPS[1–3,7–10]

1. Darkening of the skin around the eye or upper and lower eyelids
2. Excessive eyelash growth
3. Deepening of the upper eyelid 'sulcus' – or crease (aka 'DUES')
4. Flattening of the lower eyelid bags (aka 'FLEB')
5. Drooping of the upper eyelid
6. Appearance of a mildly sunken or deep set eyeball
7. Fat loss around the eye
8. Eyelids pressing firmly against the eye (aka 'tight orbit')
9. Exaggerated exposure of the lower white outer layer of the eyeball (sclera)
10. Loose and redundant eyelid that may turn inward

What do these look like?

What are PGAs?

PGAs are widely used across the world and are a common first-choice treatment for glaucoma – you may be prescribed bimatoprost, latanoprost, tafluprost, or travoprost. They are chosen because of their effectiveness in lowering pressure in the eye and their easy once-a-day regimens.[5,7]

Please talk to your eye doctor before stopping your medication(s) if you are considering it.

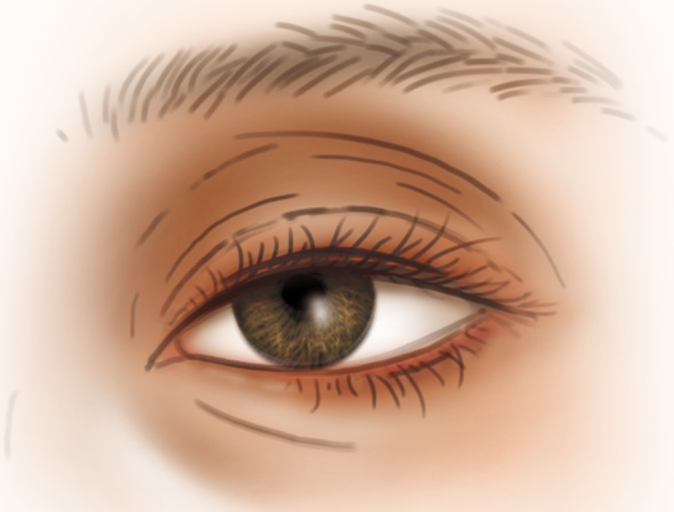
Recognizing the signs and symptoms of PAPS

HCP Patient

- The incidence of some PAPS signs and symptoms (such as DUES) will differ depending on the PGA used.[1,2,4]
  - For example, approximately 60% of individuals switching from latanoprost to bimatoprost show signs of DUES after 3–6 months, with as many as 44% showing signs as early as 1 month following the switch.[7]
  - Whereas, switching back from bimatoprost to latanoprost has been associated with improvements in PAPS.[4]

Click on any of the signs of PAPS below to discover more

1. Darkening of the skin around the eye or upper and lower eyelids (pigmentation of the periorbital skin or the eyelids)[1,7,8]
2. Excessive eyelash growth (ciliary hypertrichosis)[1,7,8]
3. Deepening of the upper eyelid 'sulcus' – or crease (aka DUES)[1–3]
4. Flattening of the lower eyelid bags (aka FLEB)[1,2]



5. Drooping of the upper eyelid (ptosis)[1–3,9]
6. Appearance of a mildly sunken or deep set eyeball (mild enophthalmos)[1–3,9]
7. Fat loss around the eye (orbital fat atrophy)[1–3,9]
8. Eyelids pressing firmly against the eye (tight orbit)[1,2]

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Recognizing the signs and symptoms of PAPS

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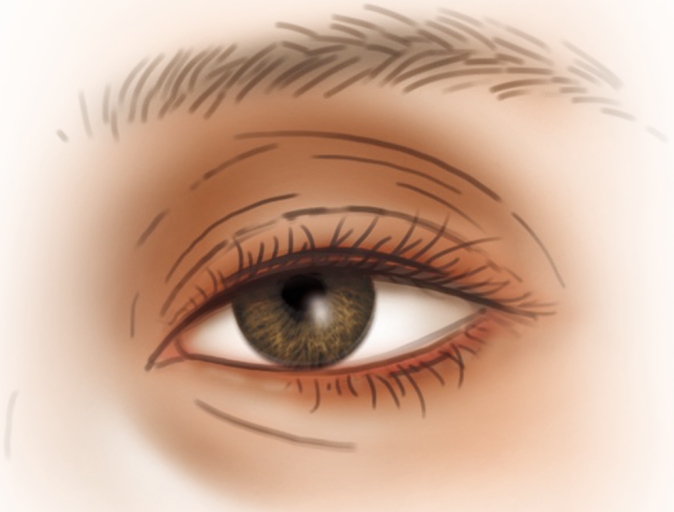

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Pigmentation of the periorbital skin or the eyelid

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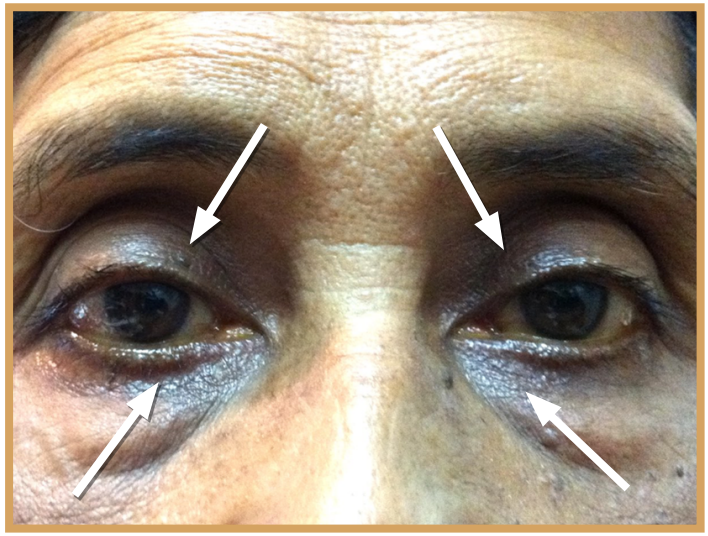
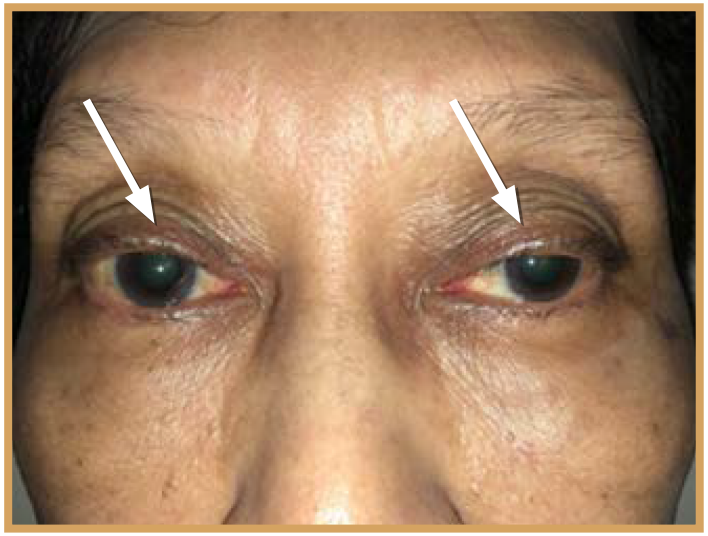
- Pigmentation of the periorbital skin or the eyelid can occur with the use of PGAs.[1,8]
- Although pigmentation is **not a common cosmetic complication** associated with the short-term use of PGAs,[13] it may be a potentially unwanted side effect. It is known that the **prolonged use of PGAs is associated with longer time to resolution**.[8]



After PGA treatment

Image courtesy of Dr Weerawat Kiddee



After PGA treatment

Image courtesy of Dr Yanin Suwan

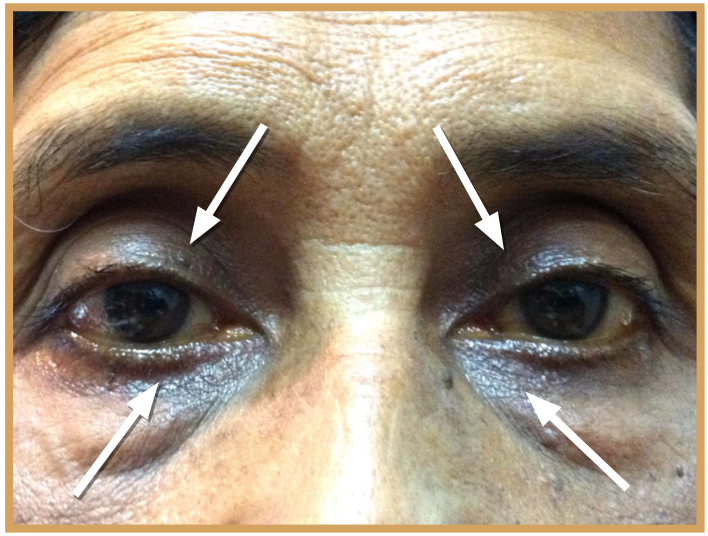
Discontinuing the causative PGA treatment, or switching to another anti-glaucoma medication (see the 'Glaucoma treatment' section), **may reverse or improve periorbital pigmentation**.[8,13]

If appropriate, you could advise your patients to take care when using tissue paper to clean the periocular area and eyelids as this can cause pigmentation and lead to what is commonly known as **'panda eyes'**.[14]

Darkening of the skin around the eye or upper and lower eyelids (pigmentation of the periorbital skin or the eyelids)

HCP Patient

- **Pigmentation is the darkening of an area of skin**. Pigmentation of the eyelids or skin around the eye can occur with the use of PGAs.[1,8]
- Although pigmentation is not a common cosmetic complication associated with the short-term use of PGAs,[13] it may be a potentially unwanted side effect.



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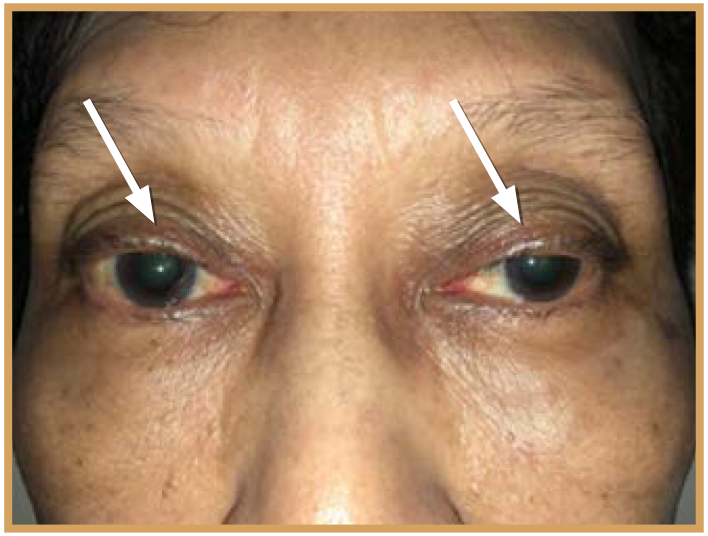


After PGA treatment

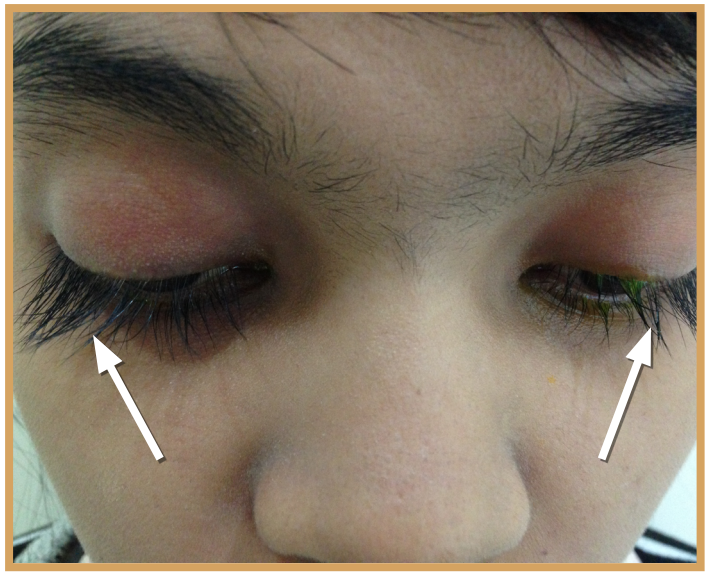
Image courtesy of Dr Yanin Suwan

Take care when using tissue paper to clean around your eye as this could further spread the eye drops on your eyelids or around your eyes, causing the skin to darken, leading to what is known as **'panda eyes'**.[14]

Ciliary hypertrichosis

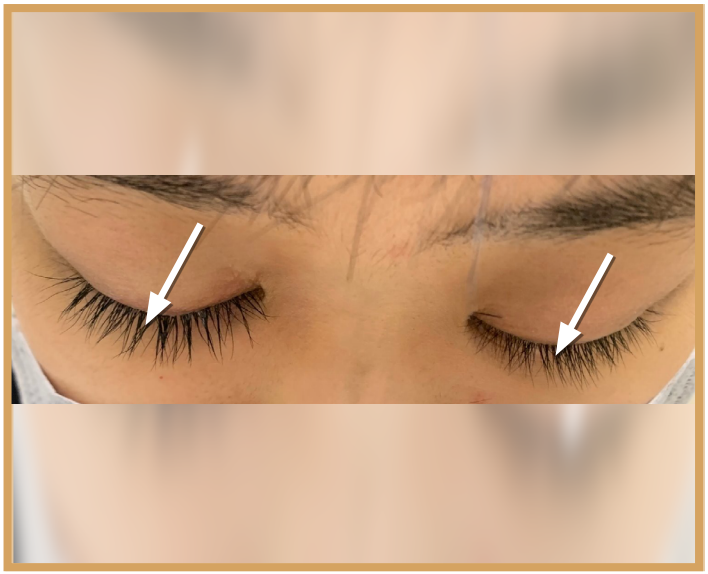
HCP Patient

- PGAs can cause ciliary hypertrichosis and growth of periocular hair,[1,7] which can manifest as the **excessive growth of eyelashes and ancillary hairs around the eyelids**.[15]
- Exposure to PGAs promotes hair cell growth, inducing a growth phase in resting follicles and hypertrophic follicle changes. These changes result in **increased length and thickness of lashes**, **additional lash rows**, and/or **conversion of vellus** (soft, short, unpigmented) **to terminal hairs** (coarse, longer, pigmented) in canthal areas.[15]
- It is important to note that the **effects of PGAs on eyelash growth rate and the hair growth cycle may be long-lasting**.[16]



After PGA treatment

Image courtesy of Dr Yanin Suwan



After PGA treatment

Image courtesy of Dr Chien-Chia Su

Patients may not raise concern on this issue as it may be seen to have **cosmetic benefit**.

Excessive eyelash growth (ciliary hypertrichosis)

HCP Patient

- PGAs can cause **excessive eyelash growth**, also known as 'ciliary hypertrichosis',[1,7] where **eyelashes may look thicker and longer, and additional rows of lashes** may also grow.[15]
- There may also be a change from soft, short, unpigmented (vellus) hair to coarse, longer, pigmented (terminal) hair.[15]
- The effects of PGAs on eyelash growth rate and the hair growth cycle may be long-lasting.[16]

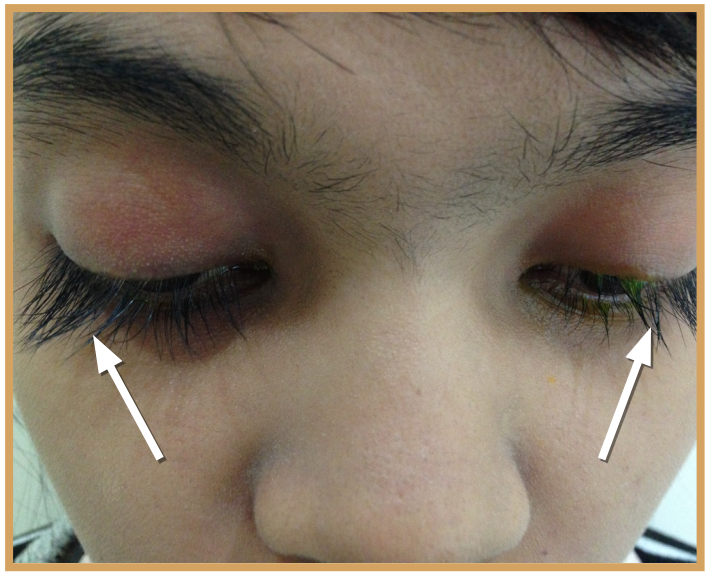


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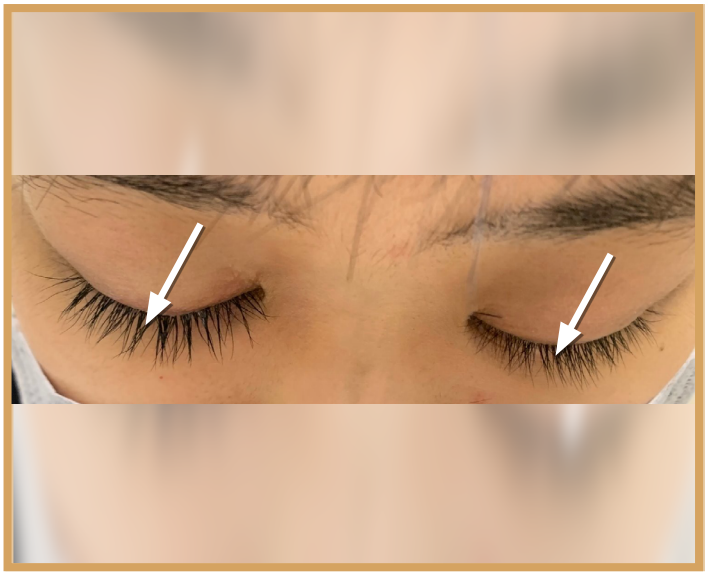
Image courtesy of Dr Yanin Suwan



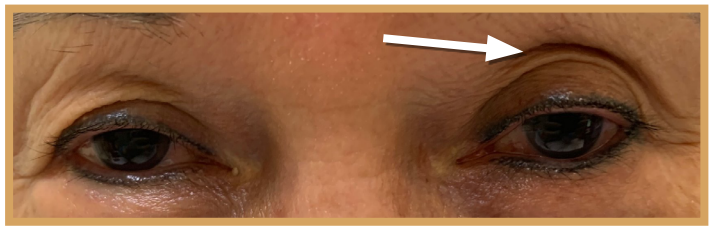
After PGA treatment

Image courtesy of Dr Chien-Chia Su

Deepening of the upper eyelid sulcus (DUES)

HCP Patient

- DUES is the most common and prominent feature of PAPS, occurring in **up to 60% of individuals after 6 months** of treatment with PGAs, particularly those treated with bimatoprost and travoprost.[1,17,18]
- It is likely caused by orbital fat atrophy; PGAs are known to inhibit the formation of adipocytes.[19] Orbital fat atrophy is considered to be the main cause of the anatomical changes observed in PAPS, including DUES.[2]



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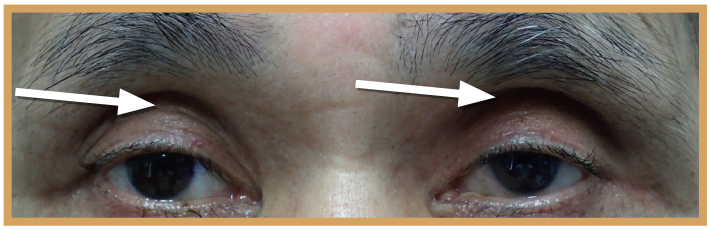

After PGA treatment

Image courtesy of Prof. Makoto Aihara

After PGA treatment

Image courtesy of Dr Grace D. Grozman

DUES, often associated with 'sunken eyes', can be a major cosmetic problem for patients (especially those check unilateral glaucoma) and could **decrease compliance to eye-drop medications**.[1]

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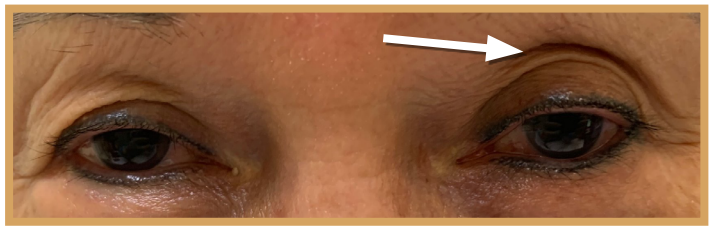
Deepening of the upper eyelid 'sulcus' – or crease (aka DUES)

HCP Patient

- DUES is the most common and prominent feature of PAPS. It occurs in up to 60% of individuals after 6 months of treatment with PGAs.[1,17]
- It is likely caused by the absence of fatty tissue around the eye; PGAs are known to prevent the formation of fat cells.[18]
- **The loss of fatty tissue around the eye adds to the 'sunken' appearance**.[10]



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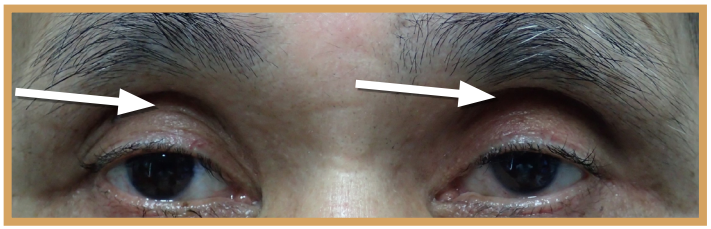


After PGA treatment

Image courtesy of Prof. Makoto Aihara

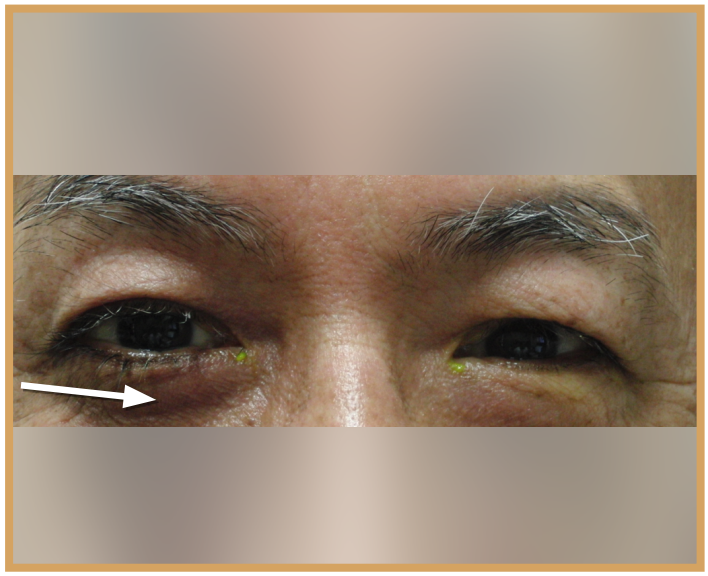
After PGA treatment

Image courtesy of Dr Grace D. Grozman

Flattening of the lower eyelid bags (FLEB)

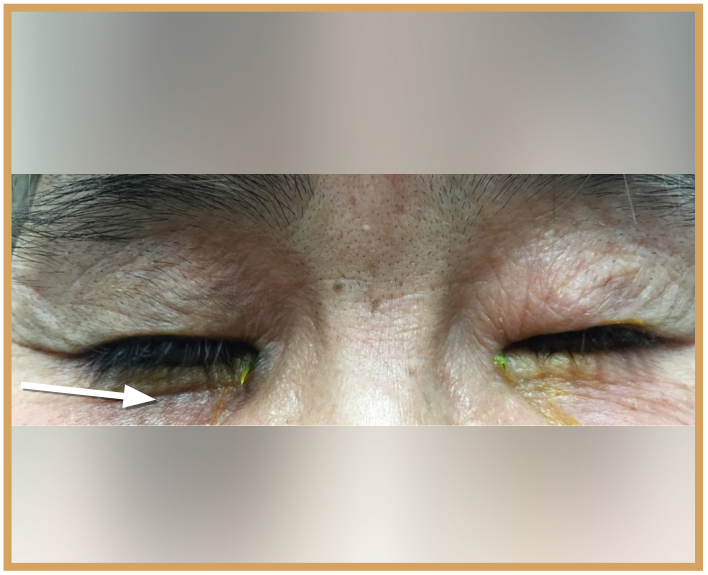
HCP Patient

- FLEB is a well recognized, but often **under-reported adverse event associated with PGA treatment**; this is because it can be seen as a **'positive' cosmetic sign in PAPS**.[1,16]
- Research shows that neither the loss of dermatochalasis or lower lid steatoblepharon (FLEB) have been found to be significantly associated with latanoprost. However, a higher incidence of these have been reported with bimatoprost and travoprost.[1]



After PGA treatment
(right eye; the left eye underwent trabeculectomy)

Image courtesy of Prof. Aihara



After PGA treatment
(right eye; the left eye underwent trabeculectomy)

Image courtesy of Prof. Aihara

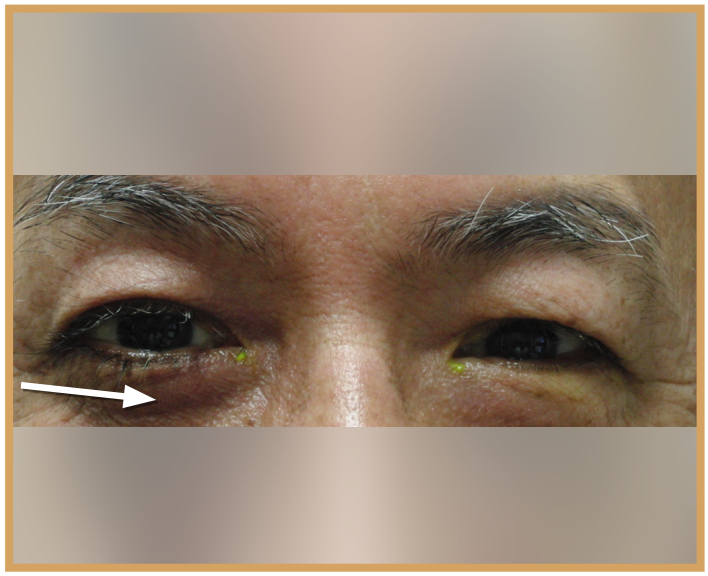
Switching treatment can offer benefits in reversing the signs of PAPS and result in **improvements in FLEB within 3 months**.[16]

Patients may not raise concern on this issue as it may be seen to have **cosmetic benefit**.

Flattening of the lower eyelid bags (aka FLEB)

HCP Patient

- Flattening of the lower eyelid bags (also known as FLEB) is a well recognized, but often **under-reported side effect of PGA treatment**; this is because it can be seen as a 'positive' cosmetic sign in PAPS.[1,16]



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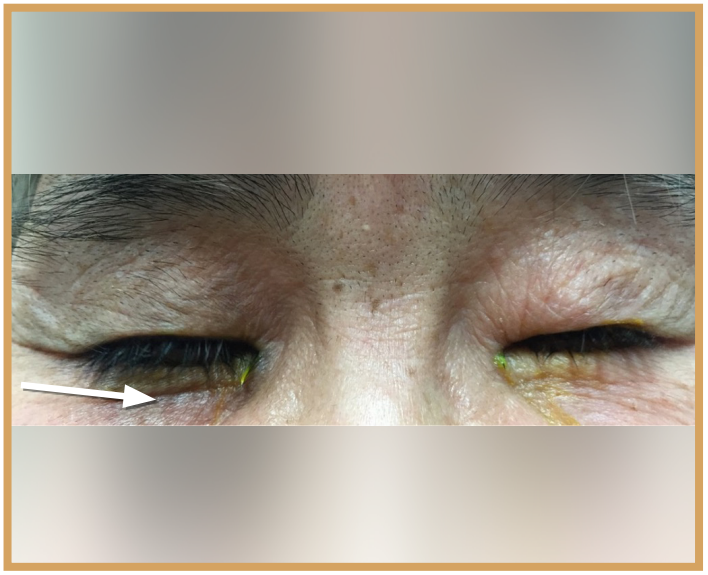
(right eye; the left eye underwent trabeculectomy)

Image courtesy of Prof. Aihara



After PGA treatment
(right eye; the left eye underwent trabeculectomy)

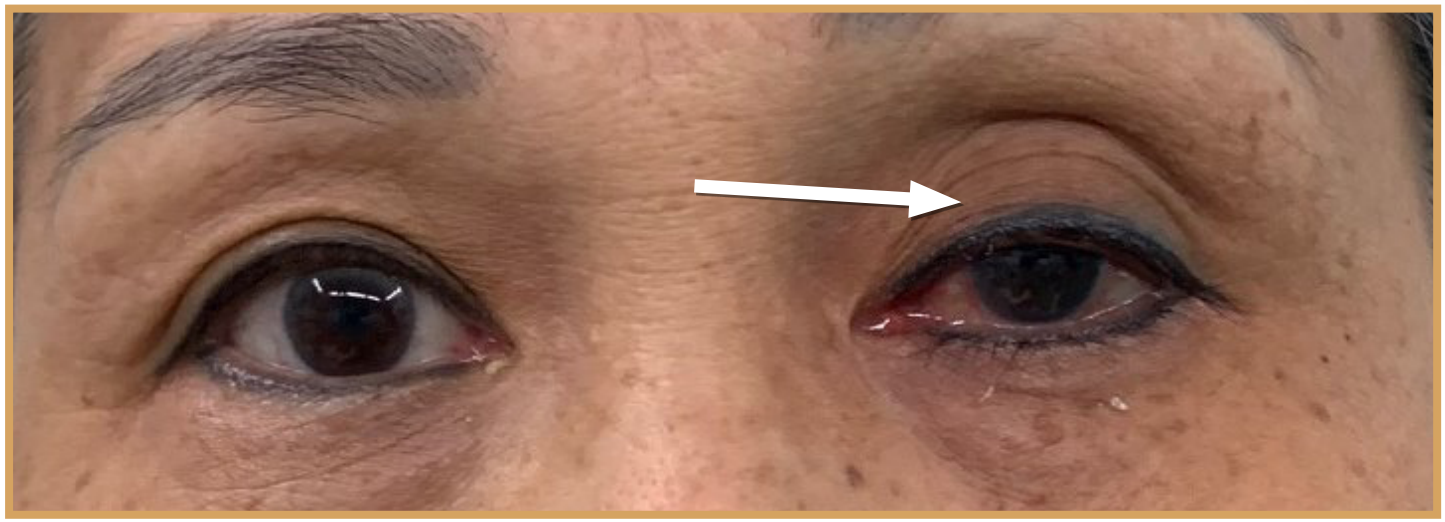
Image courtesy of Prof. Aihara

If you notice FLEB and other signs of PAPS, you may be asked to **switch treatment,** which can result in **FLEB improving within 3 months**.[16]

Ptosis

HCP Patient

- The use of PGAs can cause visually significant ptosis (also known as blepharoptosis), characterized by droopy eyelids.[3]
- The mechanism behind ptosis and dehiscence of the levator aponeurosis (or Müller muscle) in PGA users is unknown.[2,3] However, it has been hypothesized to be due to MMP activity or lid tightening.[3]
- While latanoprost use has been shown to produce the least amount of fat loss, compared with other PGAs, it is associated with ptosis.[3]



After PGA treatment

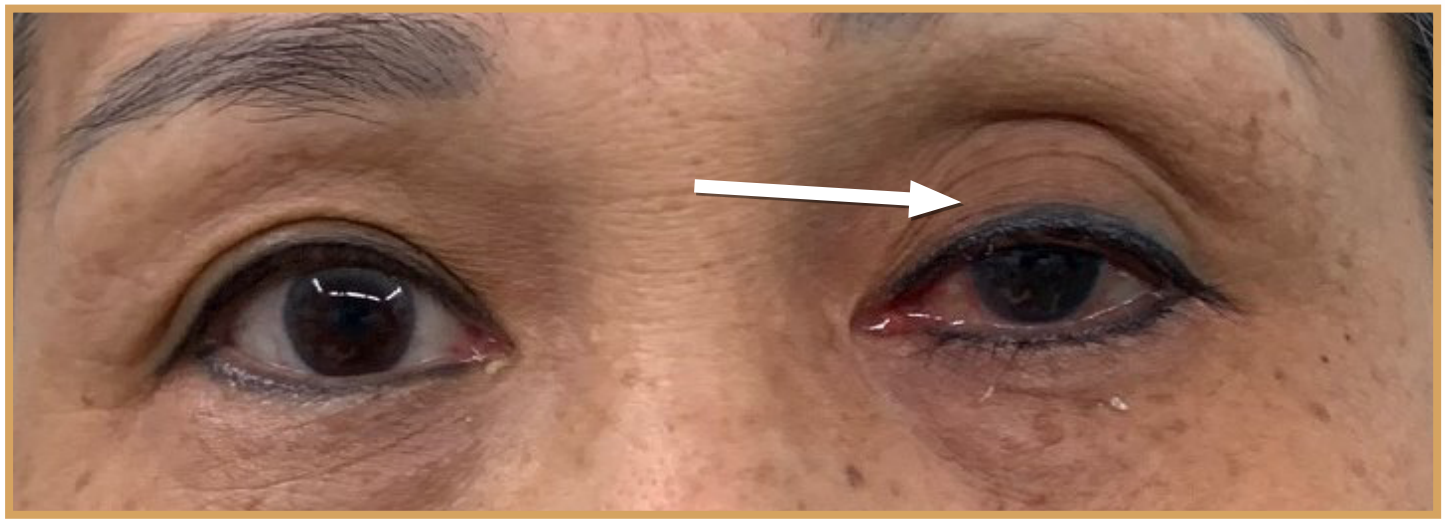
Image courtesy of Dr Chien-Chia Su

It is suspected that PGA-associated ptosis is not reversible. The risks of continued PGA use should be carefully weighed in patients with inferior visual field loss, especially as later development of ptosis could **compromise visual function.**[3]

Drooping of the upper eyelid (ptosis)

HCP Patient

- The use of PGAs can cause **droopy** (or **'floppy'**) **eyelids**, particularly the upper eyelids.[3]
- The exact cause for this in PAPS is unclear, but it is thought to be because the muscle responsible for raising the upper eyelid and maintaining its position is not working properly.[3]



After PGA treatment

Image courtesy of Dr Chien-Chia Su

Mild enophthalmos

HCP Patient

- **PGF2α-induced fat atrophy** causes inhibition of adipocyte differentiation and a decrease in fat accumulation within adipocytes (especially of the preaponeurotic and deep orbital 'fat pads').[8,17,19,20]
- Mild enophthalmos, orbital fat atrophy, DUES, FLEB, and involution of dermatochalasis are all thought to result from this acquired fat loss.[1,8,17,19,20]
- Some studies have suggested that **enophthalmos is not as common as other adverse events seen with PAPS**.[2,17]

After PGA treatment

Image courtesy of Dr Chien-Chia Su

It is important to consider any causes of enophthalmos in the differential diagnosis, such as relative enophthalmos caused by a contralateral exophthalmos. **Hertel exophthalmometry can** reveal a mild degree of enophthalmos or, at least, a relative decrease in values (versus baseline).[21]

Appearance of a mildly sunken or deep set eyeball (mild enophthalmos)

HCP Patient

- PAPS can include **mild abnormal positioning of the eyeball** (adding to the 'sunken' look).[1–3,9,17,21]
- While this may **not be as common as other side effects** seen with PAPS,[2,17] your eye doctor may want to do some tests to understand the cause of the abnormal positioning.[21] Your doctor may also assess this over time to compare the results before and after treatment.[21]

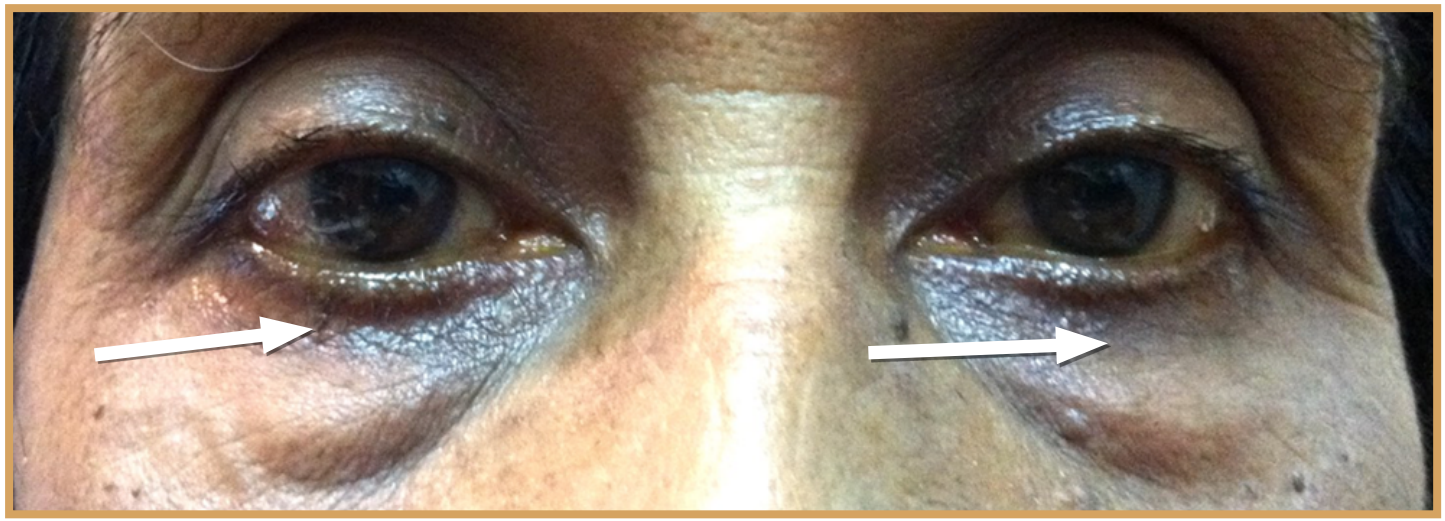
After PGA treatment

Image courtesy of Dr Chien-Chia Su

Orbital fat atrophy

HCP Patient

- PGF2α-induced fat atrophy causes inhibition of adipocyte differentiation and a **decrease in fat accumulation within adipocytes** (especially of the preaponeurotic and deep orbital 'fat pads').[8,17,19,20]
- Orbital fat atrophy, DUES, FLEB, involution of dermatochalasis, and mild enophthalmos are all considered to result from this acquired fat loss.[1,8,17,19,20]
- Bimatoprost-treated patients have been shown to have the **highest density of adipocyte cells**, suggesting adipocyte atrophy, compared with other PGAs.[20]
- **Orbital fat atrophy may be difficult to judge or is not as noticeable** as other signs of PAPS (such as eyelid or periocular pigmentation).



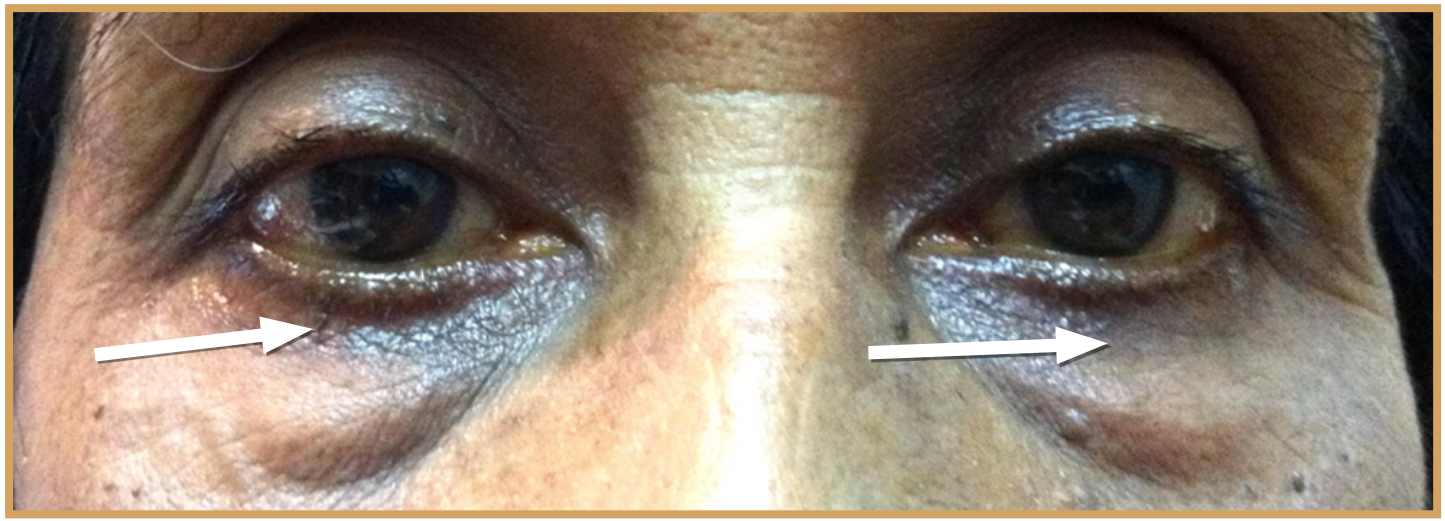
After PGA treatment

Image courtesy of Dr Weerawat Kiddee

Fat loss around the eye (orbital fat atrophy)

HCP Patient

- PGAs are known to reduce the ability of fat cells to mature and specialize. Therefore, PAPS is characterized by a **decrease in fat accumulation** around the eyes.[8]
- This fat loss around the eye (particularly the 'fat pads' underneath your eyes) may also be the cause of other clinical and cosmetic signs, such as DUES (the deepening of the upper eyelid 'sulcus' – or crease).[1,17,20]
- **Fat loss around the eye may be difficult to judge or is not as noticeable** as other signs of PAPS (such as pigmentation around the eye).



After PGA treatment

Image courtesy of Dr Weerawat Kiddee

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Tight orbit

HCP Patient

- A tight orbit is recognized as a **narrow palpebral fissure** and a feeling of tight eyelids.[1]
- **Differences in the penetration rate or concentration of each PGA within the orbital tissue**, including the eyelids, may be involved in the differences in the clinical phenotypes of DUES, **eyelid tightening**, and other signs of PAPS, all of which may result in a tight orbit.[17]
- Structural differences in the bone, orbit, or skin may also be related to the response to PGAs.[17]

After PGA treatment

Image courtesy of Prof. Makoto Aihara

A tight orbit may pose serious clinical challenges, including added **difficulty in measuring IOP** with the Goldmann applanation tonometer (GAT) and **difficulty in controlling IOP**.[1]

Eyelids pressing firmly against the eye (tight orbit)

HCP Patient

- A tight orbit is recognized as a feeling of the **eyelids being tight against the eye** and a narrow area between your open eyelids.[1]
- Different PGAs have different capacities to penetrate the fat tissue around the eyes (including the eyelids), and thus accumulate in different amounts which may be the cause of any differences seen in the signs of PAPS, including eyelid tightening and DUES.[17]

After PGA treatment

Image courtesy of Prof. Makoto Aihara

It is important to talk to your eye doctor as early as possible if you notice any tightening of your eyelids or have compromised vision as a tight orbit can impact the pressure in your eye.[9,17]

What mechanisms are behind the signs of PAPS?

HCP | Patient

Mechanism	PAPS signs
• **Potential inhibition of adipogenesis** via prostaglandin F receptor stimulation[19] • **Adipocyte atrophy** in the preaponeurotic and deep orbital fat[20]	• **Reduced orbital fat observed** in clinical DUES[19,20]
• **Dehiscence of the levator aponeurosis (or Müller muscle)**[2]	• **Ptosis**[2]
• **Elevated tyrosinase activity** through a non-cAMP pathway[22]	• **Iris and/or periocular pigmentation**[22]
• **Induction of follicle transition** from telogen (resting phase) to anagen (growth phase), and **prolonged anagen phase**[15] • **Increase in protease synthesis**[15] • **Increase in free Ca^{2+}**[15] • **Stimulation of protein kinase activity**[15]	**Induced excessive growth of lashes and ancillary hairs** around the eyelids:[15] • Increasing hair thickness and length • Converting vellus hair (soft, short, unpigmented) to terminal hair (coarse, longer, pigmented)

Most anatomical changes in PAPS may be due to orbital fat atrophy.[2,20] Bimatoprost-treated patients have been shown to have the highest density of adipocyte (undifferentiated) cells, suggesting fat atrophy.[20]

The impact of PAPS extends beyond cosmetic changes[12,14]

PAPS can complicate clinical examinations and directly impact ophthalmic surgery[23–25]

HCP Patient

Cosmetic changes, which may affect:

- Patient's quality of life and confidence[12]
- Drug adherence and/or difficulty with eye drop instillation[14]

Note: Visible facial asymmetry may be of particular concern in patients treated with PGAs for unilateral glaucoma[5]

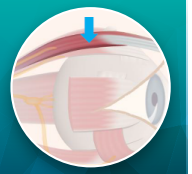
Difficulty in measuring IOP:

- Tight orbit may lead to overestimation of IOP measurements[23]

Discover more

Complexity before and during surgery:

- A tight orbit may affect surgical access and ease of surgery, including difficulty in manipulating and elevating the levator palpebrae superioris muscle during ptosis repair surgery[24]



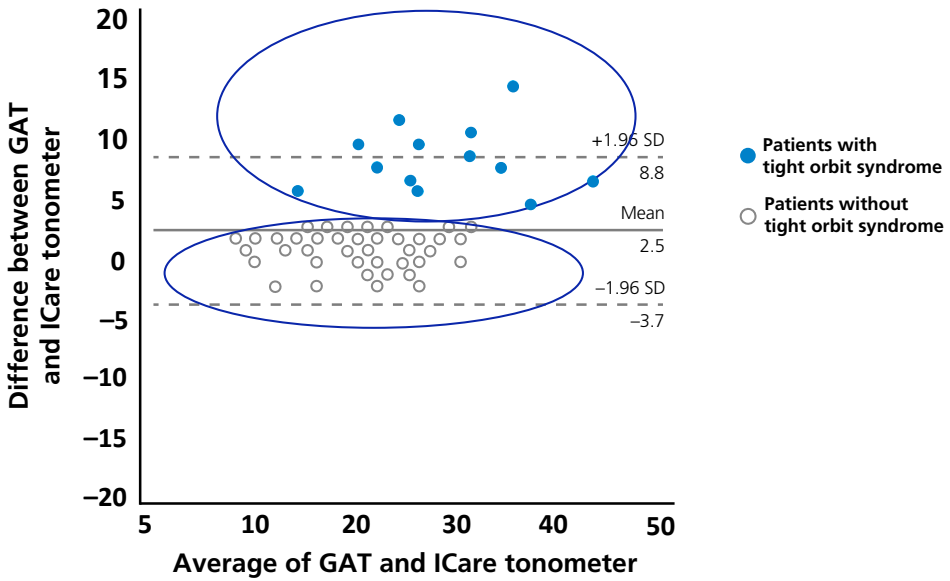
Impact on postoperative outcomes:

- A tight orbit can affect postoperative manipulations, such as laser suture lysis and bleb needling
- In patients undergoing trabeculectomy for OAG, those with DUES prior to surgery are at a significantly higher risk of recurrent IOP elevation up to 24 months after surgery, compared with patients without DUES[25†]

Discover more

Prolonged PGA use is associated with tight orbit syndrome, which can lead to overestimation of IOP measurements[23]

The difference between the GAT and ICare tonometer measurements were greater in patients with tight orbit syndrome[23]

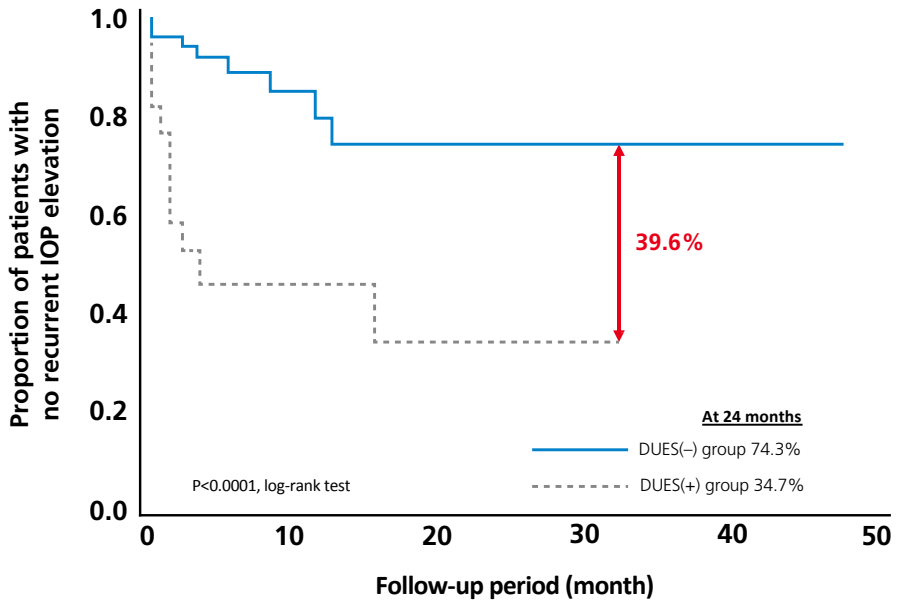


- The differences between the GAT and ICare tonometer measurements were greater in patients with tight orbit syndrome.[23]
- Multivariate regression analysis showed that PGA use was the **only factor** significantly associated with the development of tight orbit syndrome.[23]
- In patients with tight orbit syndrome, whose IOP measurements may be overestimated with the GAT, the ICare tonometer is a **suitable alternative device**.[23]

Adapted from: Lee YK, et al. *Jpn J Ophthalmol* 2014;58:496–502.

The outcome of trabeculectomy is affected by preoperative DUES[25†]

Cumulative proportion of patients with no recurrent IOP elevation according to preoperative DUES status[25]



Adapted from: Miki T, et al. *PLoS One* 2017;12:e0181550.

Effects of preoperative administration of PGAs on the outcome of trabeculectomy:[25†]

- The proportion of patients with no recurrent IOP elevation up to 24 months post-trabeculectomy was significantly lower in the DUES(+) group (34.7%) versus the DUES(–) group (74.3%) (P<0.0001).[25]
- There was a high risk of recurrent IOP elevation up to 24 months post-trabeculectomy in patients who used bimatoprost prior to surgery.[25]

Key recommendations

Be aware of PAPS, and talk to your eye doctor

Report any visible side effects as soon as they arise

HCP Patient

The symptoms of PAPS can also affect treatment outcomes, including:

- Unreliable eye pressure measurements[23]
- Added difficulty and poor outcomes related to glaucoma surgery in the future[24,25]

Don't let PAPS affect your adherence to treatment,[14] social life and confidence, and/or quality of life.[10,12]

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Recommendations for reducing the impact and/or the avoidance of PAPS symptoms

HCP Patient

Patient education

If appropriate, you could advise patients to:

- Wash their face/eyelids with water after using PGAs.
- Take care when using tissue paper to clean the periocular area or eyelids (as this may lead to pigmentation).[14]

Discontinuing treatment

- **AAO** recommends discontinuation of the causative treatment, often resulting in partial-to-complete reversal of PAPS in as early as 4–6 weeks.[21] However, treatment cessation is associated with a range of inherent issues, including increasing IOP, worsening glaucoma, and the need to resort to less efficacious medicines.

Switching treatment

- **APGS** and **EGS** recommend that patients are switched to an alternative drug class rather than considering same-class combination treatment.[26,27] As an example, omidenepag isopropyl may be an effective alternative when switching from PGAs in patients with glaucoma.[8,28]
- Despite not being a long-term solution, switching to an alternative PGA may be effective in patients who cannot discontinue treatment. For example, latanoprost may have a relatively lower rate of PAPS occurrence and longer latency of onset compared with other PGAs,[1,2] and switching to this may show improvements in PAPS.[4]

Surgery and DUES

- For patients receiving PGAs with poor IOP control, who are also considering surgery, it is important to monitor and prevent DUES onset as much as possible.[25]
- Confirm DUES status prior to trabeculectomy[25] and monitor IOP carefully in patients who are DUES(+). Equally, watch out for IOP recurrence in those who are DUES(+) after surgery.[25]

Any management decisions must be made on an individual basis and consider the benefits, risks, and convenience to the patient.
The information presented is based on expert opinion and consensus (see the 'Credits' section).

Follow-up appointments
Arrange regular check-ups with patients, prioritizing appointments with those experiencing cosmetic changes or troublesome ocular symptoms.

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What can you do?

Simple steps that could help lessen the impact of PAPS and certain symptoms

HCP Patient

Schedule regular visits with your eye doctor

- It is important to visit your glaucoma specialist or eye doctor regularly, especially if you notice the onset of any cosmetic changes or other troublesome eye symptoms.

As part of your glaucoma management plan, you could be asked to:

Wash your face and eyelids carefully with water after using PGA eye drops

- Please take note that washing your face immediately after using your eye drops could prevent them from being absorbed and working properly. But, washing too late could cause the eye drops to absorb into your skin and lead to pigmentation. Please talk to your eye doctor if you have any questions on this.

Take care when using tissue paper to wipe around your eyes

- Using tissue paper to clean around your eye could further spread the eye drops on your eyelids or around your eyes, causing the skin to darken, leading to pigmentation and what is known as ‘panda eyes’.[14]
- If you do use tissue paper regularly after applying your eye drops, please talk to your eye doctor if you begin to observe any signs of darkening of the skin around the eyes or eyelids, or if you have any questions on this.

The information presented is based on expert opinion and consensus (see the ‘Credits’ section). No significant evidence currently exists.
Any management decisions made by your doctor will be on an individual basis and consider the benefits, risks, and convenience to all.

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What glaucoma eye drops are available in my country/region?

HCP | Patient

Drug class	Drug name	Daily dose (concentration % w/v)
PGAs[30,31]	*Bimatoprost* *Latanoprost* *Tafluprost* *Travoprost* *Latanoprostene bunod*	QD (0.01%, 0.03%) QD (0.005%) QD (0.0015%) QD (0.004%) QD (0.024%)
EP2 receptor agonists[29,31]	*Omidenepag isopropyl*	QD (0.002%)
β-blockers[30,31]	*Betaxolol* *Levobunolol* *Timolol* *Carteolol* *Metipranolol*	BID (0.25%, 0.5%) QD to BID (0.5%) QD to BID (0.25%, 0.5%) BID (1.0%) BID (0.3%)
CAIs (topical)[30,31]	*Brinzolamide* *Dorzolamide*	BID (1.0%) BID to TID (2.0%)
α2-agonists[30,31]	*Apraclonidine* *Brimonidine*	TID – maximum 1 month (0.5%, 1.0%) BID (0.2%)
Miotics[30,31]	*Pilocarpine (multiple)*	Up to QID (multiple)
ROCK inhibitors[31–34]	*Netarsudil* *Netarsudil + Latanoprost* *Ripasudil*	QD (0.02%) QD (0.02%, 0.005%) BID (0.4%)
Combinations[31]	***PGA + β-blocker*** *Bimatoprost + Timolol* *Latanoprost + Timolol* *Tafluprost + Timolol* *Travoprost + Timolol* ***CAI + β-blocker*** *Brinzolamide + Timolol* *Dorzolamide + Timolol* ***α2-agonist + β-blocker*** *Brimonidine + Timolol* ***CAI + α2-agonist*** *Brinzolamide + Brimonidine*	 QD (0.03%, 0.5%) QD (0.005%, 0.5%) QD (0.0015%, 0.5%) QD (0.004%, 0.5%) BID (1.0%, 0.5%) BID (2.0%, 0.5%) BID (0.2%, 0.5%) BID (1.0%, 0.2%)

Availability and access to treatments may vary across clinics, hospitals, regions, and countries. Each treatment option should be considered in accordance with local regulations and the level of evidence available at the time of the decision.

Any treatment decisions must be made on an individual basis and consider the benefits and risks of the treatment.

Information presented is correct as of December 2021.

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This guidebook was developed in collaboration with leading experts in glaucoma

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Santen

APGS Asia-Pacific Glaucoma Society

References & additional information

Abbreviations

AAO: American Academy of Ophthalmology; APGS: Asia–Pacific Glaucoma Society; BID: twice a day; BMI: body mass index; CAI: carbonic anhydrase inhibitor; cAMP: cyclic adenosine monophosphate; DUES: deepening of the upper eyelid sulcus; EGS: European Glaucoma Society; EP2: prostaglandin E2; FLEB: flattening of the lower eyelid bags; GAT: Goldmann applanation tonometer; HCP: healthcare professional; IOP: intraocular pressure; MMP: matrix metalloproteinase; OAG: open-angle glaucoma; OHT: ocular hypertension; OR: odds ratio; PAPS: prostaglandin-associated periorbitopathy syndrome; PGA: prostaglandin analogue; PGF2α: prostaglandin F2α; QD: once a day; QID: four times a day; ROCK: Rho-associated protein kinase; SD: standard deviation; TID: three times a day.

Footnotes

*In a cross-sectional study of 134 patients with glaucoma or OHT, using topical PGAs (bimatoprost, latonoprost, travoprost) for ≥3 months resulted in a prevalence of PAPS of 44.8% (95% CI: 36.3–53.3). Eyes were photographed and independently evaluated for PAPS by two glaucoma specialists using at least four out of seven clinical appearances, including DUES, absence of dermatochalasis, a deep crease in the upper eyelid, ptosis, decreased prominence of the inferior orbital fat pads, inferior scleral show, enophthalmos, and orbital fat atrophy. Older age (>60 years of age) (OR: 3.0; 95% CI: 1.2–7.8), bimatoprost (OR: 4.0; 95% CI: 1.6–9.5), travoprost (OR: 3.3; 95% CI: 1.1–10.1), and timolol (OR: 2.9; 95% CI: 1.3–6.8) were all independent risk factors for the development of PAPS. In addition, BMI ≥23 kg/m^2 (OR: 0.3; 95% CI: 0.1–0.7) was negatively associated with PAPS.[6]
†In a retrospective review of 74 patients with primary OAG, whose IOP was inadequately controlled by PGAs, and who subsequently underwent primary trabeculectomy, the proportion of patients with no recurrent IOP elevation up to 24 months after trabeculectomy was significantly lower in the DUES(+) group (34.7%) versus the DUES(–) group (74.3%) (P<0.0001). Bimatoprost (n=13) was considered the most unfavourable PGA treatment (compared alongside latanoprost, tafluprost, and travoprost), and only significant independent risk factor, for post-trabeculectomy recurrence of IOP elevation.[25]

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Prostaglandin-associated periorbitopathy syndrome (PAPS): Addressing an unmet clinical need

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ABSTRACT

Background: Topical prostaglandin analogs (PGAs) are widely approved and preferred first-line options for glaucoma and elevated intraocular pressure (IOP). However, prostaglandin-associated periorbitopathy syndrome (PAPS) is now a well-recognized clinical and cosmetic concern for patients receiving PGAs, especially during long-term and unilateral therapy. PGA-associated periocular changes occur in a substantial proportion of patients, with older patients (>60 years) at greater risk of clinical presentation. PAPS may hinder long-term management of glaucoma, including treatment adherence, ophthalmic surgery outcomes, and reliable IOP measurements. Recommendation: New therapeutic approaches may address this unmet clinical need. Omidenepag isopropyl (OMDI) is a novel, non-prostaglandin, selective EP_2 receptor agonist in ongoing development, which provides a unique pharmacological mechanism of action. OMDI appears to provide IOP reductions comparable to PGAs, but without PAPS-related undesirable effects. OMDI may offer a suitable long-term option for patients who demonstrate decreased efficacy, or failure, of PGAs, plus patients with significant PAPS, while fulfilling international guidelines.

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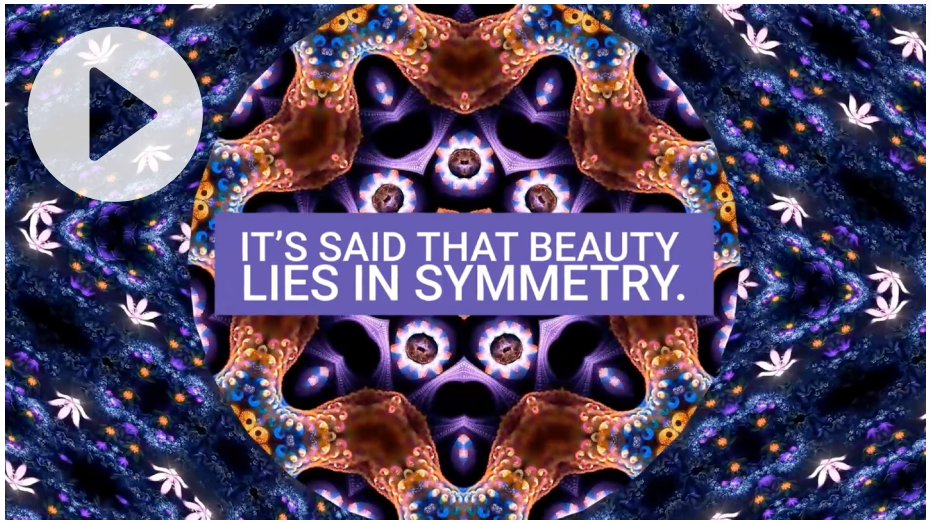

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