Issues associated with generic drugs used in children

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Disclosure

- I have nothing to disclose

Questions About Generic Drugs in the Care of Children

- How do generic drugs differ from branded drugs?
- Is cheaper usually or always just as good?
- Can we maintain quality & reduce health care costs with greater use of generics?
- What criteria help guide switching from branded to generic drugs?
- Generic switch and therapeutic switch: what are these and how do they differ?

How Generic Approval Differs From That of the Branded Drug

- Generics for pediatric indications are usually tested in adults, due to ethical constraints
  - Can't give a child "volunteer" a drug they don't need or aren't likely to need
  - Can't justify taking 12+ blood samples twice
- BIOEQUIVALENCE based on kinetics and pharmaceutics (dissolution, absorption, etc.)
  - Doesn't test repeated doses to steady state
  - Doesn't compare therapeutic effectiveness of drug A to drug B

Bioequivalence Evaluation: Study Design

- General approach:
  - Carefully controlled, crossover study
  - Carefully selected patients: healthy, young, adult often males
  - Compares AUC & C_{max} generic to AUC & C_{max} Innovator measured twice, several half-lives apart
    - 10-12+ serum samples/AUC, same times
    - Measured over at least 3 half-lives
    - 24-36 pts, studied twice in crossover design

Substitution: It's Not All The Same

- Generic substitution: substitutes a drug without market exclusivity, but with the same active ingredient as a branded product
- Therapeutic substitution: substitutes a drug considered therapeutically equivalent to the one that was ordered
  - Basis for that similarity is not always clear or focused on pediatric patients

When Might You Want to Fight, Not Switch?

- Branded formulation is pediatric friendly (available as a solution, suspension, chewable tablet, etc.) and the generic has a different taste, smell, etc.
- Pediatric therapeutic studies of the branded drug support treatment of similar age patients for the same indication as your patient and the generic has not been as successful in your patients
- The drug has a narrow therapeutic index

Example

3 Month Old with Probable GERD

Prevacid Ordered, Omeprazole Dispensed

- Are these therapeutically equivalent?
  - Omeprazole suspension was never labeled for <1 yr
  - PPI's have quite variable absorption kinetics in all ages and the extemporaneous formulation of pantoprazole hasn't been tested in 3 month olds

3 Month Old with GERD

Prevacid Ordered, Omeprazole Dispensed

- Other Differences
  - PPI's are cleared mostly by CYP2C19, less by CYP3A4 that have different developmental maturation patterns, but which are not mature at 3 months

Is Therapeutic Switching Appropriate? What are the Data?

- Are these drugs interchangeable?
- Are the kinetics known for a 3 month old patient?
- Is omeprazole suspension therapeutically equivalent to Prevacid ® for 3 month olds?

Generic Drugs: In the Care of Children

- Therapeutic switches require a knowledge of pharmacology and clinical trials in appropriate population, similar to your patient
- Specific areas of concern: AEDs, psychoactive drugs, cardiac drugs, antidepressants, drugs used following transplant or in oncology

Generic Drugs: In the Care of Children

- Generics have a role in Pediatric medicine, but it must be carefully considered
- Generics usually reduce medication costs, but sometimes create unanticipated healthcare costs
- Few pediatric studies compare Drug A vs Drug B for effectiveness, much less cost-effectiveness
- Without pediatric studies or a pediatric label before a drug becomes generic, it is very unlikely to undergo pediatric studies for pediatric labeling
- Generic switches are seldom based on pediatric data

Summary Slide

Need more research/support for studies in pediatrics to:

1. Look at differences between testing of innovator and generic drugs and how it affects substitutions
2. To distinguish therapeutic and generic substitutions when treating children
3. Identify general factors in children to consider for a therapeutic or generic switch
4. Select therapeutic areas where generic substitution increases AEs and may worsen outcomes

Thank you for your attention