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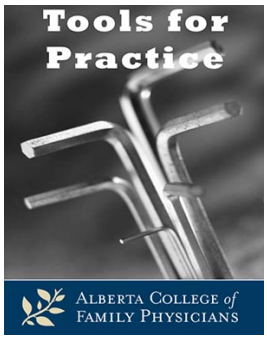
Updated: Jan 17, 2020
Evidence updated: Addition of four systematic reviews
Bottom Line: No change
Original: July 7, 2014



Generic Versus Brand Name: The other drug war

Clinical Question: Is there any benefit to prescribing brand name medications versus generic brands?

Bottom-line: Based on the best available evidence, generic medications are bioequivalent and produce similar clinical outcomes to brand name medications.

Evidence:

- Bioequivalence:[1]
    - Regulators require 90% confidence intervals (CI) for the maximum peak concentration (Cmax) and total drug exposure over time (AUC) of generic drug be within limits of 0.80-1.25.
        - This means the absolute differences in bioequivalence must be ≤~5-7%.
    - Between 1996-2007, 2070 single-dose bioequivalence studies showed the average difference in Cmax and AUC was 4.35% and 3.56%, respectively.
    - 98% of studies showed AUC of generic and innovator products' differed by <10%.
    - Generic and brand name levothyroxine have been shown to be bioequivalent.[2]
    - One study found that of 42 randomly selected brand-generic drug comparisons, 98% met AUC criteria and 88% met Cmax criteria for bioequivalence.[3]
- Clinical outcomes (brand name versus generic medications):
    - Two systematic reviews [38-74 randomized control trials (RCTS)] of cardiovascular medications including anti-hypertensives, statins, anti-platelets, anticoagulants:[4,5]
        - Both showed no difference in clinical outcomes.
        - The largest and most recent SR:[5]
            - Composite of soft outcomes (e.g. systolic blood pressure, LDL): no statistical difference.
            - Major adverse cardiovascular events (MACE) or death (3 RCTs): no statistical difference.
            - Adverse effects:

        - Mild/moderate: no difference.
        - Serious: no difference.
    - Systematic review of warfarin:[6]
        - Five trials (higher level evidence): No statistically significant difference in INR or dosage changes required.
        - Six observational studies (lower level evidence): Inconsistent results at higher risk of bias.
    - Systematic review of clopidogrel (3 studies, mixed design) [7]. For RCT data, no differences observed for:
        - MACE: 5% versus 4% generic, no statistical difference.
        - Bleeding: 2% versus 1%, no statistical difference.
        - Withdrawal: 4% versus 7%, no statistical difference.
    - Systematic review of antiepileptic drugs (7 RCT, 204 patients)[8]:
        - Uncontrolled seizures: no difference.

Context:

- Of 43 editorials on generic medication issues, 23 (53%) expressed a negative view of generic substitution,[4] while only 8% of trials found any differences in any outcomes.[4]
- If there were important clinical differences between generic and brand name medications, companies would do studies to prove brand name superiority and prevent losing millions of dollars from generic substitution.
    - In fact, one company tried to suppress data demonstrating equivalence of its product and related generics.[9]
- Brand name and generic medications may contain different inactive components (fillers and binders) and may look different.

Original Authors: James McCormack BScPharm PharmD, John T Chmelicek MD CCFP FAAFP FAWM

Update: Samantha Moe, PharmD **Review:** G Michael Allan MD CCFP

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