medSask
YOUR MEDICATION INFORMATION SERVICE

College of Pharmacy and Nutrition
University of Saskatchewan
Saskatoon SK S7N 5C9
www.medsask.usask.ca

Generic vs. Brand Name Drugs: What are the differences?

A recent news article, found here, has once again sparked the debate of whether generic drugs are just as good as brand name drugs. To answer this question, it is important to understand the approval process of drugs in Canada to see how generic drugs come to market.

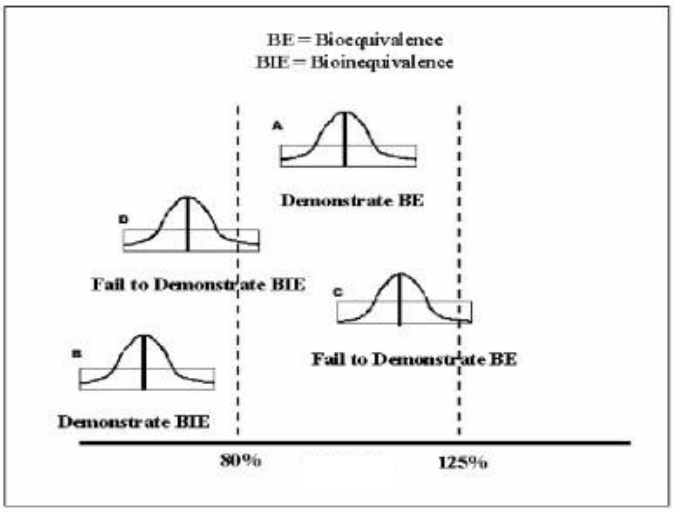
Health Canada decides which drugs are allowed to be sold in Canada. Drug manufacturers, whether in Canada or internationally, must prove their product contains exactly what is labelled and abide by strict "Good Manufacturing Practice" guidelines. Both brand name drugs and generic drugs are subject to the same criteria; there are not two separate approval processes.

Generic drugs must have the same amount of active ingredient as the brand name drug, but are allowed to have different non-active ingredients or "fillers", which are ingredients that help hold the tablet together, make it easier to swallow, make it gentler on the stomach, or preserve the drug, etc. If the generic drug is produced with different fillers, then the manufacturer must prove "bioequivalence" – that is, they must prove that the product delivers the same amount of drug to the body over a period of time compared to the brand name product. In most cases, if the generic drug has the same fillers, a bioequivalence test is not necessary (1).

To perform a bioequivalence test, usually between 30 and 70 healthy people are tested in two groups. An individual will receive either the brand or generic drug and the amount absorbed is measured. The procedure is then repeated with the other drug. If the drugs are absorbed and removed by the body at a similar extent over a period of time, they are deemed bioequivalent (2). So, what is "a similar extent"?

People commonly claim bioequivalence requirements are too loose, that the amount of active ingredient in a generic drug is allowed to be from "80 to 125%" of that in the brand name product; thus, a possible 45% variance in the active ingredient is allowed. This is untrue; the "80 to 125%" figure refers to a statistical term called the 90% confidence interval for the "area under the curve (AUC)" (3). The confidence interval takes into account the absorption and excretion differences between people in the study, and the AUC is a measure of the concentration of a drug over time as it is absorbed into the body and then slowly removed from the body. Putting it together, this means that when a generic drug is taken, the entire AUC (taking into account the differences between people being studied), must always fall between a small range of values which lie entirely between 80 to 125% of the stated amount, or it fails the equivalency test; practically, this means the actual variance is less than 5% (4), with studies finding an average variance of 3-4% (5).

The graph below may help illustrate this point (3):



Only "A" passes the bioequivalence test, since the entire range of AUC values for individuals in the study lie between 80 and 125%. The rest fail because their range of values cross the acceptable variance.

A variance of 3-4% must be put into perspective; different batches of the same brand name drug are allowed to have the same variance (6), thus, the potential variation from switching to a generic version is no different than the variation of receiving the same brand at different times.

Some argue that since some drugs must be dosed very accurately, the 3-4% variation can be important. This is true, and so Health Canada has labelled some drugs as "critical dose drugs", which means the range of AUC values must lie between 90 and 112%, rather than 80 to 125% (7); thus, the range in the graph above would be even tighter, creating an even smaller allowable variance.

Another misconception is that since generic drugs are less expensive than their brand name counterparts, they must be of poorer quality. When a company develops a new drug, they spend a substantial amount on research and development of the drug, and must perform expensive studies to prove the safety and efficacy of the new drug. This takes many years and an average of $1.1 billion (8). The brand name manufacturers are rewarded for this investment with a patent – a time during which no other manufacturer can produce the drug. The price set by the brand name manufacturer factors in the money spent in research and development. Once patent expires, the generic drug companies are free to produce the drug. Since they do not have to invest in research and development they can bring their version of a drug to market for a much lower cost—it has nothing to do with a lower quality product or substandard manufacturing.

The advantage of generic drugs versus brand name drugs is lower cost. In Canada, since the government helps pay for many people's medications, when a lower cost version is routinely given, it amounts to significant savings for the struggling health care system; approximately $7 billion was saved in 2010 (9). Switching to generic medications to save all this money has NOT caused an increase in harm to patients; two large studies show no differences in outcomes when using generic drugs for patients with cardiovascular disease (10) or infections (11).

Certainly, from time to time, there are reports that a switch from one brand to another (from brand name to generic or from one generic to another generic) result in adverse effects. This might mean that someone might experience a side effect that did not happen before the switch, or the drug may not work as well—but this is very rare. Extra caution is suggested when switching between brands of "critical dose drugs" (e.g., anti-seizure drugs, warfarin, lithium, thyroid

hormone, etc.) and extended release formulations (12). If the medication does not seem to be working as well as normal or if side effects appear after a switch, contact your doctor. However, when starting on a new medication, a generic version is just as good as the brand version (13).

If generic drugs are just as good, why are there reports of people doing worse on them? They may have different fillers, so if the generic version contained something like a sulfite and the brand name did not, an allergic reaction could be possible, though very rare. More likely, there is significant bias at play; if a person has negative expectations about a generic drug, any issue will likely be blamed on the generic, instead of the real cause. One has to consider that in almost all cases, no difference is noticed; these cases don't make it to the news.

For the vast majority of people, generic drugs are just as good as the brand name drugs, and have enormous cost saving potential for our health care system and need to be utilized as much as possible. Be confident taking a generic medication, as Health Canada has stringent regulations in place to ensure only safe and effective products are marketed.

Prepared by Terry Damm, BSP

Reviewed by Carmen Bell, BSP; Darcy Lamb, BSP, MSc; Karen Jensen, BSP, MSc

December 2013

References:

1. Health Canada. Biopharmaceutics Classification System Based Biowaiver. Accessed online Dec 2013. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/consultation/drug-medic/bcs_draft_guide_ebauche_ld_scb-eng.pdf

2. Canadian Generic Pharmaceutical Association. Bioavailability and Bioequivalence – What Are They? Accessed online Dec 2013. http://www.canadiangenerics.ca/en/resources/docs/09.16.13%20Bioequivalence2013_Eng.pdf

3. Generic drug variability. Pharmacist's Letter/Prescriber's Letter 2008;24(7):240704.

4. The Canadian Agency for Drugs and Technologies in Health. Similarities and Differences Between Brand Name and Generic Drugs. Accessed online Dec 2013. http://www.cadth.ca/en/resources/generics/similarities

5. Davit BM, Nwakama PE, Buehler GJ, et al. Comparing generic and innovator drugs: a review of 12 years of bioequivalence data from the United States Food and Drug Administration. *Ann Pharmacother*. 2009;43(10):1583-1597.

6. Health Canada. Good Manufacturing Practices Guidelines. Accessed online Dec 2013. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/compli-conform/gmp-bpf/docs/gui-0001-eng.pdf

7. Health Canada. Comparative Bioavailability Standards: Formulations Used for Systemic Effects. Accessed online Dec 2013. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/bio/gd_standards_ld_normes-eng.php#a2.1.1.6

8. Deloitte. Measuring the Return from Pharmaceutical Innovation 2012. Accessed online Dec 2013. http://www.deloitte.com/view/en_GB/uk/research-and-intelligence/deloitte-research-uk/deloitte-uk-centre-for-health-solutions/b47f30374ca4b310VgnVCM2000003356f70aRCRD.htm

9. Canadian Generics Pharmaceutical Assocation. Accessed online Dec 2013. http://www.canadiangenerics.ca/en/

10. Aaron S. Kesselheim, MD, JD, MPH, Alexander S. Misono, BA, Joy L. Lee, et al. Clinical Equivalence of Generic and Brand-Name Drugs Used in Cardiovascular Disease. JAMA. 2008 December 3; **300(21)**: 2514–2526.

11. Snyman JR, Schoeman HS, Grobusch MP, Henning M, et al. Generic versus non-generic formulation of extended-release clarithromycin in patients with community-acquired respiratory tract infections: a prospective, randomized, comparative, investigator-blind, multicentre study. Clin Drug Investig. 2009;29(4):265-74.

12. Lewek, P., Karsas, P. Generic drugs: The benefits and risks of making the switch. The Journal of Family Practice. Accessed online Dec 2013. http://www.jfponline.com/index.php?id=22143&tx_ttnews[tt_news]=175484#5911JFP_Article4-tab1

13. *Gregory M. Peterson.* Generic Substitution of Antiepileptics: Need for a Balanced View. Accessed online Dec 2013. http://www.cnsspectrums.com/aspx/articledetail.aspx?articleid=3603

University of Saskatchewan

Telephone: 1-800-667-3425 (SK); 966-6340 (Saskatoon)
Fax: (306) 966-2286 Text: (306) 260-3554