

Inside *Therapeutics: Medicines Update p18 Side-effects of anti-epilepsy drugs p27*

Optician; the British optical and instrument
v. 223, no. 5853 (May 31 2002)
General Collection
W1 OP861
2002-06-12 12:05:49

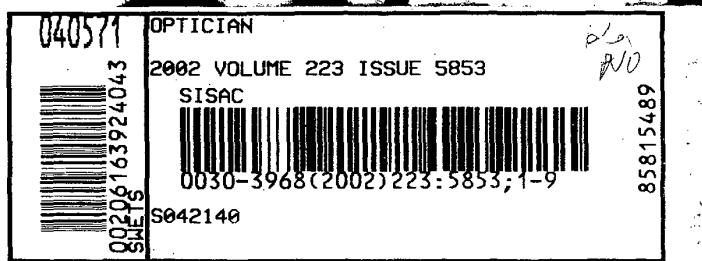
May 31 2002 £3.25

Optician

The Weekly Journal for OPTOMETRISTS & DISPENSING OPTICIANS

www.optometryonline.net

'Fresh,
cool eye
thanks
my optician!'



**Recommend Refresh® eye drops
to your customers –
they'll thank you for it.**



This week's front cover features Allergan. For further details please telephone 01494 444722



A Reed Business Information Publication

Optician

www.optometryonline.net

Contents

Features

- 8 Opportunity knocks**
John Wilkinson says get ready for the new NHS.
- 16 The making of a modern practice**
Rob Moss reports on Cambridge-based optometrist Angela Gould's progress as she establishes herself as owner of one of the university town's oldest practices.
- 18 Medicines Update – Part 11**
Professor Michael Doughy provides an overview of eye medicines and other eye care products introduced in the last three months.
- 23 Ocular pharmacokinetics**
Dr John Lawrenson discusses ocular pharmacokinetics and the significance it has for drug delivery and toxicity.
- 26 Drugs database**
OPTICIAN describes the City Ocular Adverse Reactions to Drugs database.
- 27 Effects of anti-epileptic drugs on visual performance**
Emma Roff Hilton, Sarah Hosking and Tim Betts describe the impact that drugs prescribed to treat epilepsy can have on a patient's vision.
- 31 Clinical Audit Patient Survey**
Dale Harris and Bob Hutchinson look at the dispensing process in practice.
- 32 OPTICIAN Index**
April saw slower growth than is usual for spring.

Regulars

- 4 News**
10 Products
12 Letters/Comment
How to contact OPTICIAN
14 Omen
35 Appointments
43 Optical Suppliers' Guide
47 A-Z of anterior eye disease

Next Issue

Contact lens monthly

- ◆ *John Meyler and Cristina Schnider* discuss the dangers of ultraviolet light and suggest UV-blocking contact lenses as protection.
- ◆ The second part of our pilot CET series on Visual Recognition in Contact Lens Practice covers fitting characteristics.
- ◆ *Lyndon Jones* takes a look at equipping your practice ready for contact lens practice.



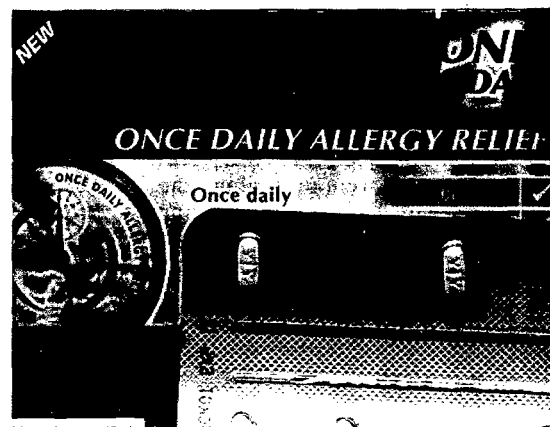
Shake-up in the NHS p8 ▲



The making of a modern practice p16 ▲



Letters p12 ▲



New drugs p18 ▲



'Fresh, cool eye drops - thanks my optician!'

Recommend Refresh eye drops to your customers - they'll thank you for it.

This week's front cover features Allergan. For further details please telephone 01494 444722

Innopharma EX1032, Page 2

Medicines Update

for optical practitioners – Part 11

MEDICINES UPDATE for optical practitioners is designed to keep the UK optometrist up to date with all aspects of eye medicines and other eye products that can be used to manage a range of minor-to-moderate non sight-threatening conditions or diseases that can affect the external eye.

In addition, the series is designed to keep the optometrist fully informed of the availability and developments of ophthalmic medicines for the management of severe eye diseases and in systemic medicines that could have an impact on the eye or vision, including those medications likely encountered in shared-care schemes.

This part includes several new products

Professor Michael Doughty provides an overview of eye medicines and other eye care products introduced in the past three months

and a brief review of the role of oral antihistamines in the management of seasonal allergic conjunctivitis.

TEN NEW OPHTHALMIC PRODUCTS

This quarter sees the introduction of another option in re-wetting solutions, a generic carbomer gel, several options for management of seasonal allergic conjunctivitis (including a new topical ocular multiple-acting antihistamine, another generic mast cell stabiliser, and several

products containing the oral antihistamine cetirizine), a new gel formulation of timolol and third prostaglandin analogue for management of open-angle glaucoma (Table 1). Some changes in product availability have also occurred (Table 2).

A new option in re-wetting solutions is available – Blink-n-clean (Figure 1). The idea for this product, as emphasised by its name, is that the combination of the surfactant (tyloxapol) and the substantial quantity of chemical buffer (tromethamine) is designed to disperse

TABLE 1. New ophthalmic pharmaceuticals for UK (May 2002)

Drug name	conc	C	Pharmaceutical	co	Presentation
hydroxypropylmethylcellulose 0.15%, tyloxapol 0.025%, ¹ tromethamine 1.2%, EDTA and preserved with polyhexamethylene biguanide 0.0001%		SL CE	COMPLETE BLINK-N-CLEAN	32	15ml multi-use bottle
² carbomer 980, sorbitol 4%, EDTA and preserved with cetrimide 0.01 %	0.2%	SL CE	CARBOMER GEL	65	10g multi-use tube
ketotifen, glycerol and preserved with benzalkonium chloride	0.025%	PoM	ZADITEN	40	5 ml multi-use bottle
³ Na cromoglycate, sorbitol, polysorbate 80, EDTA and preserved with benzalkonium chloride	2%	P	VIVICROM EYE DROPS	66	10 ml multi-use bottle
cetirizine	10mg	GSL P	PIRITIEZE ALLERGY TABLETS	67	7 tablets (GSL) 30 tablets (P)
cetirizine	10mg	P	BENADRYL ONE-A-DAY	70	14 tablets
cetirizine	10mg	P	CETIRIZINE HAYFEVER RELIEF	51	7 tablets
cetirizine	10mg	GSL P	HAYFEVER AND ALLERGY RELIEF	68	7 tablets (GSL) 30 tablets (P)
timolol, sorbitol, lysine, in a carbomer 974P – polyvinyl alcohol gel vehicle, preserved with benzalkonium chloride 0.008 %	0.1%	PoM	NYOGEL EYE GEL	40	5g multi-use bottle
bimatoprost, NaCl, citrate and phosphate buffers, and preserved with benzalkonium chloride	0.03%	PoM	LUMIGAN	32	2.5 ml multi-use bottle

¹ also known as trometamol ² also known as carbopol ³ also known as Na cromoglycate

protein that can accumulate on the surface of soft contact lenses, and so reduce discomfort associated with a soiled lens.

This issue of buffer ingredients has been raised before with the inclusion of citrate in rewetting solutions to promote protein dissolution.¹ Further comparative studies with tromethamine would be useful. The hypromellose should provide some comfort as well.

The first generic carbomer gel, a true ocular lubricant,² for use in the management of dry eye is available, Carbomer gel (Figure 2). It is not a P Medicine, but is CE marked. The product is referred to by its chemical name, polyacrylic acid eye ointment, in the generic listings. As with other products with similar indications, it is the new carbomer 980 that is included (as opposed to the carbomer 934 that was once available in these ocular lubricants).

This new product is not recommended for use while wearing contact lenses, but its licence is 'to relieve eye discomfort and eye dryness in wearers and non-wearers of contact lenses'.

In time for the new allergy season, readers should note that the well-known P Otrivine-Antistine, listed in the College of Optometrists' Formulary, has been repackaged (Figure 3).

The same company has also introduced a completely new PoM option for manage-

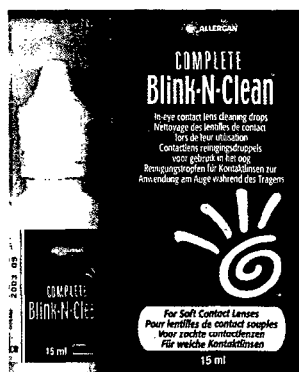


Figure 1. Re-wetting drops for soft contact lenses

ment of seasonal allergic conjunctivitis (SAC), namely ketotifen 0.025 per cent (as PoM Zaditen, Figure 4).

Ketotifen is not a new drug since it was assessed and introduced in the 1980s.³ It is presented as having three mechanisms by which it can reduce the signs and symptoms of SAC, namely as a histamine H_1 blocking drug, as a mast cell stabiliser and as an anti-eosinophil drug.³ More recent studies indicate that its affinity for H_1 receptors is the highest reported for topical ocular antihistamines, with an estimated K_i of around 1nM,⁴ although it is not as selective for H_1 receptors as some other drugs. Like another 'second generation' mast-cell stabiliser (ie lodoxamide),⁵ it is considered able to reduce histamine release from mast cells as well reduce eosinophil recruitment and activation (company literature), but neither of these other activities appear to be very substantial.⁶

Notwithstanding, as an antihistamine, it can produce substantial reduction in symptoms to an allergen challenge within minutes (company literature) and is considered as comparing very favourably to the use of two other topical ocular antihistamines, namely levocabastine, available as PoM Livostin and P Livostin Direct,⁷ and emedastine, available as PoM Emaxine.⁸

In the UK, ketotifen 0.025 per cent eyedrops are indicated for use on a *bds* basis, and the only real limitation is that the current licence is for individuals over 12 years of age. There are no limits to the time period over which it can be used.



Figure 2. Generic carbomer gel lubricant for dry eye



Figure 3. Topical decongestant/antihistamine for hay fever

When used as a 0.05 per cent solution (as available in the US), some 75 per cent of patients using the product reported adequate control of ocular itching and lacrimation within seven days, with the reduction in eye redness (hyperaemia) being slightly less.⁹

An issue that has arisen, especially in comparative studies, is whether the ketotifen eyedrops, presumably the vehicle

characteristics, are as comfortable (ie as based on the amount of stinging) as other products.^{10,11} It can be noted, however, that while some irritation can be expected, this is a general problem with many eyedrops and the reported effects with ketotifen eyedrops do not appear to be really clinically significant, for example causing very substantial numbers of patients to discontinue therapy.^{8,9}

Another sodium cromoglycate eyedrops product is available, P Vivicrom Eye Drops (Figure 5). As with similar products containing this first-generation mast-cell stabiliser, it is indicated for use for both seasonal and perennial allergic conjunctivitis, but not for contact lens wear-related conjunctivitis. It is noteworthy that the package insert stresses that the eye drops 'should be used every day during the hay fever season, even when you are not suffering from any symptoms'. This use should be on a *qds* basis.

With the new allergy season, for grass pollens etc, now under way, there has been a veritable explosion in the options available for oral antihistamines for seasonal allergic conjunctivitis; all of the new products contain cetirizine, a new

Corporate (co) identification for tables

1 Ciba Vision Ophthalmics 2 Typharm, 3 Rhone-Poulenc-Rorer, 4 Forley, 5 Martindale, 6 APS/Berk 7 C-Pharma, 8 Cox Pharms, 9 Hillcross Pharms, 10 Norton Healthcare, 11 Stevendent Healthcare, 12 Cusi, 13 Schering-Plough, 14 Dominion, 15 Distriphar, 16 Leo Pharms, 17 Wyeth Labs, 18 Chauvin, 19 Hoechst-Marion Roussel, 20 Crookes Healthcare, 21 Mentholatum, 22 Alcon, 23 Abbott, 24 Johnson & Johnson, 25 ASTA Medical, 26 Norton Consumer, 27 Boots, 28 Baker Norton Pharms, 29 NuCare, 30 Opus Pharms, 31 Genus Pharms, 32 Allergan, 33 Stafford-Miller, 34 Sussex Pharms, 35 Cross-Pharma, 36 NuMark, 37 Warner Lambert Consumer, 38 UCB Pharma, 39 Novartis Consumer Health, 40 Novartis Ophthalmics (Pharms), 41 Surgical Designs, 42 Bausch & Lomb Surgical, 43 Wellcome, 44 Regent Labs, 45 Merck Sharpe & Dohme, 46 Bioglan, 47 Generics UK, 48 Medeva-Pharma, 49 Pharmacia & Upjohn, 50 Mid-Optic, 51 Peach Ethical Pharmaceuticals, 52 Chrome-X, 53 Chemmedica, 54 Florizel, 55 Roche, 56 SSL, 57 Aventis Pharma, 58 Glaxo-Wellcome, 59 Lagap Pharma, 60 Spectrum Ophthalmics, 61 Vision Pharmaceuticals, 62 VXL, 63 Optecs (Euro), 64 Pharmacia, 65 Tubilux Pharma, 66 Pharma-Global, 67 GlaxoSmithKline Consumer, 68 Galpharm, 69 Celltech Pharms, 70 Pfizer Consumer Healthcare

TABLE 2. Changes in ophthalmic pharmaceuticals for UK (May 2002)

Drug name	conc	C	Pharmaceutical	co	Presentation
chloramphenicol	0.5%	PoM	SNO-PHENICOL	18	discontinued
betamethasone	0.1%	PoM	BETNESOL	69	10ml multi-use bottle now available again
betamethasone c neomycin	0.1% 0.5%	PoM	BETNESOL-N	69	10ml multi-use bottle now available again

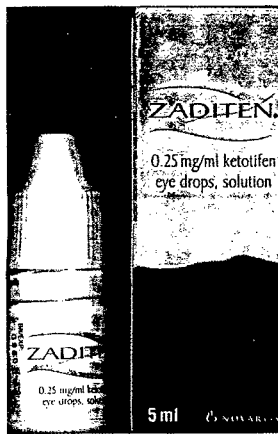


FIGURE 4. Topical antihistamine/mastocell stabiliser eye drops for hayfever

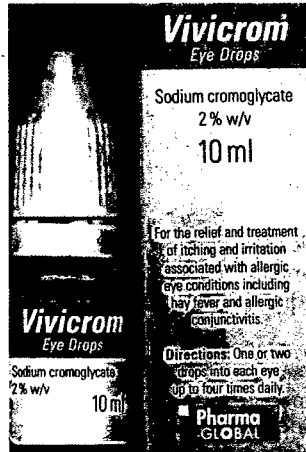


FIGURE 5. Sodium cromoglycate eyedrops for hayfever and perennial allergic conjunctivitis

generation 'non-drowsy' antihistamine.

These options are the direct result of further deregulation on the access to 'medicines' in that several of these can be added to the ever-growing list of GSL options being made available in small pack sizes of seven tablets.^{12,13}

Cetirizine, a histamine H₁-blocking drug, has a well-established efficacy in reducing the signs and symptoms of seasonal allergic conjunctivitis, as well as nasal symptoms.

Based on both patient reports and external eye assessments with grading schemes, cetirizine 10mg *qd* treatment can produce a clinically significant improvement,^{14,15} for example on ocular irritation, itching, lacrimation and conjunctival redness. Newer research indicates that sufficient quantities of cetirizine reach the tear film after oral administration (10mg BDS) to have an impact on polymorphonuclear leukocytes reacting at the conjunctival surface.¹⁶

The first two cetirizine products on the list should be noted carefully before jumping to conclusions about errors in the listings. Now available as both a P Medicine (30 tablets) and GSL (7 tablets) is Piriteze Allergy Tablets (Figure 6). The product contains cetirizine, and not as might be expected, the older generation antihistamine chlorpheniramine (as found in P Piriton, marketed by the same company).

As with the other products, they are not recommended for use by children under the age of 12 years, but some of the package inserts note that use in children between the ages of six and 12 years can be done under the supervision of a doctor. It is left to the reader to decide if 'doctor' would include one's 'eye doctor'.

A new option from the Benadryl line,

again containing cetirizine 10mg, has also been introduced as Benadryl One-a-day Allergy Relief (Figure 7). It should not be confused with Benadryl Allergy Tablets that contain acrivastine 1.3mg. Several generic options containing cetirizine are also now available. These are an addition to the

Pollonase line, namely P Cetirizine Hayfever Relief (Figure 8), and a completely new line from Galpharm, namely Hayfever and Allergy Relief (Figure 9). As with the first new option, the latter generic option is also available in a small pack size as a GSL product for the local supermarket.

At least two other generics for cetirizine, in pack sizes of 30 tablets, have also been

marketed (companies 6 and 46). For all these products, while there are still small print warnings about the possibility of drowsiness as an ADR, when used at the recommended doses cetirizine is considered to have a very low potential for such side effects.¹⁷ Notwithstanding, should optometrists be recommending the use of these products to their patients, time should still be given to consideration of ADRs, and even though some of them may well be attributable to the allergy condition itself,¹⁸ the anti-histamine could still exacerbate the patient's condition.

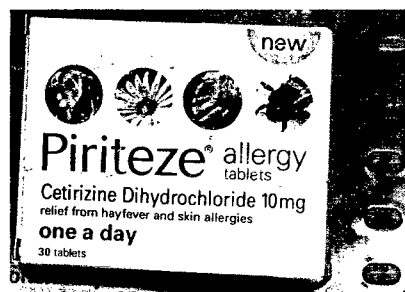


FIGURE 6: Branded cetirizine anti-allergy tablets for hayfever and perennial allergic conjunctivitis

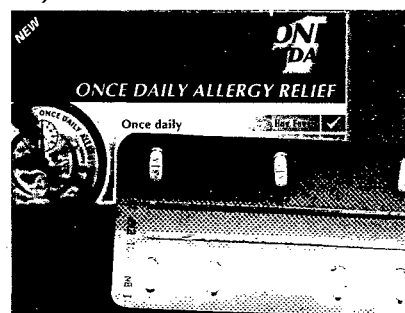


FIGURE 7: Branded cetirizine anti-allergy tablets for hayfever and perennial allergic conjunctivitis

A new option is available for timolol, a non-selective beta-blocker, for management of open-angle glaucoma. The new gel formulation, PoM Nyogel (Figure 10) has timolol 0.1 per cent in a carbomer gel-polyvinyl alcohol (PVA) mixture. The carbomer is carbomer 947P rather than 980 as used in dry-eye products.

This new timolol eye 'gel', also known as 'T-gel', is also different to the on-eye-setting gel used as the vehicle PoM Timoptol LA that contains timolol 0.5 per cent. The gellan gum (also known as Gelrite) solution which is the vehicle for Timoptol LA interacts with divalent cations in the tear film to produce a gel, an ophthalmic gel-forming solution or GFS.¹⁹

The new timolol gel works on a different principle by interacting with ocular surface mucins. The timolol itself is 'trapped' in the carbomer-PVA polymer and the interaction with the ocular surface, via mucins, is presented as a 'mucoadhesive' gel.²⁰

The idea behind the first gel-based ophthalmic timolol product (Timoptol LA or Timoptic XE outside of the UK), was to promote ocular contact time in order to increase ocular drug delivery so as to allow for routine once-daily dosing.²¹ An added benefit, partly related to the once-daily dosing, was that systemic cardiovascular effects might be slightly reduced.^{22,23} The new timolol 0.05 per cent ophthalmic gel, based on carbomer (polyacrylic acid polymer), has been reported to provide improved ophthalmic delivery in animal models.²⁴ In clinical trials on non-glaucomatous human eyes, the efficacy of T-gel 0.1 per cent as an ocular hypotensive agent has been reported to be equivalent to timolol 0.5 per cent.²⁵ As with the older timolol gel, the new product, PoM Nyogel, is indicated for once-daily use, preferably in the morning to hopefully avoid nighttime bronchial effects.

The limitation for use in asthmatics is well established, but it should be noted that the list of cardiovascular medications under (S/P) gets longer and longer and now specifically

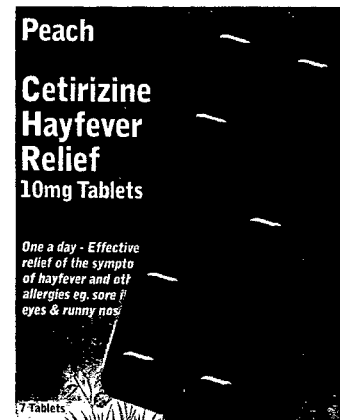


FIGURE 8: Generic cetirizine anti-allergy tablets for hayfever and perennial allergic conjunctivitis

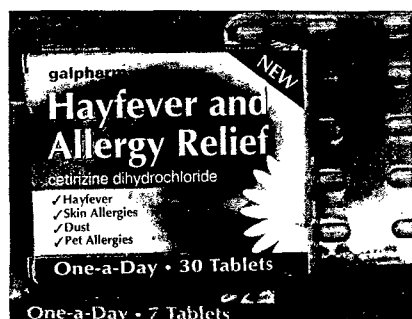


FIGURE 9. Generic cetirizine anti-allergy tablets for hayfever and perennial allergic conjunctivitis



FIGURE 10. New eye gel formulation of timolol for open-angle glaucoma

includes digoxin, adrenergic neurone blockers (such as reserpine), the calcium blockers used for angina or high blood pressure or Reynaud's syndrome (for example, nifedipine and verapamil), anti-arrhythmia drugs (eg quinidine and disopyramide), as well as other beta-blockers.

In summary, therefore, as with the use of other topical ophthalmic beta-blockers, the new timolol gel is generally not for use in patients with any form of significant bronchial or cardiovascular disease, but with the use of the gel formulation and the reduction in timolol concentration to 0.1 per cent, the chance of adverse reactions in those with borderline diseases of these types should be reduced. The outcome of substantial open-label clinical trials with PoM Nyogel on patients with glaucoma have yet to be published.

A third 'prostaglandin analogue' for open-angle glaucoma has been marketed, namely bimatoprost 0.03 per cent (0.3mg/ml) in PoM Lumigan (Figure 11). Its introduction will likely re-open the debate as to why different prostaglandin-type substances and/or drugs can have different effects on IOP.²⁶ The term prostaglandin analogue is presumably still

acceptable for the UK (since this is the term used in the latest edition of *MIMS*),²⁷ but this new drug is being referred to as a prostamide. The question to be asked is whether this distinction is important, or whether all three drugs (ie latanoprost, travaprost and bimatoprost) can all be considered together as 'new generation'

anti-glaucoma medications that improve aqueous outflow via the uveoscleral route.

Bimatoprost was developed as drug AGN 192024, and was originally presented as a unique class of drugs called OHLs (ocular hypotensive lipids).²⁸

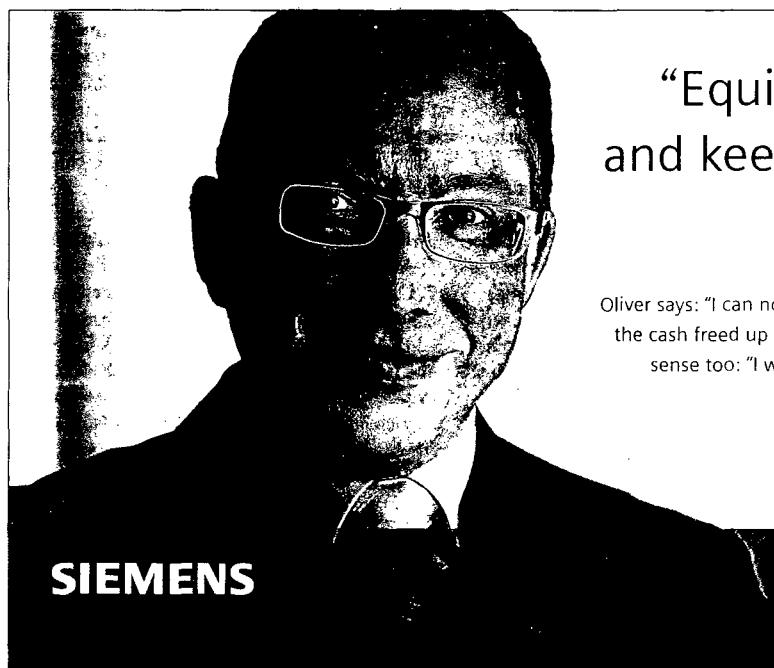
Company-supported pre-clinical evaluation literature appears to be at pains to point out further that bimatoprost should not be simply considered as

another alternative to the other prostaglandin analogues.²⁹ Firstly, unlike latanoprost (an isopropyl ester form of prostaglandin $F_{2\alpha}$), bimatoprost is not a pro-drug, ie it does not need to be converted from the ester into its active acid form once absorbed by the anterior segment tissues.

The ester derivatisation, however, provides improved corneal penetration.



FIGURE 11. Third option of a prostaglandin type drug for open-angle glaucoma



"Equipment finance is simple and keeps cash in the business."

*Oliver Judge, Optician
Siemens Financial Services customer*

Oliver says: "I can now afford to invest in the designer frames I need because of the cash freed up by finance." And choosing Siemens Financial services made sense too: "I was impressed by their service, rates and market know-how."

To find out how we can help your practice
Call now on: 0800 092 6451
www.siemensfinancialservices.co.uk

**Siemens
Financial Services**

Partner in creating value.

Bimatoprost actually is a synthetic phenyl derivative of a fatty acid amide rather than an ester, although both drugs are still 17-phenyl derivatives of prostaglandin $F_{2\alpha}$.^{26,29} The issue being raised is whether bimatoprost not only passively improves the non-conventional outflow facility (also now being referred to as the pressure-insensitive aqueous humour outflow pathway) but also has an ocular hypotensive effect that is proportionately larger for higher IOP values.^{28,29}

This latter phenomenon is being referred to as a pressure-sensitive aqueous humour outflow pathway that is indirectly linked to the resistance to outflow in relation to the actual aqueous production and flow rate. This new pathway is, however, largely theoretical and cannot be directly measured.²⁸ Time will tell as to whether this prostaglandin analogue, as with the others, will not only offer superior control of both daytime and nighttime IOP to topical ocular beta-blockers³⁰ but an even greater efficacy as a result of a dual effect on outflow.

Notwithstanding the likely confusion and controversy surrounding such a refinement of the possible mechanism of action of these types of drugs, the new drug is indicated for use as an option in management of open-angle glaucoma or ocular hypertension when other anti-glaucoma medications are either contraindicated (eg beta-blockers) or are failing to produce the desired effects on IOP. Bimatoprost can also be used in combination with topical ocular beta-blockers (timolol etc). It thus has the same status as the first prostaglandin analogue, latanoprost (PoM Xalatan) when it was introduced (although the indications for latanoprost have now been changed – see below).

In company-supported clinical trials, the efficacy of bimatoprost (AGN 192024) have been compared to placebo in non-glaucomatous eyes²⁸ and in patients with open-angle glaucoma or ocular hypertension.^{31,32} The latter studies have included comparisons with latanoprost 0.005 per cent *qd*,³¹ and to timolol 0.5 per cent *qd* or *bids*.³² The IOP lowering effects averaged between 25 and 35 per cent, making bimatoprost clinically comparable to the other prostaglandin analogues.³³

It was from these studies that it has been established that the recommended dosing, as with the other two drugs, is once-daily and preferably in the evening. It should be noted, however, that an (S/P) is asthma (respiratory impairment). This is mainly because there is inadequate data available on the use of this or other topical ocular prostaglandin analogues in asthmatic patients, and not because there is considered to be a substantial problem.^{33,34} The indications for use of the first prostaglandin analogue introduced for glaucoma, latanoprost (as PoM Xalatan) have now been revised for it to be used as

a first line option in management of open-angle glaucoma and ocular hypertension.

Acknowledgements

The author wishes to acknowledge the timely assistance from the various companies who have provided samples for review and answered questions.

REFERENCES

- 1 Hong B-S, Bilbault TJ, Chowhan MA *et al*. Cleaning capability of citrate-containing vs non-citrate containing lens cleaning solutions: An *in vitro* comparative study. *Int Contact Lens Clinics*, 1994; 21: 237-240.
- 2 Doughty MJ. *Drugs, Medications and the Eye*, 2002; 8th Edn (January). Smawcastellane Information Services, 23A Henry Bell St, Helensburgh G84 7HL, Scotland.
- 3 Mikuni I, Fujiwara T, Togawa K *et al*. Therapeutic effects of a new, anti-allergic ophthalmic preparation. *Tokai J Exp Clin Med*, 1982; 7: 279-294.
- 4 Sharif NA, Su SX, Yanni JM. Emedastine: A potent, high affinity histamine H_1 -receptor-selective antagonist for ocular use: Receptor binding and second messenger studies. *J Ocular Pharmacol*, 1994; 10: 653-664.
- 5 Bonini S, Schiavone M, Bonini S *et al*. Efficacy of lodoxamide eye drops on mast cells and eosinophils after allergen challenge in allergic conjunctivitis. *Ophthalmology*, 1997; 104: 849-853.
- 6 Yanni JM, Stephens DJ, Miller ST *et al*. The *in vitro* and *in vivo* ocular pharmacology of olopatadine (AL-4943A), an effective anti-allergic/antihistaminic agent. *J Ocul Pharmacol Ther*, 1996; 12:389-400.
- 7 Doughty MJ. Levocabastine, a topical ocular antihistamine available as a Pharmacy Medicine – a literature review. *The Pharmaceutical J*, 2002; 268: 367-370.
- 8 D'Arienzo PA, Leonardi A, Bensch G. Randomized, double-masked, placebo-controlled comparison of the efficacy of emedastine difumarate 0.05% ophthalmic solution and ketotifen fumarate 0.025% ophthalmic solution in the human conjunctival allergen challenge model. *Clin Ther*, 2002; 24:409-416.
- 9 Aguilar AJ. Comparative study of clinical efficacy and tolerance in seasonal allergic conjunctivitis management with 0.1 % olopatadine hydrochloride versus 0.05 % ketotifen fumarate. *Acta Ophthalmol Scand*, 2000; 78:52-55.
- 10 Artal MN, Luna JD, Discepolo M. A forced choice comfort study of olopatadine hydrochloride 0.1% versus ketotifen fumarate 0.05%. *Acta Ophthalmol Scand*, 2000; 78: 64-65.
- 11 Kurosawa A, Kuretake Y, Tachihara R *et al*. Comparison of eye irritation caused by seven antiallergic eyedrops (in Japanese). *Folia Ophthalmol Jpn*, 2001; 52: 220-223.
- 12 Medicines (Products other than veterinary drugs) (General Sale List) Amendment (No 2) Order 2001. SI 2001. No 4111.
- 13 *Chemist & Druggist* (2002), January 5, pp 6.
- 14 Davies BH. Prophylactic treatment of seasonal allergic rhinitis. *Clin Ther*, 1991; 13: 87-91.
- 15 Katalin S, Margit V, Follmann P *et al*. The role of cetirizine in the out-patient treatment of allergic conjunctivitis (in Hungarian). *Szemeszet*, 1993; 130: 111-113.
- 16 Kantar A, Oggiano N, Coppa GV *et al*. Cetirizine reduces the priming capacity on neutrophilic polymorphonuclear leukocytes of lacrimal fluid from subjects with allergic conjunctivitis after specific challenge.

Clin Drug Invest, 1997; 14: 346-352.

- 17 Volkerts ER, Van Willigenburg APP, Van Laar MW *et al*. Does cetirizine belong to the new generation of antihistamines? An investigation into its acute and subchronic effects on highway driving, psychometric test performance and daytime sleepiness. *Human Psychopharmacol*, 1992; 7: 227-238.
- 18 Spaeth J, Klimek L, Mösges R. Sedation in allergic rhinitis is caused by the condition and not by antihistamine treatment. *Allergy*, 1996; 51: 893-906.
- 19 Greaves JL, Wilson CG, Rozier A *et al*. Scintigraphic assessment of an ophthalmic gelling vehicle in man and rabbits. *Curr Eye Res*, 1990; 9: 415-420.
- 20 Krishnamoorthy R, Mitra AK. Mucoadhesive polymers in ocular drug delivery. In (Mitra AK, ed) *Ophthalmic Drug Delivery Systems*. Marcel Dekker Inc, New York, 1993, pp. 199-221.
- 21 Laurence J, Holder D, Vogel R *et al*. A double-masked, placebo-controlled evaluation of timolol in a gel vehicle. *J Glaucoma*, 1993; 2: 177-181.
- 22 Dickstein K, Hapnes R, Aarsland T. Comparison of aqueous and gellan ophthalmic timolol with placebo on the 24-hour heart rate response in patients on treatment for glaucoma. *Am J Ophthalmol*, 2001; 132:626-632.
- 23 Dickstein K, Aarsland T. Comparison of the effects of aqueous and gellan ophthalmic timolol on peak exercise performance in middle-aged men. *Am J Ophthalmol*, 1996; 121:367-371.
- 24 von der Ohe N, Stark M, Mayer H *et al*. How can the bioavailability of timolol be enhanced? A pharmacokinetic pilot study of novel hydrogels. *Graefes Arch. Clin Exp Ophthalmol*, 1996; 234:452-456.
- 25 Mayer H, von der Ohe N. Efficacy of a novel hydrogel formulation in human volunteers. *Ophthalmologica*, 1996; 210:101-103.
- 26 Camras CB, Bito LZ, Toris CB. Prostaglandins and prostaglandin analogues. In (Zimmermann TJ *et al* eds) *Textbook of Ocular Pharmacology*. Lippincott-Rave, Philadelphia, 1997; pp. 315-328.
- 27 MIMS (2002), May, pp. 14.
- 28 Brubaker RF, Schoff EO, Nau CB *et al*. Effects of AGN 192024, a new ocular hypotensive agent, on aqueous dynamics. *Am J Ophthalmol*, 2001; 131: 19-24.
- 29 Woodward DF, Krauss AH-P, Chen J *et al*. The pharmacology of bimatoprost (Lumigan TM). *Surv Ophthalmol*. 2001; 45 (suppl. 4):S337-S345.
- 30 Doughty MJ. Medicines Update for Optical Practitioners, Part 10. OPTICIAN, 2002; 223 (no 5839): p21-23.
- 31 DuBiner Hm Cooke D, Dirks M *et al*. Efficacy and safety of bimatoprost in patients with elevated intraocular pressure: A 30-day comparison with latanoprost. *Surv Ophthalmol*, 2001; 45 (suppl 4): S353-S360.
- 32 Brandt JD, VanDenburgh AM, Chen K *et al*. Comparison of once- or twice-daily bimatoprost with twice-daily timolol in patients with elevated IOP: a 3-month clinical trial. *Ophthalmology*, 2001; 108:1023-1031.
- 33 Alexander CL, Miller SJ, Abel SR. Prostaglandin analog treatment of glaucoma and ocular hypertension. *Ann Pharmacother*, 2002; 36:504-511.
- 34 *Medicines Compendium*. Datapharm Communications Ltd, 2002.

◆ Michael J Doughty is professor of ocular pharmacology and physiology at the Department of Vision Sciences Glasgow-Caledonian University. The author has no proprietary interest in any of the drugs mentioned.

Innopharma EX1032, Page 7