Generics are Cheaper and Just as Effective

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Disclosures

• No current pharmaceutical industry connections
• Data & Safety Monitor for Cypass - Chair - Transcend Medical
  • (now Alcon Surgical with no current connection)
• Sight Sciences - Unpaid consultant

In this season of often highly emotional opinions, it is wise to consider that there may be multiple ways of looking at each situation.

Generic Drug

• Same active ingredient(s)
• Purity
• Sterility
• Approved by FDA for same indication
• Does not require same safety and efficacy clinical studies as original branded agent (as much as $100 million)
**US FDA Requirements for Generic Drug**

- For solutions, same active and inactive ingredients
- For generic eye drop solutions since 1992: exact same ingredients as original branded agent
- Same strength, concentration (+5%)
- Same dosage form(s)
- Same routes of administration
- Same labelling
- Same indications
- Since 1992, for generic glaucoma suspensions, gels, emulsions, ointments, whose original medication was introduced after 1962, therapeutic equivalence (+1.5mm Hg at all 4 diurnal time points at all 4 measurement days up to 12 weeks) in randomized control trial
- N.B. generics from other countries may not adhere to these rather stringent requirements

**What Can be Different?**

- Excipients (except eye drops)
  - Excipients can be an important part of drug efficacy, absorption, side effects
  - Excipients could (at least theoretically) interfere with pharmacodynamics or pharmacokinetics of active agents
  - Almost all use BAK as preservative
- Bottles
- Plastic - physical or chemical properties
- Size of drop delivered

**What about Efficacy and Tolerance**

- In Korean study of branded dorzolamide/timolol fixed combination (Cosopt) vs generic dorzolamide/fixed combination
  - 112 patients switched from branded to generic dorzolamide/timolol
  - IOP at various time points up to 12 weeks same
  - Side effects and tolerance same
- In Lithuania/U Indiana study, no difference in diurnal IOP values between generic and branded latanoprost at 4 weeks. However, branded drug had a few more patients whose IOP was under 14mm Hg. Generic drug was not US FDA approved.
- Indian studies have shown significant variation in Indian generic latanoprost in chemistry and efficacy.

**UCSF Study**

- Retrospective study
- IOP increased by about 1mm Hg when company decreased branded dosage of bimatoprost from 0.03% to 0.01%
- IOP decreased from baseline by an average 1 mm Hg when patients switched from bimatoprost 0.01% to generic bimatoprost 0.03%
What About Cost?

- Cost per bottle
  - Does not take into account drop size or size of fill
- Best is cost per unit time (e.g. day, month or year)
  - In England, 3 year study total costs
    - Branded glaucoma = £1000 > Generic per year
  - In U.S. for latanoprost
    - Branded $1198, Generic ~$200 (takes into account fill size and drop size)
- US vs Canada
  - Branded glaucoma medication study
    - US brand on average 4x Canadian wholesale prices
    - US generic about same as Canadian
    - From 2006-2013, US wholesale brand prices increased 29-349%; Canadian brand wholesale prices increased slightly 9-16%.
    - US Generic wholesale prices increased 23-58%, generic Canadian prices decreased -38-0%.

Do Costs Affect Behavior?

- U Michigan study of 8500 patients
- Compared to patients switching to generic latanoprost, patients who continued brand name PGA’s were 28% LESS likely to improve adherence and 39% MORE LIKELY to have reduced adherence.
- Reduced co-pay was associated with improved adherence
- 7% discontinued all glaucoma meds after introduction of generic latanoprost into regimen.

Cost Important for Adherence

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Less Important ———> More Important

Generics are used Commonly

- Prostaglandins Most Common Primary Drug for POAG
  - Prostaglandin analogues: 61%
  - Bimatoprost: 23%
  - Latanoprost: 22%
  - Combiphas: 18%

- Generics are used more commonly to start
  - Monthly: 48%
  - Monthly: 46%
  - Combination: 50%
Interesting Tidbits

• Some generic drugs are made by the branded manufacturer and are exactly the same
  • E.g. Xalatan and Greenstone latanoprost
• Some generic bottles use a “floppier” or stiffer plastic than the branded agents and so may administer too many or not enough drops with each squeeze. If more drops, the bottle may run out sooner than insurance allows replacement. If less drops or stiffer plastic, patient may miss eye more often and get less efficacy.
• Bottle shape, size and stiffness may be easier or more difficult for some patients especially with arthritis or tremor
• Retail price of drug is complicated
  • Pharmacists get rebates from pharm mfrs
  • Pharmacists may get incentives from insurers for generics
• These rebates rarely get passed on to patients
• Occasionally savings from generics may be small

More interesting Tidbits

• 66% of eye care drugs are generic
• Eyecare practitioners are MORE likely to prescribe BRANDED products than other doctors.

What About Preservative-Free Drops?

• Theory: Preservatives have negative effect on ocular surface
• Reality:
  1. The vast majority of patients tolerate BAK quite well.
  2. RCT clinical studies fail to prove any efficacy in improving OSD with “kinder preservatives”
    • Whitson JT: Oc Pharm Ther 2010
    • Dubiner, Hubatsch: BMC Ophthalmol 2014
  3. Or Preservative free
    • Cucherat, M: J Glaucoma, 2014 23:69-75
    • Day et al: BJO 2013 97:989-93

Summary I

• Generic eyedrop formulations in the US MUST by FDA rule have exactly the same chemical formulation both as to drug, preservative and excipients as the original branded drug or a fully tested drug
• The generic drug, if a suspension, ointment, gel, etc., must show similar diurnal IOP control to branded drug up to 12 weeks in an RCT
• The side effect profile must be similar
• Most independent studies show similar clinical efficacy, safety and patient tolerance
• Generic drugs can be up to 6 times less expensive than the branded one
• Lower costs may be associated with better adherence
  • (although 1 in 14 inexplicably may stop taking drops altogether after being switched to generic)
Summary II

• Therefore, in most cases, generic anti-glaucoma drugs are equivalent in efficacy and safety to branded agents.
• Cost is an important issue and should be considered in making medication Rx decisions.
• As always, the patient’s informed opinions need to be included in the decision making process.
• Also, there are always exceptions, so each patient should be monitored for potential idiosyncratic response. A small percent of patients may benefit from PF formulations. Treatment should be individualized.

Thank you

References

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References II

• Stein JD, Shekhawat N, Talwar N, Balkrishnan R: Impact of the introduction of generic latanoprost on glaucoma medication adherence. Ophthalmology. 2015; 122:728-47