CATANIA, 3-4 febbraio 2014

I farmaci generici nel glaucoma: una nuova realtà su cui riflettere

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- European Advisory Board of Alcon and Allergan -AMO
- Speakers' bureau of Allergan, MSD and Alcon

Generic drugs in glaucoma therapy, a new reality to deal with

Clinical and Experimental Ophthalmology 2013;

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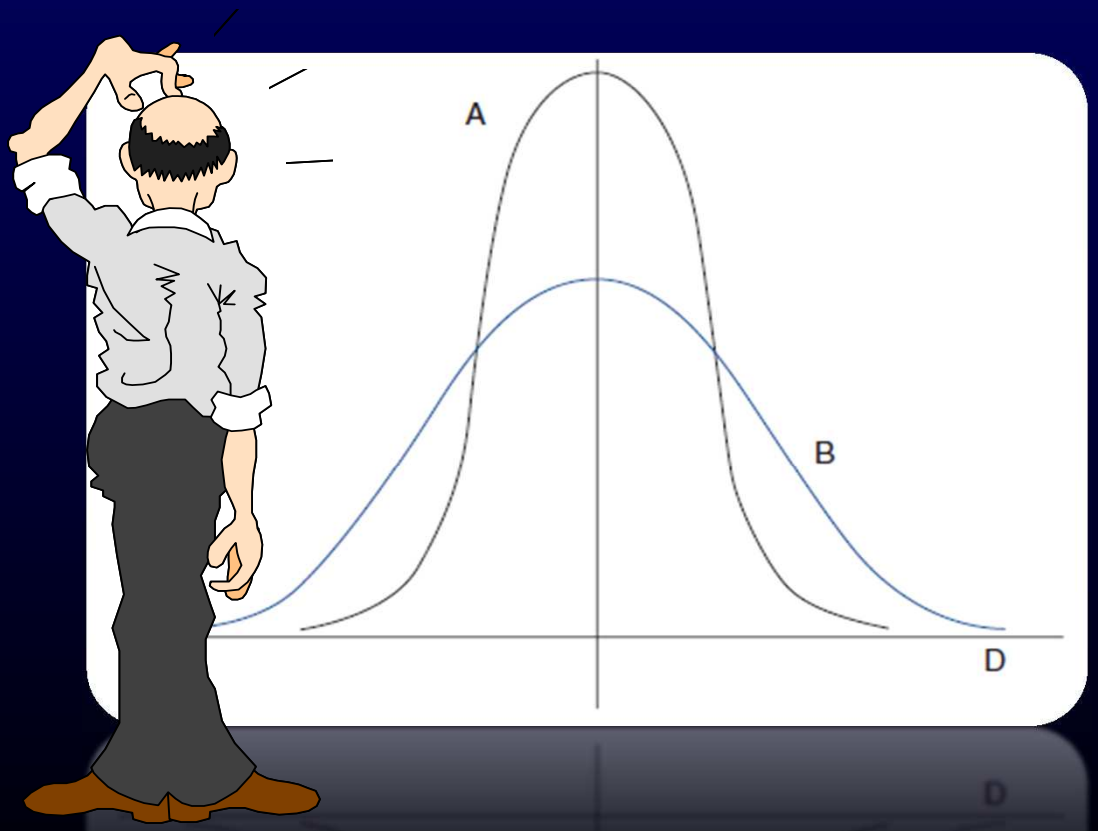


GENERICI

EQUIVALENTI

Vibrione !


Altri avvisi di reato a Napoli:
'diffusione colposa di epidemia'

Today's Treatment Algorithm - Choices*

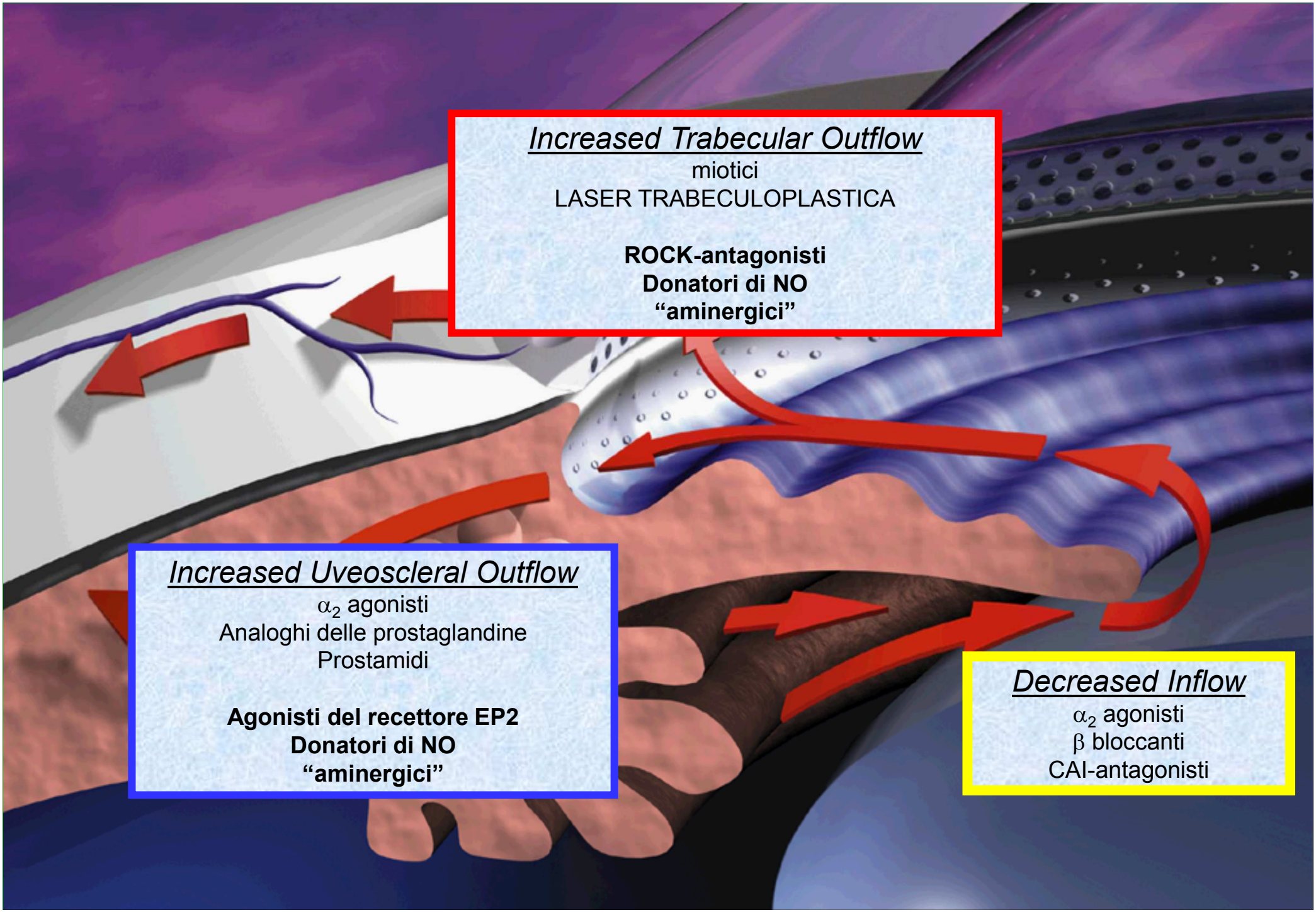
- 12 Beta-blocker options X 8 CAI's X 4 Lipids X 7 Adrenergic Agonists X 11 miotics

- For each class, patient is on one of the agents or not, so the number of choices per class is one more than the available number of agents in the class:

13 Beta-blocker options X 9 CAI's X 5 Lipids X
8 Adrenergic Agonists X 12 miotics = 56,160 - 1=

56,159 *ways to reach max. tolerated med. therapy*

**Editorial; "56,000 Ways to Treat Glaucoma" T. Realini, R. Fechtner, Opthalmology Nov. 11, 2002*


Increased Trabecular Outflow
miotici
LASER TRABECULOPLASTICA
ROCK-antagonisti
Donatori di NO
“aminergici”
Increased Uveoscleral Outflow
α_2 agonisti
Analoghi delle prostaglandine
Prostamidi
Agonisti del recettore EP2
Donatori di NO
“aminergici”
Decreased Inflow
α_2 agonisti
β bloccanti
CAI-antagonisti

Quality of Generic Ophthalmic Drugs

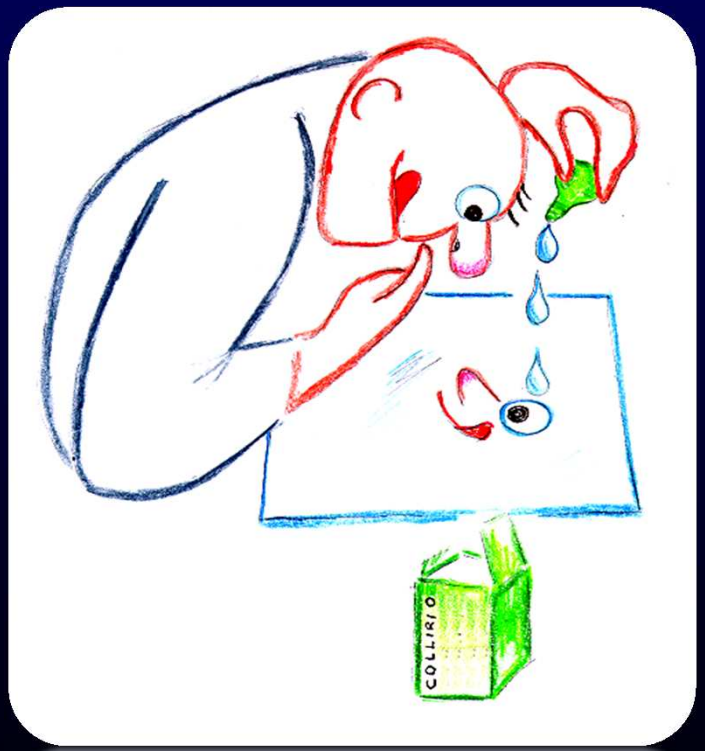
THE OCULAR SURFACE / JANUARY 2013, VOL. 11 NO. 1

GARY D. NOVACK, PHD

The relationship between the chemistry of the product, the pharmacokinetics, and the therapeutics might be viewed from a caffeine analogy in choice of coffee providers. Do Starbucks, Peet's and Kirkland coffee all have the same amount of caffeine? That is chemistry. Do the three brands produce similar maximal and total caffeine bloods levels? That is pharmacokinetics. Do the three brands produce similar increases in mental functioning? That is therapeutics.

Punti da chiarire :

- Il generico, che mi è stato prescritto, ha le identiche caratteristiche del “brand” ?

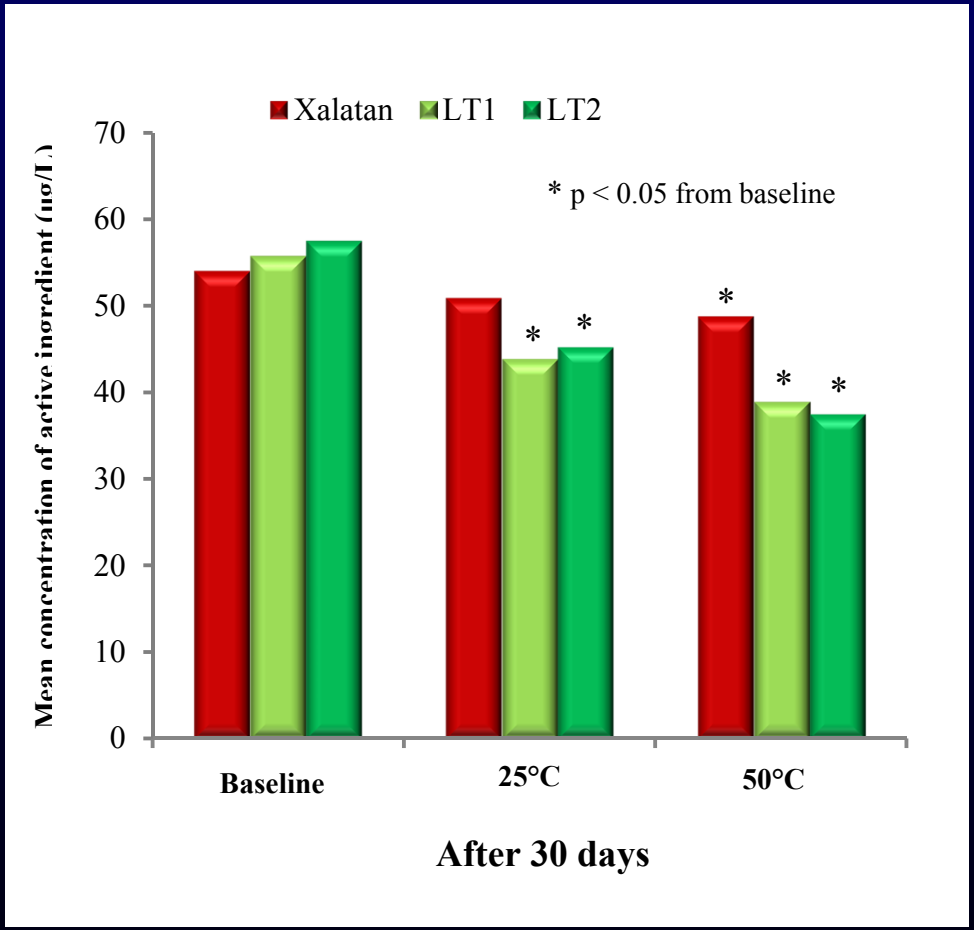


A Comparison of Active Ingredients and Preservatives Between Brand Name and Generic Topical Glaucoma Medications Using Liquid Chromatography-Tandem Mass Spectrometry

Malik Y. Kahook[1], Robert D. Fechtner[2], L. Jay Katz[3], Robert J. Noecker[4], David A. Ammar[1]

Curr Eye Res, Febuary 2012, Vol. 37, No. 2 , Pages 101-108

- Brand name formulations contained active ingredients and BAK in concentrations that were generally in agreement with their package inserts at baseline.
- The two generic formulations of latanoprost contained baseline levels of active ingredients that were 10% greater than their labeled value.
- Generic latanoprost formulations had significant loss of active ingredient concentration after exposure to 25°C and 50°C for 30 days.
- Both generic and brand name dorzolamide-timolol appeared relatively resistant to degradation. BAK concentrations remained stable at 25°C but decreased in some bottles at 50°C.
- Bottles of both generic medications had higher levels of particulate matter compared to brand name versions.



Comparative Evaluation of Physical Properties of 3 Commercially available Generic Brands of Latanoprost with Xalatan

Madhura Joag[1A], *Velpandian Thirumurthy*[1B], *Bhaskar Jha*[1A], *Anubha Rathi*[1A], *Meenakshi Wadhwani*[1A], *Tanuj Dada*[1A]. [A]Glaucoma Services, Dr R P Center for Ophthalmic Sciences, [B]Ocular Pharmacology, Dr R P Center for Ophthalmic Sciences, [1]All India Inst Of Med Sci, New Delhi, New Delhi, India.

Purpose: The aim of the study was to compare the eye drop volume dispensed, total number of drops dispensed per vial and physical properties (pH, density and relative viscosity of the drop) of 2.5ml vials of 3 commercially available brands of Latanoprost, with Xalatan.

Methods: At the standardized temperature of 25° C, drop size, pH, relative viscosity and total drops per vial were calculated for the four brands of Latanoprost. Drop size was measured by weighing 10 drops individually from 5 different vials of each brand. An average of the values for each experiment was calculated. pH estimation was done by automated pHmeter and Relative Viscosity was calculated by taking an average of three readings using Oswaldt's Viscometer. On basis of the above values, estimated absolute drug concentration per drop was derived. ANOVA was used to compare between the parameters of the 3 brands and xalatan.

Results: There was a significant difference in the mean drop size and number of drops per bottle of each generic brand as compared to Xalatan ($p < 0.001$) The physical properties and absolute drug concentration also varied significantly between the 3 generic brands as compared to Xalatan (Table)

Conclusions: Significant differences were been found between the drop size, number of drops per bottle and physical properties of 3 generic commercially available brands of Latanoprost as compared to Xalatan. This study underscores the unmet need for a better quality control in the production of generic prostaglandin analogues and has implications for the IOP lowering efficacy, adverse effect profile and cost of glaucoma therapy with these drugs.

Drug	Viscosity (Poise)	pH	Specific Gravity	Amount of solution per bottle (ml)	Number of drops per bottle	Mean drop size (µl)	µg of absolute drug per drop
Xalatan	1.075	6.61	1.02	2.91	107.58	26.5	1.33
Brand 1	1.043	7	0.95	2.58	85.17	31.8	1.59
Brand 2	1.085	6.61	1.03	2.33	97.39	23.5	1.17
Brand 3	1.049	6.6	1.03	3.20	117.25	26.6	1.33

Commercial Relationships: **Madhura Joag**, None; **Velpandian Thirumurthy**, None; **Bhaskar Jha**, None; **Anubha Rathi**, None; **Meenakshi Wadhwani**, None; **Tanuj Dada**, None

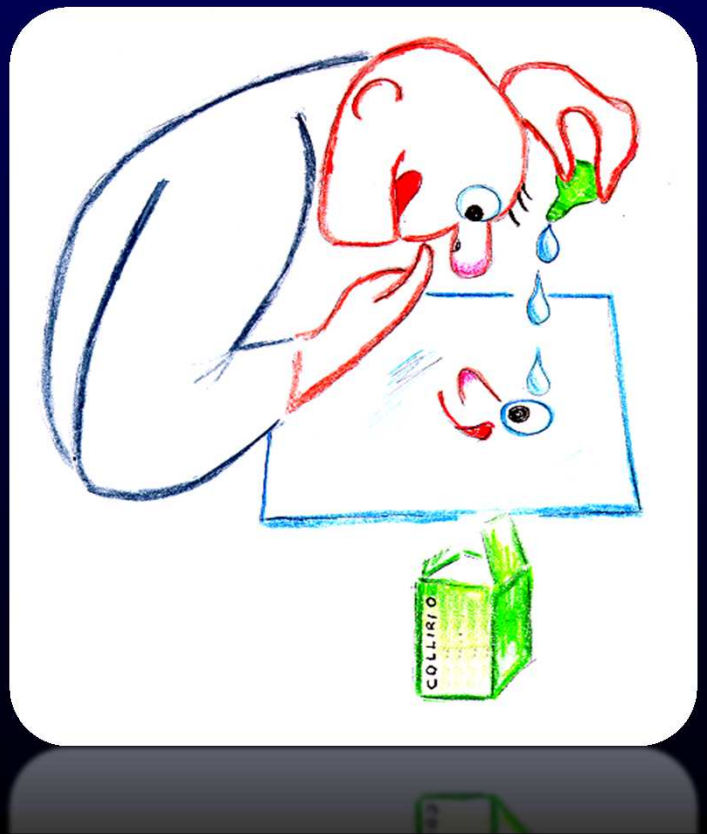
Support: None

ARVO 2012

Cortesia del Dr. De Natale

Punti da chiarire :

- Del generico, che mi è stato prescritto, ne entrerà nel mio occhio la stessa quantità del “brand” ?

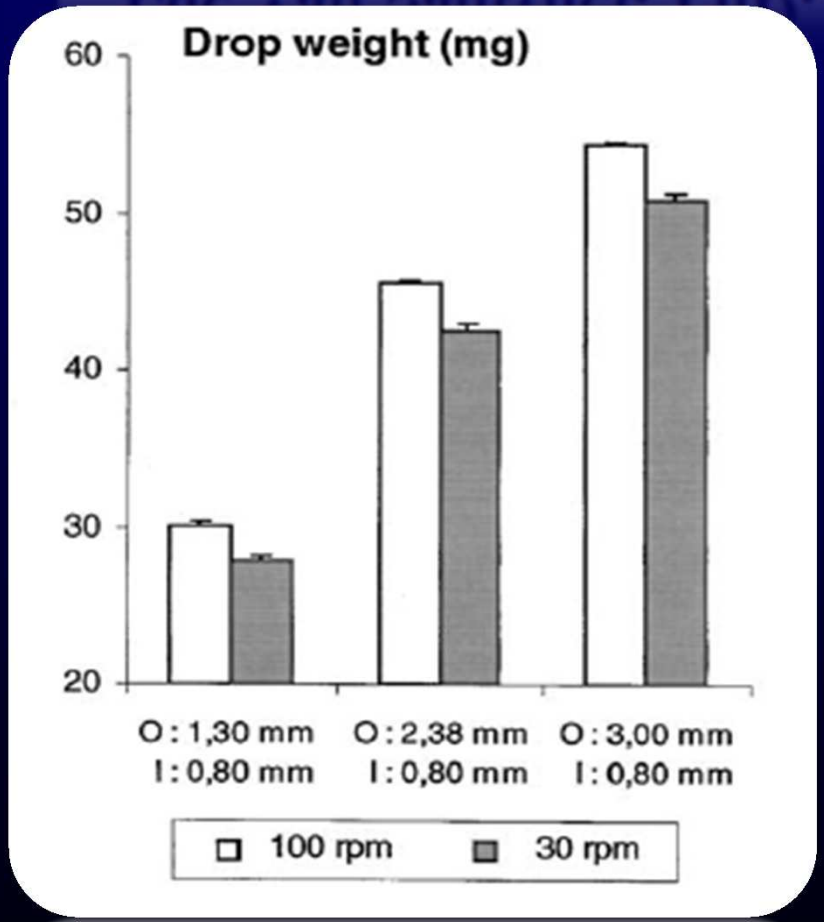


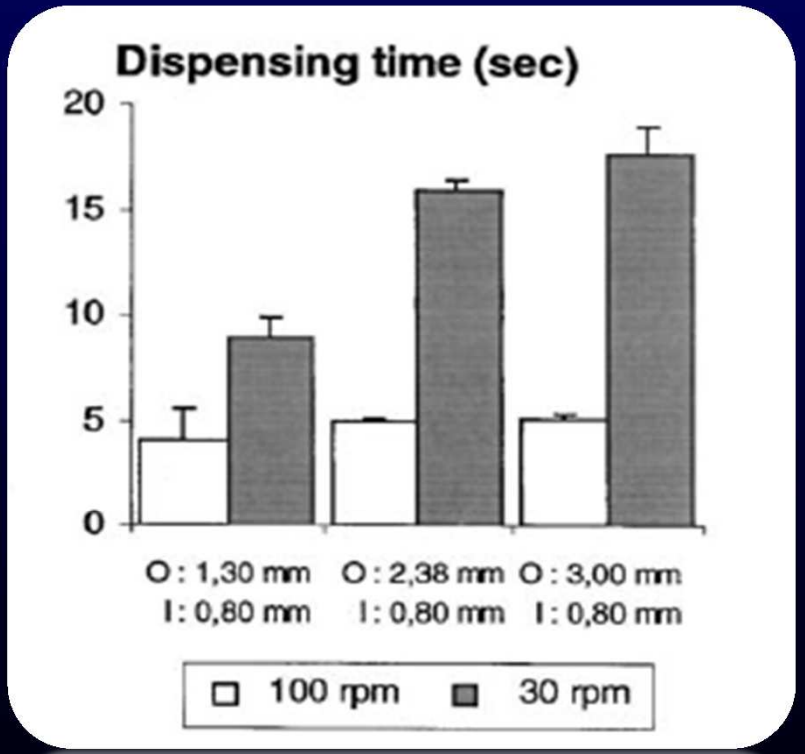
LINK VIDEO

SURVEY OF OPHTHALMOLOGY VOLUME 49 • NUMBER 2 • MARCH–APRIL 2004

Determinants of Eye Drop Size

Luc Van Santvliet, PhD, and Annick Ludwig, PhD





SURVEY OF OPHTHALMOLOGY VOLUME 49 • NUMBER 2 • MARCH–APRIL 2004

Determinants of Eye Drop Size

Luc Van Santvliet, PhD, and Annick Ludwig, PhD

TABLE 1

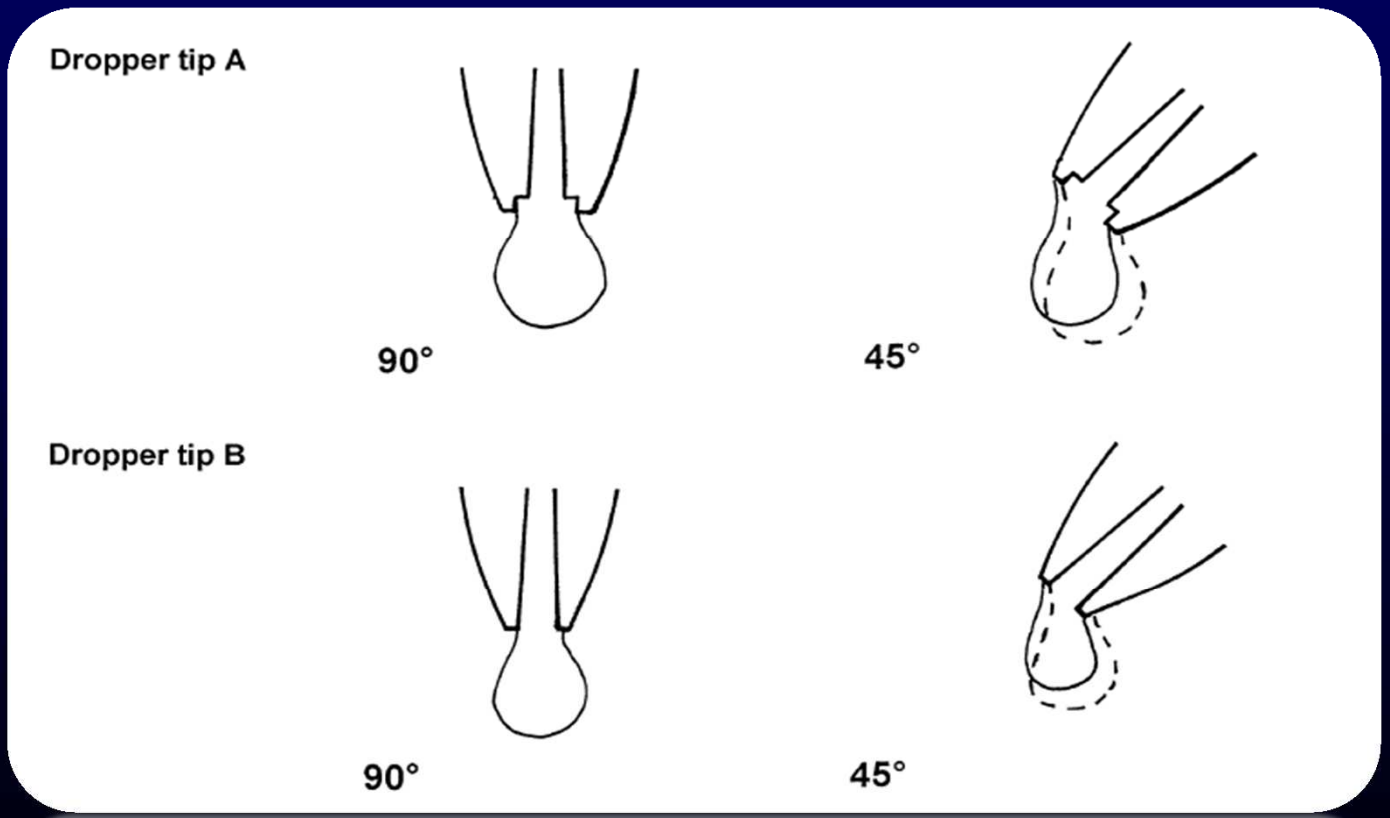
Effect of Surface Tension on Drop Size from a Plastic Dropper Bottle

Solution		Surface tension (mN/m)	Drop volume (µl ± SD)
Phosphate buffer solution pH 7.4		71.9	43.57 ± 0.48
Drugs			
Tetracaine HCl	16.6 mM	50.5	33.85 ± 0.27
Preservatives			
Phenylmercuriborate	0.002%	73.1	43.90 ± 0.16
Chlorobutanol	0.5%	53.1	34.11 ± 0.31
Benzalkonium chloride	0.01%	45.0	31.52 ± 1.17
Viscolyzers			
Hydroxyethylcellulose (Natrasol 250G)	1%	63.9	40.26 ± 0.61
Hydroxypropylcellulose (Klucel G)	1.2%	41.7	28.29 ± 0.65
Penetration enhancers			
Polysorbate 80	0.01%	63.0	39.81 ± 0.21
Tyloxapol	0.1%	46.6	37.32 ± 0.90
Polidocanol	0.1%	32.0	25.07 ± 0.83

SURVEY OF OPHTHALMOLOGY VOLUME 49 • NUMBER 2 • MARCH–APRIL 2004

Determinants of Eye Drop Size

Luc Van Santvliet, PhD, and Annick Ludwig, PhD



SURVEY OF OPHTHALMOLOGY VOLUME 49 • NUMBER 2 • MARCH–APRIL 2004

Determinants of Eye Drop Size

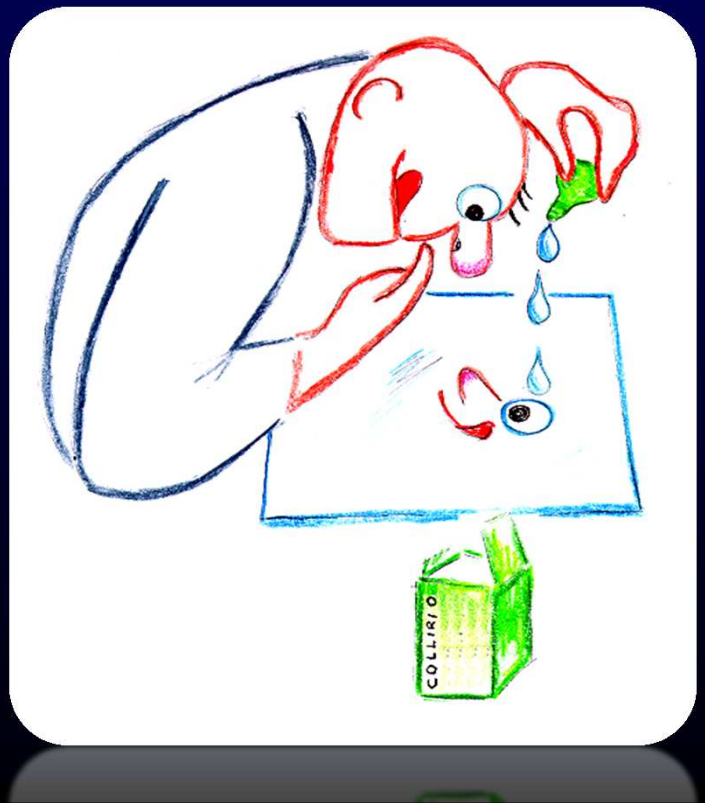
Luc Van Santvliet, PhD, and Annick Ludwig, PhD

Conclusions

Dropper tips should deliver small-volume eye drops. The ideal dropper tip consists of a small diameter outer orifice with a design clearly defining the surface area from which the drop will fall. By adding to the formulation an agent that reduces surface tension, the manufacturer can further reduce drop size. Increasing the solution's viscosity up to 15 mPa·s does not increase drop size. The patient can help minimize drop size by holding the dropper bottle as vertically as possible. Squeezing the bottle gently and slowly induces a low drop formation rate, ensuring that only one drop of the medication will be formed, and that that drop will have a reduced volume. Alternative administration techniques and aids can be recommended to patients encountering difficulties with instilling eye drops.

Punti da chiarire :

- Il generico, che mi è stato prescritto, funzionerà , su di me, allo stesso modo del “brand” ?



Latanoprost 0.005% test formulation is as effective as Xalatan® in patients with ocular hypertension and primary open-angle glaucoma.

Eur. J. Ophthal., 2012 Jan-Feb;22(1):19-27.

Allaire C, Dietrich A, Allmeier H, Grundmane I, Mazur-Piotrowska G, Neshev P,Kahle G.
Author information: European Pharmaceutical Clinical Sciences, Bausch & Lomb, Evry, France.
catherine.allaire@bausch.com

- **PURPOSE:**
- To determine if a test formulation of latanoprost 0.005% (Bausch & Lomb) eyedrops reduced intraocular pressure (IOP) as well as Xalatan® (latanoprost 0.005%) in patients with ocular hypertension (OH) or primary open-angle glaucoma (POAG).
- **METHODS:**
- This multicenter, randomized, investigator-masked, parallel-group study allocated **266 patients** with OH or POAG in a 1:1 ratio to latanoprost or Xalatan administered once daily for 6 weeks. The primary endpoint was the mean change in 8:00 AM IOP of the study eye from baseline to week 6. Secondary endpoints included mean change in 8:00 AM IOP from baseline to week 2, and in 12:00 noon and 4:00 PM IOP from baseline to week 2 and week 6. The safety and tolerability of both drugs were also assessed.
- **RESULTS:**
- Both study groups had comparable demographics and baseline characteristics. The mean (SD) change in 8:00 AM IOP from baseline to week 6 was -7.29 (2.61) and -7.54 (2.80) mmHg with latanoprost and Xalatan, respectively. Latanoprost was found noninferior to Xalatan in the primary analysis (mean [SEM] treatment difference, 0.252 [0.504] mmHg; 95% confidence interval [CI] -0.408, 0.913; p = 0.0001; noninferiority margin, 1.5 mmHg) and met the predefined definition of equivalence to Xalatan (95% CI within [-1.5, 1.5 mmHg] margin). The IOP-lowering effects of latanoprost and Xalatan were comparable at all assessed time points. Both study treatments demonstrated a comparable safety and tolerability profile.
- **CONCLUSIONS:**
- Bausch & Lomb latanoprost 0.005% is clinically equivalent to Xalatan for treating OH and POAG as demonstrated through this unique comparative trial.

An Evaluation of Therapeutic Noninferiority of 0.005% Latanoprost Ophthalmic Solution and Xalatan in Patients With Glaucoma or Ocular Hypertension

Maurizio Digiuni, MD, Gianluca Manni, MD,† Michele Vetrugno, MD,‡ Maurizio Uva, MD,§ Giovanni Milano, MD,‖ Nicola Orzalesi, MD,* Paolo Fogagnolo, MD,¶ Marco Centofanti, MD,†¶ Emilio Campos, MD,# and Luca Rossetti, MD**

(*J Glaucoma* 2013;22:707–712)

TABLE 4. IOPs During the Trial

	Latanoprost*, N = 91	Xalatan, N = 93	*P*
Baseline			
Mean (SD)	22.8 (1.90)	22.8 (1.80)	0.8
Range	17.8-29.1	17.7-28.5	—
9 AM, mean (SD)	23.5 (1.92)	23.4 (1.83)	0.8
1 PM, mean (SD)	22.8 (2.24)	22.8 (2.00)	0.9
5 PM, mean (SD)	22.4 (2.31)	22.2 (2.32)	0.7
12 weeks			
Mean (SD)	16.6 (2.31)	16.5 (2.45)	0.8
Range	11.0-24.0	11.3-24.7	—
9 AM, mean (SD)	16.7 (2.33)	16.3 (2.46)	0.4
1 PM, mean (SD)	16.5 (2.25)	16.6 (2.57)	0.8
5 PM, mean (SD)	16.2 (2.29)	16.4 (2.74)	0.6

Comparison of intraocular pressure in glaucoma subjects treated with Xalatan® versus generic latanoprost

ACTA OPHTHALMOLOGICA 2013

Patrick Egan,[1] Alon Harris,[1] Brent Siesky,[1] Leslie Abrams-Tobe,[1] Austin L. Gerber,[1] Joshua Park,[1] Steven Holland,[1] Nathaniel J. Kim[1] and Ingrida Januleviciene[2]

Table 1. p-values of paired t-tests comparing differences in IOP drop between subsequent measurement trials respective to each drug's effect on each eye

	8 am versus 12 noon	12 noon versus 4 pm	4 pm versus 8 pm
Xalatan® (OD)	0.183	0.319	0.006*
Xalatan® (OS)	0.519	0.023*	0.582
Generic (OD)	0.825	0.103	0.084
Generic (OS)	0.783	0.144	0.012*

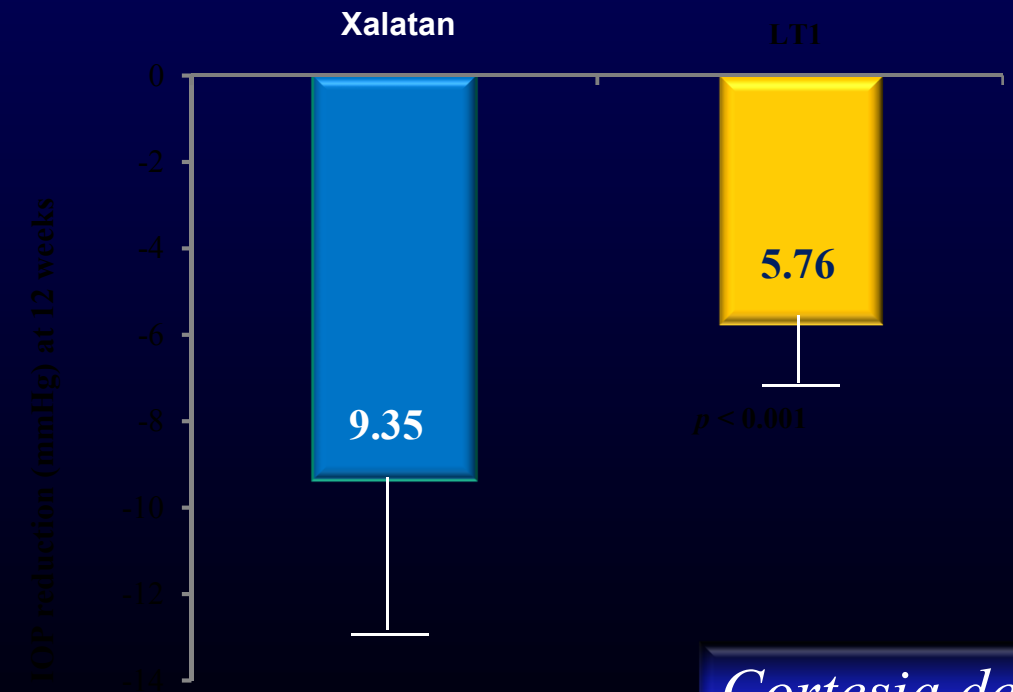
OI
* T

prost. Additionally, Xalatan® induced a significantly greater number of IOP reductions below 14 mmHg than generic latanoprost ($p = 0.013$). Drug tol-

A randomized, crossover, open label pilot study to evaluate the efficacy and safety of Xalatan in comparison with generic Latanoprost (Latoprost) in subjects with primary open angle glaucoma or ocular hypertension

Narayanaswamy et al. IndianJ Ophthalmol 2007;55:127–31.

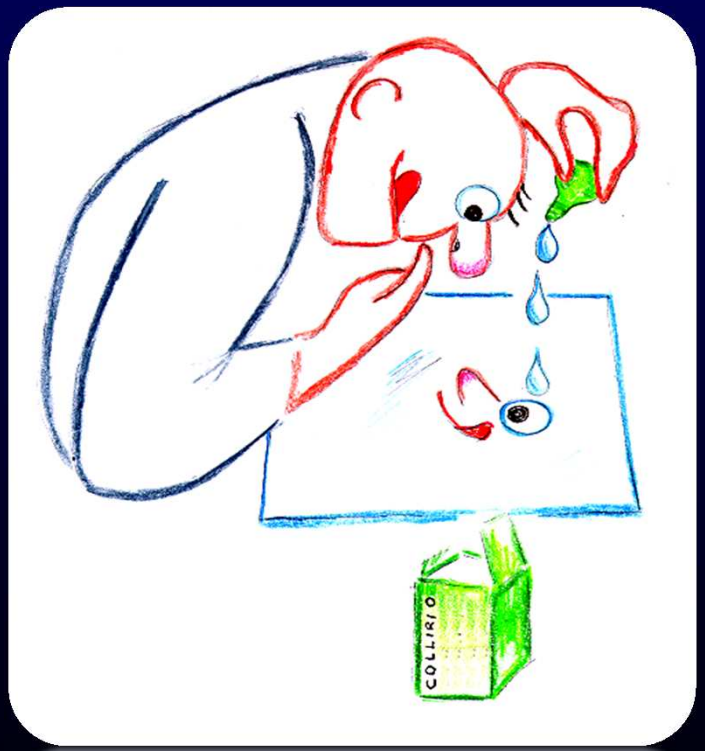
IOP reduction of Xalatan vs generic latanoprost[1]



Cortesia del Dr. De Natale

Punti da chiarire :

- Il mio medico, può scegliere quale generico darmi ?



Prescrizione dei farmaci equivalenti

A far data dal 15 agosto 2012, **il medico** che curi un paziente **per la prima volta**, per una patologia cronica, ovvero, per un nuovo episodio di patologia non cronica, per il cui trattamento sono disponibili più medicinali equivalenti:

1. è tenuto ad indicare nella ricetta SSN **la sola denominazione del principio attivo** (accompagnata ovviamente dagli altri elementi identificativi: dosaggio, forma farmaceutica e, se necessaria, via di somministrazione). Tale indicazione è necessaria e sufficiente ai fini della spedizione della ricetta con onere a carico del SSN e va riportata solo per i medicinali per cui è scaduto il brevetto (per i medicinali a brevetto ancora valido, il medico continuerà ad indicare nella ricetta esclusivamente il nome commerciale del medicinale);
2. ha facoltà di aggiungere all'indicazione del principio attivo, sempre obbligatoria, **la denominazione di uno specifico medicinale** a base dello stesso principio attivo. Tale indicazione non è tuttavia vincolante per il farmacista;
3. può infine indicare, oltre alla denominazione del principio attivo e dello specifico medicinale, **la dicitura "non sostituibile", corredata obbligatoriamente da una sintetica motivazione** riportata in ricetta, che ne giustifichi tale scelta. Tale indicazione è vincolante per il farmacista.

Cortesia del Dr. De Natale

Modalità di prescrizione e dispensazione di farmaci a carico del SSN

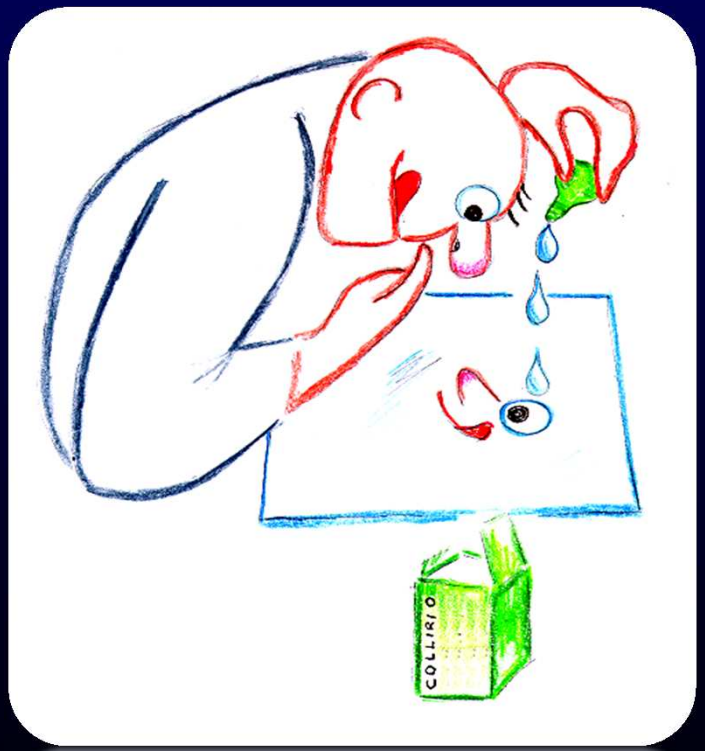
	Clausola di non sostituibilità indicata in ricetta	Medico	Farmacista
Prima prescrizione per patologia cronica o acuta	NO	▪ indicazione nella ricetta del solo principio attivo accompagnato da altri elementi identificativi del medicinale (es. dosaggio e forma farmaceutica); ▪ indicazione oltre che del principio attivo (sempre obbligatorio), anche della specialità o del medicinale con denominazione generica da consegnare al paziente (non vincolante per il farmacista).	⇒ consegna al paziente del medicinale con il prezzo più basso. [*]
	SI	▪ indicazione oltre che del principio attivo (sempre obbligatorio), della specialità o del medicinale con denominazione generica da consegnare al paziente, anche dell'indicazione della motivazione della *"non sostituibilità"*.	⇒ consegna al paziente del medicinale specificato in ricetta. L'eventuale differenza dal prezzo di riferimento è a carico dell'assistito.
Prosecuzione di terapia già in atto per patologia cronica	NO	▪ indicazione nella ricetta della specialità o del medicinale con denominazione generica.	⇒ consegna al paziente del medicinale con il prezzo più basso. [*]
	SI	▪ indicazione della specialità o del medicinale con denominazione generica da consegnare al paziente.	⇒ consegna al paziente del medicinale specificato in ricetta. L'eventuale differenza dal prezzo di riferimento è a carico dell'assistito.

[*] *Resta ferma la possibilità da parte dell'assistito di chiedere al farmacista un corrispettivo farmaco a prezzo più alto assumendosi l'onere della differenza dal prezzo di riferimento.*

Cortesia del Dr. De Natale

Punti da chiarire :

- …per non parlare di …..



DRUG THERAPY

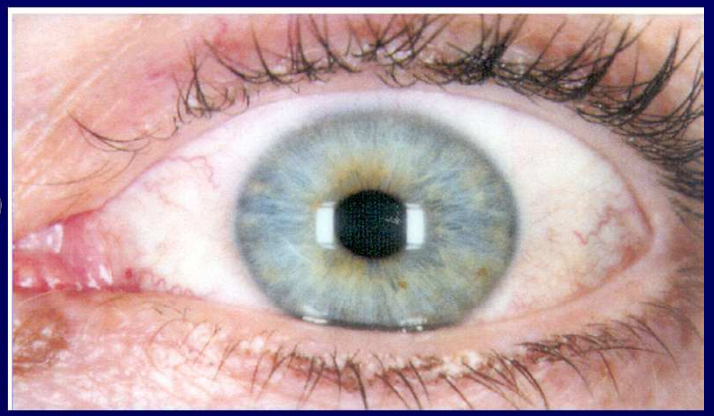
Adherence to Medication

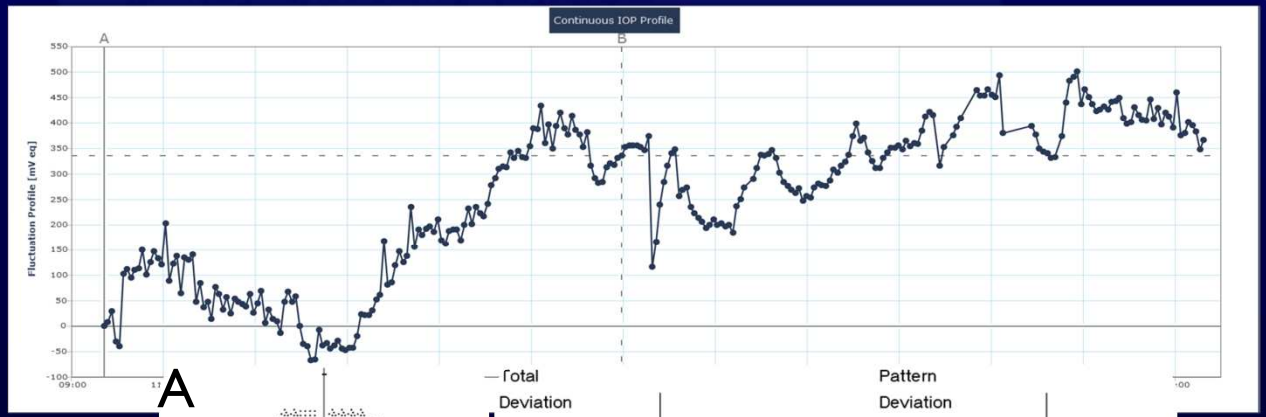
Lars Osterberg, M.D., and Terrence Blaschke, M.D.

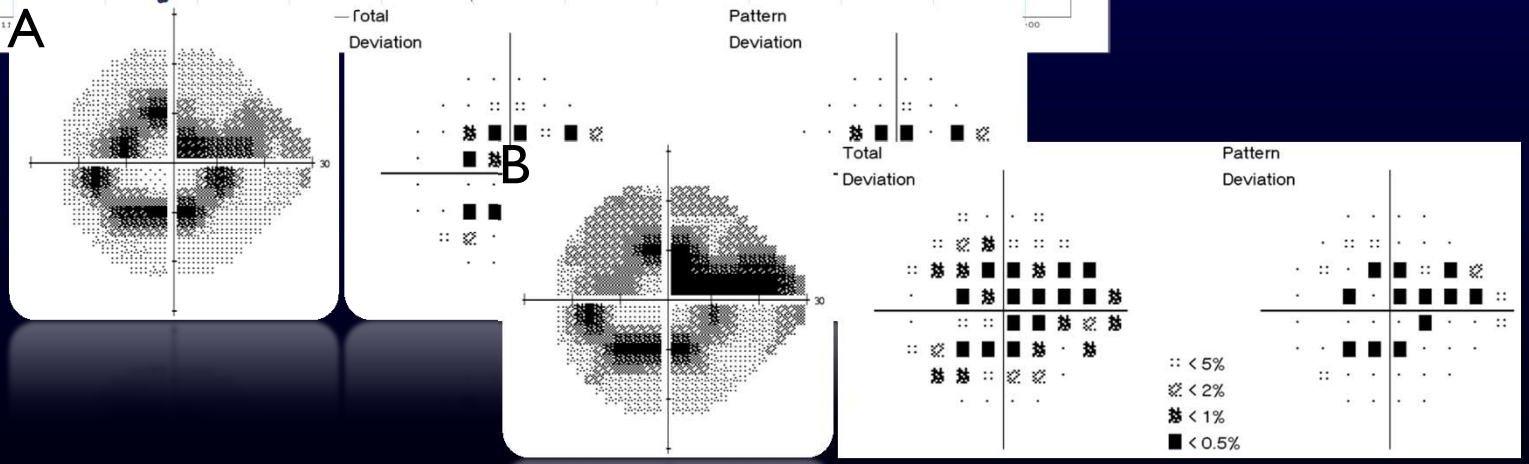
N Engl J Med 2005;353:487-97.

Drugs don't work in patients who don't take them.

— C. Everett Koop, M.D.







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Research in Social and
Administrative Pharmacy 8 (2012) 574–578

RESEARCH IN SOCIAL & ADMINISTRATIVE PHARMACY

Research Briefs

Generic medications for you, but brand-name medications for me

Amy J. Keenum, D.O., Pharm.D.[a,*], Jennifer E. DeVoe, M.D., D.Phil.[b], Deena J. Chisolm, Ph.D.[c], Lorraine S. Wallace, Ph.D.[d]

[a]*Department of Family Medicine, University of Tennessee Graduate School of Medicine, 1924 Alcoa Highway, U-67, Knoxville, TN 37920, USA*

[b]*Department of Family Medicine, Oregon Health & Science University, Portland, OR 97239, USA*

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[d]*Department of Family Medicine, The Ohio State University, Columbus, OH 43201, USA*

Concludendo….

GRAZIE !