CLINICAL INNOVATION: Fair & Effective Incentives for New Uses of Established Drugs

Should the US system be changed?

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New Indications for Approved Drugs: Changing the U.S. System*

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* For more on my idea, see "Paper Promises" on my SSRN page.

Overview

- I view the problem differently.
- U.S. federal law has incentives in place.
- We don't know if they would work, because we have allowed the healthcare delivery system to run roughshod over them.
  - We have acquiesced in a state of affairs that basically treats them as a joke. At this point, the problem is inertia more than anything else.
- My solution?
  - Simple and elegant. Leaves the details to private ordering.
  - Will be wildly unpopular.

Premise – What should be non negotiable?

- First, new uses are both theoretically and in fact excludable.
- Second, generic drugs are otherwise approved, prescribed, automatically substituted, and dispensed.

How Did We Get Here?

Federal incentives contemplate excludability.

- 3-year new use exclusivity
- 7-year orphan drug (use) exclusivity
- Patents on new methods of use

And yet, not excluded. Why? A **combination** of

- FDA policies and practices
- State laws
- Prescriber, generic industry, and payer practices

working together

Skinny Labeling

- Bristol-Myers Squibb v. Shalala (D.C. Circuit 1996
  - Capoten (captopril) approved for hypertension (no protection) as well as diabetic nephropathy (exclusivity) and left ventricular dysfunction following myocardial infarction (exclusivity)
  - FDA may approve generics labeled only for hypertension

- Sigma-Tau v. Schwetz (4th Circuit 2002)
  - Metabolism errors (oral & injectible)
  - End stage renal disease (injectible) under orphan exclusivity
  - 80 percent of innovator's injectible sales were for ESRD
  - FDA may approve generic injectible labeled only for metabolism errors

plus therapeutic equivalence determination

- FDA deems a generic drug therapeutically equivalent to reference listed drug if (a) pharmaceutically equivalent and (b) bioequivalent
  - Same route of administration, dosage form, strength
- FDA lists all approved drugs and therapeutic equivalence ratings in the Orange Book

- Orange Book does not state indications for which a drug is approved
- Orange Book does not distinguish between a generic approved for all RLD indications and a generic approved for some RLD indications
- TE ratings do not specify the indications

plus state laws and regulations

- Therapeutic equivalence ratings facilitate (and sometimes trigger) substitution under state pharmacy law
- State medical practice rules don't require the physician to specify the intended use in the prescription
- State pharmacy laws and regulations don't require the pharmacist to inquire about the intended use
- **plus** payers generally require substitution without regard to patient's condition or scope of dispensed drug's approvals

or in some cases prescribing decisions

- Physician might decide prescribe generic for unapproved use for which RLD holds patent or exclusivity
- FDA doesn't interfere in prescribing decisions, deeming them practice of medicine
- State laws generally permit physicians to prescribe approved drugs for unapproved uses

plus impediments

- Can't persuade physician to write "dispense as written" simply to ensure that innovator receives reward / return on investment
- Can't use same arguments to persuade patient to insist on the more expensive brand product
- Very difficult to obtain judicial relief enforcing exclusion
- E.g., regulatory exclusivity binds only the agency
- Patent doesn't block FDA approval (carve out)

More impediments

- Patent infringement litigation theoretical but patient, physician, and pharmacist are unappealing defendants.
- Secondary infringement cases against generic manufacturer are hard to win.

Solutions . . .

- Federal law already has incentives in place.
  - Rather than creating radical new incentives, rethinking basic approach to patents and exclusivity, throwing scarce public funds into new use research, etc.
  - **Why not see if existing incentives work (to encourage new uses), when we actually allow them to operate properly?**

- Desired end state:
  - New uses are excluded.
  - Generic drugs are otherwise dispensed.
- Means of accomplishing this
  - Sale / no-sale decision based on use for which prescribed
- Who is in best position to make the sale / no-sale decision?
  - The pharmacist
  - The payer
- Who has the information to make the right sale / no-sale decision?
  - The same parties. Payers do prior authorization already.
- How do we nudge / motivate them ?

First, provide the information.

- FDA should revise approach to therapeutic equivalence determinations
  - AB rated only if full labeling?
  - Differentiated AB ratings (AB-Limited, AB-Full)?
  - AB ratings indication by indication?
  - Part of a broader overhaul of the OB (e.g., why not deem a 20mg capsule AB to a 20 mg tablet)
- Won't work alone (given state laws and payer policies) but an important first step

Other steps FDA could take

- Prohibit companies from discussing unapproved uses that are protected by another company's patents or exclusivity
  - Needs to be squared with First Amendment
  - And can be
- If no change to the OB, then resurrect guidance on generic drug promotion and ban claims of therapeutic equivalence with partial labeling

Other steps FDA could take

- Rewrite essay at front of Orange Book to emphasize importance of preserving new use excludability
- Require generic drugs to proactively disclaim carved out uses and remind pharmacies and physicians about potential patent infringement
- Clarify that "practice of medicine" policy is meant to protect clinical decisions

Step(s) by Congress

- Prohibit pharmacy from dispensing a generic drug for a use that does not appear in its labeling, if the innovator holds patent or exclusivity for the use.
- Unprecedented? Actually, no.
  - 21 U.S.C. § 353(b)(1): "The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale."

What happens?

- Gives pharmacist motive to work with other parties in healthcare system to ensure that s/he has the information needed.
  - Might refuse to dispense/substitute generic drug with partial labeling without assurance of intended use
  - Would affect contract negotiations between pharmacies and payers as well as pharmacies/payers and generic companies
  - Should motivate payers to develop a system in which all generic drug sales require a diagnosis that corresponds to the drug's labeling

Or, try this . . .

- Make it easy for innovators to sue payers for induced patent infringement when generic dispensed.
- How? Prohibit pharmacies from dispensing a (partially labeled) generic drug without disclosing the sale and diagnosis to [x]

I suppose…

- Require payment by the generic companies whose drugs are sold and used for the indications that are supposed to be excludable
  - Objection: this acquiesces to the state of non-exclusion.
  - Patent and regulatory exclusivity become (more of) a sham.

These are hammers, yes, but:

- Idea here is not to penalize pharmacies (first idea) or have payers paying for induced infringement (second idea). The desired end-state is no-sale decisions.
- These ideas will be unpopular. But:
  - Motivates the right parties to construct systems that prevent dispensing for protected uses.
  - And gets us to the right end state: generic companies will get the right sales, innovators will get the right sales.
- Lots of great ideas at this conference, but **why not try first for a world where "exclusivity" means what it says?**