Public Assessment Report

Intraoperative Floppy Iris Syndrome (IFIS) and α-1 adrenoceptor antagonists—a class effect?

Executive summary

In April 2005, patients given tamsulosin—a highly selective α-1A adrenoceptor antagonist—for treatment of benign prostatic hyperplasia were identified as having an increased risk of Intraoperative Floppy Iris Syndrome (IFIS)—a newly diagnosed syndrome that can lead to surgical complications during cataract surgery.

The Pharmacovigilance Working Party (PhVWP) of the Committee for Medicinal Products for Human Use (CHMP) first considered the issue of IFIS in December 2005. PhVWP concluded that a causal association between IFIS and tamsulosin was plausible, and advised that a warning should be added to the Summary of Product Characteristics (SPC) for products that contained tamsulosin.

In May 2006, PhVWP agreed with the conclusions of an assessment by Finland that at the time, there was insufficient evidence to suggest that IFIS was a class effect of α-1 adrenoceptor antagonists. However, PhVWP proposed further investigation, and stimulated a review of a potential class effect, given the occurrence of isolated spontaneous cases of IFIS with alfuzosin and doxazosin in the UK.

This report discusses the data used in the assessment of a potential class effect α-1 adrenoceptor antagonists and development of IFIS. These data suggest that IFIS can develop in a few patients given these medicinal products. Given the nature of IFIS and the ease of its management, it would be prudent to advise patients to notify their ophthalmic surgeon in advance of surgery of current and past use of α-1 adrenoceptor antagonists, which will enable preparations for any complications that might arise.

The UK Pharmacovigilance Expert Advisory Group (PEAG) of the Commission on Human Medicines (CHM) considered IFIS as a possible class effect of α-1 adrenoceptor antagonists in October 2006. PEAG advised that it would be prudent to add a warning to the product information, advising patients to inform their cataract surgeon about past and current use of α-1 adrenoceptor antagonists before surgery to ensure appropriate measures are in place should IFIS occur.

In November 2006, PhVWP considered whether IFIS is a class effect of α-1 adrenoceptor antagonists. PhVWP agreed that the SPC and Patient Information Leaflet (PIL) for α-1 adrenoceptor antagonists should be updated. The proposed wording is given on page 15 of this Public Assessment Report.

Introduction

In April 2005, patients given tamsulosin—a highly selective α-1A adrenoceptor antagonist—for treatment of benign prostatic hyperplasia were identified as having an increased risk of Intraoperative Floppy Iris Syndrome (IFIS)—a newly diagnosed syndrome that can lead to surgical complications during cataract surgery.[1]

IFIS

IFIS is newly identified, and is characterised by loss of muscle tone in the iris (the part of the eye that controls pupil dilations and contractions and thus the amount of light entering the eye). During cataract surgery, IFIS is characterised by three features: a floppy iris that billows in response to normal irrigation currents in the anterior chamber; a marked tendency for the iris to prolapse to the phaco and side-port incisions; and progressive pupil constriction.[1] Because the pupil must remain stable and dilated properly for effective cataract removal, IFIS is a potentially serious problem because it might cause surgical complications and might increase the risk of posterior capsular rupture.

Chang and Campbell[1] discussed data from a retrospective study and a prospective study, which support an association between tamsulosin and IFIS. The retrospective study assessed 706 eyes in 511 patients who underwent cataract surgery, 27 (5%) of whom were receiving systemic α-1 adrenoceptor antagonists (16 tamsulosin, and 11 prazosin, terazosin, or doxazosin). The researchers noted a so-called floppy iris in 10 of the 16 patients given tamsulosin, and recorded poor or moderately poor preoperative dilation in patients taking prazosin, terazosin, or doxazosin (but no actual cases of IFIS were identified). In the prospective study, IFIS was diagnosed in 21 of 900 cataract surgeries, and in 16 of 741 patients (about 2%). 14 of the 16 patients were taking tamsulosin at the time of cataract surgery, and 1 patient had stopped tamsulosin 1 year before surgery. Of the 725 patients who did not have IFIS patients, none were receiving tamsulosin. Frequency of IFIS in both studies, totalling more than 1600 eyes and 1250 patients, was reported as 2% of patients having cataract surgery, and was regarded as associated with tamsulosin.

Chang and Campbell[1] suggest that tamsulosin has a particular high affinity and specificity for the α-1A receptor, which might account for the difference between tamsulosin and other selective α-1 adrenoceptor antagonists and risk of IFIS. Tamsulosin not only blocks α-1A receptors in the prostate, but also is thought to block selectively α-1A receptors that are common in the iris dilator muscle as shown in animals.[2,3] A lack of dilator smooth-muscle tone can cause iris billowing and a tendency for the iris to prolapse.

Regulatory assessments

The Pharmacovigilance Working Party (PhVWP) of the Committee for Medicinal Products for Human Use (CHMP) first considered IFIS in December 2005. PhVWP concluded that a causal association between IFIS and tamsulosin was plausible. PhVWP advised that: cataract surgeons should be informed of tamsulosin use in patients before surgery; that treatment with tamsulosin for patients awaiting cataract surgery should not be recommended; that the benefits of withdrawing treatment before surgery remain unknown; and that a warning should be added to the Summary of Product Characteristics (SPC) for products that contained tamsulosin—final SPC wording to reflect this advice was agreed in May 2006. In the UK, this advice was communicated by an article in the drug-safety bulletin *Current Problems in Pharmacovigilance* in May 2006 (see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=368), and by a Dear Healthcare Professional letter to ophthalmologists, urologists, and general practitioners in July 2006 (see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2024695&ssTargetNodeId=221).

The box below shows the SPC wording for tamsulosin:

Section 4.4: Special warnings and special precautions for use

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients for whom cataract surgery is scheduled is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of requirement of stopping the therapy prior to cataract surgery has not yet been established.

During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being, or have been, treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

Section 4.8: Undesirable effects

During cataract surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been associated with therapy of tamsulosin during post-marketing surveillance (See also Section 4.4).

Also in May 2006, PhVWP agreed with the conclusions of an assessment by Finland that at the time there was insufficient evidence to suggest that IFIS was a class effect of α-1 adrenoceptor antagonists; other drugs in this class include alfuzosin, doxazosin, prazosin, and terazosin. However, PhVWP proposed further investigation, and stimulated a review of a potential class effect, given the occurrence of isolated spontaneous cases of IFIS with alfuzosin and doxazosin in the UK.

The MAHs for alfuzosin, doxazosin, and terazosin were asked to submit: a cumulative review of ocular disorders reported spontaneously, in clinical trials, or in the literature associated with alfuzosin, doxazosin, or terazosin, with particular focus on IFIS; an assessment of the potential mechanism by which alfuzosin, doxazosin, or terazosin might cause IFIS, and whether a class effect is likely; and a discussion of any potential benefits to withdrawal of treatment 1–2 weeks before cataract surgery in patients with IFIS.

Data assessed

The MAH for tamsulosin provided data for an association between IFIS and α-1 adrenoceptor antagonists, which were reviewed by the Finnish Regulatory Agency and considered by PhVWP in May 2006. Some of these data are included in a report by Ohtake and colleagues, which showed that tamsulosin and other α-1 adrenoceptor antagonists inhibit phenylephrine induced mydriasis and cause miosis to an equal extent and duration in an animal study.[4]

Finland considered the evidence to be insufficient to suggest that IFIS is a class effect of α-1 adrenoceptor antagonists. Differences between drugs in this class—eg, dosing; treatment duration; and pharmacokinetic properties such as half-life, active metabolites, and intraocular levels—are potentially important for development of IFIS. Furthermore, individual patient susceptibility may play a part, and the usage of particular α-1 adrenoceptor antagonists may affect frequency of IFIS reports. In conclusion, the role of α-1 antagonists in the development of IFIS should be monitored closely.

In May 2006, PhVWP endorsed the conclusion of the Finnish assessment report, but in addition proposed that the UK should investigate whether there is an increased risk of IFIS with alfuzosin, doxazosin, and terazosin.

Cumulative reviews of ocular disorders

Alfuzosin

The MAH identified case reports of floppy iris syndrome associated with alfuzosin from launch in 1988 to June 30 2006. One of the cases was subsequently published by Settas and Fitt.[5] Patient exposure during this period is more than 7·5 million patient-years; alfuzosin is currently marketed in 86 countries.

About 12 000 patients received alfuzosin during clinical trials, and more than 235 000 patients were exposed to different alfuzosin formulations for up to 4 years in post-licensing studies and surveys. No cases suggestive of IFIS were identified from phase I to IV clinical trials and observational studies done up to June 30 2006.

A literature search done on July 26 2006 for IFIS associated with alfuzosin identified only the case report by Settas and Fitt.[5] An analysis of the Food and Drug Administration (FDA) Adverse Event Rreporting System from Jan 1 2005 to Sept 30 2005 identified isolated cases suggestive of IFIS with tamsulosin, doxazosin, terazosin. and finasteride.

Doxazosin

Case reports associated with doxazosin submitted up to May 31 2006 were analysed, and 1 report suggestive of IFIS was identified.

Prazosin

Case reports associated with prazosin submitted up to May 31 2006 were analysed. No cases were indicative of IFIS.

Terazosin

None of the identified case reports describe events that reflect the characteristics of IFIS, or describe operative findings or complications that specifically refer to IFIS. Terazosin was first licensed in Germany on Nov 30 1984, and is currently approved in more than 50 countries. Worldwide patient exposure of terazosin for the period July 1 2002 to March 31 2006 was about 3 329 881 patient-treatment years, assuming an average of one tablet or capsule per day per patient.

All literature reports of IFIS exclude terazosin from the list of α-1 adrenergic drugs implicated as causative agents of IFIS. In conclusion, there seems to be no direct evidence to date of a case of IFIS associated with terazosin.

Changes to reference safety information

Warnings about IFIS have previously been added to the US product information for terazosin, doxazosin, and alfuzosin at the request of the US Food and Drug Administration. This wording should be within the Core Safety Information (CSI) of the Company Core Data Sheet (CCDS) for these products.

For instance, in July 2005, the following wording was incorporated into the CSI for Hytrin® (terazosin).

PRECAUTIONS, General*:*

Cataract Surgery

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on/or previously treated with alpha-blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative miosis despite preoperative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's ophthalmologist should be prepared for possible modifications of their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping alpha-1 blocker therapy prior to cataract surgery."

The following revision was added to the ADVERSE REACTIONS, Post-Marketing Experience *section of the CCSI:*

"During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported in association with alpha-1-blocker therapy (see PRECAUTIONS)."

Potential mechanism

Alfuzosin

Several pharmacological differences between alfuzosin and tamsulosin suggest that IFIS should not be considered a class effect—eg, differences in chemical structure, ability to cross the blood–brain barrier, selectivity and affinity for α-1A adrenoceptor subtypes, and affinities for non-adrenergic receptors (ie, dopaminergic and serotoninergic). Alfuzosin has no structural similarities with tamsulosin, which gives alfuzosin specific biochemical properties.[6–10] Alfuzosin has a balanced binding affinity for the α-1 adrenoceptor subtypes,[11–13] only tamsulosin shows selectivity for the α-1A subtype compared with other α-1 blockers.[14]

Alfuzosin,[15] terazosin,[16] and prazosin[17] are pure competitive antagonists in human prostatic smooth muscle. Prazosin is a competitive antagonist in iris dilator smooth muscle.[18] The effect of alfuzosin on iris smooth muscle has not been studied, but its similar structure to prazosin might mean that alfuzosin also behaves as a competitive antagonist in iris smooth muscle. By contrast, tamsulosin is an irreversible antagonist of α-1 adrenoceptors.

Tamsulosin is a chiral molecule, and an animal study showed one form to be 140-times more potent in the prostate than the other.[19] The more-potent form is an irreversible antagonist to norepinephrine in human isolated prostate[16] and the iris dilator muscle in an animal study.[20] Thus, a wash-out period of 3–7 days for patients taking tamsulosin might not prevent IFIS in some patients.

Although the exact mechanism by which tamsulosin induces IFIS has yet to be established, the role of other receptors (eg, serotoninergic and dopaminergic receptors) in inducing pupillary changes warrants consideration.[21–25] Alfuzosin has a selective binding profile in favour of α-1 adrenoceptors and has little or no affinity at serotoninergic or dopaminergic receptors.[26] By contrast, tamsulosin seems to have potent affinity for dopaminergic receptors.

Doxazosin and prazosin

The mechanism by which tamsulosin causes IFIS may be more complicated than the original mechanism presented by Chang and Campbell.[1] IFIS is thought to develop as a result of tamsulosin's greater affinity for α-1A and 1D receptors compared with other α-1 receptor antagonists; the α-1A receptor is thought to be the main receptor subtype in iris dilator muscle.[2,3] Moreover, an additional α-receptor, the 1L subtype, might mediate iris dilation, and tamsulosin is a more-potent antagonist of the α-1L receptor than is terazosin or doxazosin.[27]

Terazosin

Terazosin is a non-selective α-1 adrenoceptor antagonist for the subtypes α-1A, α-1B, and α-1D. By contrast with tamsulosin, terazosin has no selectivity towards the α-1A receptor (which

is thought to predominate in the iris) and towards the α-1A and α-1D receptors (which are thought to be uroselective). Terazosin is structurally unrelated to tamsulosin and alfuzosin.

Withdrawal of treatment

In humans, tamsulosin is an irreversible antagonist of α-1 adrenoceptors, and thus a withdrawal period of several days may not be sufficient to suppress the blockade of α-1 adrenoceptors.

Chang and Campbell[1] found that discontinuation of tamsulosin 4–7 days before surgery was helpful, but did not prevent completely. Settas and Fitt[5] reported no benefit to temporarily stopping alfuzosin treatment before surgery. Discontinuation of tamsulosin for 1 week or less before surgery might be insufficient because the elimination half-life for tamsulosin is about 48–72 h.

Chang and Campbell[1] suggested that IFIS might be semi-permanent, and that blockade of α-1A receptors in the iris dilator muscle could result in disuse atrophy of the muscle because IFIS was still evident in some patients despite drug withdrawal. In other patients, however, preoperative dilation and iris floppiness seemed to improve after drug withdrawal. Chang and Campbell advised temporary withdrawal of tamsulosin treatment 2 weeks before surgery.

Michel and colleages[28] have assessed the effects of α-1 adrenergic receptor antagonists on pupil size and intraurethral pressure, and Schwinn and Afshari[29,30] have discussed the effect of therapeutic blood level of any α-1 adrenergic receptor antagonist given up to the day of surgery. Schwinn and Afshari advise that it would be prudent to stop all α-1 adrenergic receptor antagonists before cataract surgery to avoid the possibility of IFIS, although the exact time and effectiveness of this action still need to be determined by careful recording of drug doses and plasma levels in future prospective studies. Schwinn and Afshari consider the implications of withdrawing α-1 adrenergic receptor antagonist treatment, and add that restarting of α-1 adrenergic antagonists immediately after cataract surgery seems to carry little or no risk.

In conclusion, the benefits of withdrawing treatment before cataract surgery remain unclear. Until studies show clearly the benefit or absence of benefit of withdrawing tamsulosin before cataract surgery, the current PhVWP SPC wording proposed for section 4.4 for tamsulosin remains appropriate:

> "Discontinuing tamsulosin 1-2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of requirement of stopping the therapy prior to cataract surgery has not yet been established."

Discussion

In 2005, tamsulosin treatment was implicated as a causative factor for the new ocular syndrome IFIS observed during cataract surgery.[1] Although the precise mechanism by which tamsulosin can lead to IFIS remains unknown, Chang and Campbell suggest that tamsulosin has high affinity and specificity for the α-1A adrenergic receptor, which is thought to be the dominant receptor in the iris. One of the distinguishing features of IFIS is that miosis does not respond to standard intraoperative treatment to dilate the pupil.[1]

This review aimed to investigate whether IFIS is a class effect of α-1 adrenergic receptor antagonists. Structural differences and the distinct mechanisms of action of α-1 adrenoceptor antagonists might account for the substantial differences in cases of IFIS noted thus far for other α-1 adrenoceptor antagonists compared with tamsulosin.

Tamsulosin is a third-generation α-1 adrenoreceptor antagonist with greater affinity for α-1A receptors than for α-1B receptors.[31] Terazosin and doxazosin are long-acting second-generation α-1 adrenoreceptor antagonists that inhibit α-1A receptors found mainly in the prostate and α-1B receptors found mainly in vascular epithelium. Prazosin is a second-generation α-1 receptor inhibitor with a shorter half-life than terazosin and doxazosin.

Alfuzosin has similar uroselectivity to tamsulosin, and it inhibits competitively and selectively α-1 adrenergic receptors in the prostate, bladder base, and prostatic urethra. Alfuzosin has been reported to show selectivity only for the α-1A subtype,[14] and to behave as a pure competitive antagonist in human prostatic smooth muscle,[15] as do terazosin[16] and prazosin.[17] Similar to prazosin,[18] alfuzosin might act as a competitive antagonist in human iris smooth muscle. Settas and Fitt suggest that the overall affinity of α-1 adrenoceptor antagonists towards α-1A receptors might explain IFIS.

Chang and Campbell[1] recorded poor or moderately poor preoperative dilation, but no actual cases of IFIS, in patients taking prazosin, terazosin, and doxazosin. Previous regulatory assessment concluded that evidence was insufficient to suggest that IFIS was a class effect of α-1 adrenoceptor antagonists. Since then, isolated cases of IFIS associated with other α-1 adrenergic receptor antagonists have emerged.

Some studies have attempted to quantify the risk of IFIS with tamsulosin and to clarify the role of other α-1 adrenergic receptor antagonists in the development of IFIS. In a UK-based observational prospective study of 2390 cataract procedures, Cheung and colleagues[32] identified 3 eyes with IFIS and 6 eyes with some features of IFIS out of 15 patients (17 eyes) given tamsulosin; duration of tamsulosin did not correlate with severity of IFIS.

Another UK prospective study reported greater use of doxazosin (n=11) than of other α-1 adrenoceptor antagonists—indoramin (n=8), prazosin (n=5), terazosin (n=2), and tamsulosin (n=3)—in 100 patients awaiting cataract surgery. Of this unselected population, no patients developed IFIS and 1 had a constricted pupil.[33]

Chadha and colleagues[34] assessed the association of floppy-iris behaviour during cataract surgery with use of α-1 adrenoceptor antagonists and with diabetes mellitus in 1786 patients (1842 eyes). 11 eyes in 11 patients had complete IFIS, and 18 eyes in 18 patients had incomplete IFIS. 12 of 21 patients given tamsulosin had signs of complete or incomplete IFIS; however 17 cases of IFIS (5 complete, none of whom had ever taken an α-1 adrenoceptor antagonist, and 12 incomplete, 1 of whom was receiving doxazosin) were noted for patients who were not given tamsulosin. None of the other patients taking doxazosin (n=48), or those taking alfuzosin (n=2) or terazosin (n=1) had signs of IFIS. No relation between diabetes and IFIS was found. The researchers conclude that non-selective α-1 adrenoceptor antagonists are unlikely to be associated with IFIS, but they suggest that other factors besides tamsulosin may play an important part.

By contrast, Schwinn and Afshari[29,30] propose that all α-1 adrenoceptor antagonists might be associated with IFIS, and they suggest that other drugs should be considered as potentially associated with this syndrome. These researchers suggest that iris contraction and relaxation is the result of a balance of competing neural pathways, and pathways regulated by prostaglandin and nitric oxide.[35,36] The role of the serotoninergic and dopaminergic receptors in inducing pupillary changes is discussed in the section on potential mechanisms, page 8.[23–26] Tiwari and colleagues[27] have also proposed an important role for the 1L subtype α-receptor in mediation of iris dilation in the human eye, and tamsulosin is thought to be a more-potent antagonist of this receptor subtype than is terazosin or doxazosin.

Furthermore, in-vivo studies have shown that α-1 adrenoceptor antagonists can affect miosis. In an animal study, injections of alfuzosin, doxazosin, naftopidil, prazosin, tamsulosin, and terazosin relaxed the iris dilator smooth muscle, causing pupil constriction, 15–30 min after administration. All these agents also can inhibit the effects of phenylephrine on pupil size and intraurethral pressure.[28]

The American Society of Cataract and Refractive Surgeons (ASCRS, http://www.ascrs.org) have formed a Flomax (tamsulosin) Task Force and have started a multicentre trial to assess the frequency of IFIS complications in patients who take tamsulosin. Preliminary results presented at the ASCRS annual symposium (March 17–22, 2006; San Francisco, CA, USA) showed that if the surgeon knew about tamsulosin use in advance and if modified surgical techniques were used, the surgical success rate was excellent and the complication rate was not increased compared with surgery for patients not taking Flomax. In July 2006, the

ASCRS, the American Academy of Ophthalmology (AAO), and the American Urological Association (AUA) alerted patients about potential difficulties during cataract surgery caused by IFIS, and list terazosin, doxazosin, alfuzosin, and tamsulosin as treatments that might be associated with this syndrome (see, for instance, http://news.auanet.org/article_display.cfm?article_id=140).

Conclusion

With forewarning of a patient's current and past drug history, IFIS can be managed easily by a proficient cataract surgeon. The α-1 adrenoceptor antagonist tamsulosin is recognised to increase risk of IFIS; however, the causes of this syndrome remains under investigation. Not all patients given tamsulosin develop IFIS; cases have been reported in the absence of treatment; and for some, IFIS improves after drug withdrawal, whereas others have symptoms years after treatment has stopped.

In addition to tamsulosin, other α-1 adrenergic receptor antagonists and therapeutic agents that mediate relaxation of iris dilator smooth muscle have been postulated to cause IFIS. Moreover, roles have been suggested for the serotoninergic and dopaminergic receptors and of the 1L subtype of the α-receptor.

To date, isolated cases of IFIS have been observed with the other α-1 adrenoceptor antagonists, but to a much lesser extent than for tamsulosin. These cases and in-vivo studies suggest that these agents act on iris dilator smooth muscle and induce miosis, perhaps to a lesser extent than does tamsulosin.

From a regulatory perspective, the safety of the patient remains paramount. Evidence of a causal association of IFIS with other α-1 adrenoceptor antagonists, besides tamsulosin is limited, but the data suggest that the syndrome can develop in a few patients given these medicinal products. Given the nature of IFIS and the ease of its management, it would be prudent to advise patients to notify their ophthalmic surgeon in advance of surgery of current and past use of α-1 adrenoceptor antagonists, which will enable preparations for any complications that might arise.

The UK Pharmacovigilance Expert Advisory Group (PEAG) of the Commission on Human Medicines (CHM) considered IFIS as a possible class effect of α-1 adrenoceptor antagonists in October 2006. PEAG advised that it would be prudent to add a warning to the product information, advising patients to inform their cataract surgeon about past and current use of α-1 adrenoceptor antagonists before surgery to ensure appropriate measures are in place should IFIS occur.

In November 2006, PhVWP considered whether IFIS is a class effect of α-1 adrenoceptor antagonists. The PhVWP agreed that the SPC and Patient Information Leaflet (PIL) for α-1 adrenoceptor antagonists should be updated. Final PhVWP SPC and PIL wording should be as follows:

SPC wording:

Section 4.4 Special warnings and precautions for use

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. Isolated reports have also been received with other alpha-1 blockers and the possibility of a class effect cannot be excluded. As IFIS may lead to increased procedural complications during the cataract operation current or past use of alpha-1 blockers should be made known to the ophthalmic surgeon in advance of surgery.

PIL wording:

If you are undergoing eye surgery because of cataract (cloudiness of the lens) please inform your eye specialist before the operation that you are using or have previously used xxxxx. This is because xxxxx may cause complications during the surgery which can be managed if your specialist is prepared in advance.

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