LIVING WELL

Are Generic Medicines Really the Same?

The broad answer is reassuring, but transplant medicines show why some switches deserve a closer conversation.

The box changed. Should you worry?

You collect a refill and the medicine looks unfamiliar. The name is different, the packaging has changed, and the price may be lower. It is reasonable to wonder whether you have been given the same treatment-or a cheaper approximation of it.

The broad answer is reassuring: generic medicines are intended to be bioequivalent alternatives to brand-name drugs. They are not outside the drug-safety system. In the United States, prescription and over-the-counter medicines must be approved by the Food and Drug Administration (FDA), which considers effectiveness, safety, manufacturing and labelling before a drug can be sold.

But "generic" does not make every question disappear. Medicines can cause side effects and interact with food, alcohol or other medicines whether they carry a familiar brand name or not. What matters is not simply the word on the box, but the particular medicine, how you take it and whether a switch needs monitoring.

What "equivalent" can prove

Bioequivalence asks whether a generic produces sufficiently similar drug exposure to its reference medicine. In a 2018 review of transplant immunosuppressants, the required range used for approval was 0.80 to 1.25 for measures including peak concentration and overall exposure. The pooled results for cyclosporine, tacrolimus and mycophenolate mofetil fell within that range.

That is stronger evidence than a vague assurance that two products are "basically alike." Across 20 crossover trials involving 641 healthy volunteers, the review found no significant differences between generic and brand medicines in the time to peak concentration or terminal half-life. Six randomised trials involving 594 kidney transplant recipients also contributed evidence about clinical outcomes.

Yet bioequivalence does not prove that every patient will have an identical experience, or that every formulation performs alike in every setting. In subgroup analyses, some generic

cyclosporine formulations did not meet bioequivalence criteria. The authors concluded that evidence about the efficacy and safety of generic immunosuppressants remained inconclusive and argued for tighter requirements for medicines with a narrow therapeutic index.

The evidence supports caution around the switch, not a blanket rejection of generics.

Heart medicines tell a messier story

A large 2020 review examined 72 studies of brand-name and generic cardiovascular medicines, representing more than one million patients. Sixty per cent of the studies found no difference between the two. Twenty-six per cent favoured the brand-name medicine for effectiveness or safety, 13 per cent were inconclusive, and 1 per cent favoured generics.

At first glance, hospital visits appeared more common among people exposed to generic cardiovascular drugs. But the studies differed enormously from one another, making that combined result difficult to interpret. When the reviewers considered only four randomised controlled trials, the difference in hospital visits was not statistically significant.

The honest conclusion is not that generics failed, or that brands won. The reviewers said the evidence was too heterogeneous and insufficient for a firm conclusion about comparative effectiveness and safety. Real-life studies can reveal patterns, but a pattern does not necessarily show that the type of medicine caused the outcome.

That leaves you with a less dramatic but more useful answer: the best available cardiovascular evidence does not establish that brand-name medicines are clinically superior. It also does not justify pretending that every comparison has been settled beyond doubt.

Some switches need more care

Transplant medicines show why the details matter. A 2021 review of generic tacrolimus included 17 studies and 1,412 liver or kidney transplant recipients. Overall, there was no significant difference in biopsy-proven acute rejection between generic and innovator tacrolimus. Most included studies reported the same or lower rejection rates with generics.

The picture shifted when researchers separated people starting treatment from those converted from another product. Studies of new use found a lower rejection risk with generic tacrolimus, while conversion studies found an increased risk. Those findings do not establish that switching caused rejection: the evidence was mostly observational, and some studies had a risk of bias.

A separate 2018 review found generic cyclosporine non-inferior to the brand counterpart for

acute rejection, infections and death in randomised kidney-transplant trials. Even so, it concluded that not all generic immunosuppressants had similar relative bioavailability and that the overall safety and effectiveness evidence was inconclusive.

This is where a routine price question becomes a medical one. If you take an immunosuppressive medicine after a transplant, do not treat an unexpected product change as an administrative detail. Ask your transplant team about it rather than changing how you take the medicine yourself. The evidence supports caution around the switch, not a blanket rejection of generics.

Check the medicine, not the reputation

Generic use has produced substantial savings: a 2018 systematic review reported that generics saved an estimated $254 billion in the United States in 2014. That review also found that lower-income patients were more likely to use generics. Use did not differ clearly by gender, age or race and ethnicity, although the evidence outside income was heterogeneous.

Price and reputation are poor substitutes for checking what you were actually dispensed. A familiar brand does not remove the ordinary risks of medicines, and a generic label does not make a medicine unsafe. Taking it correctly still matters. So does checking for interactions with food, alcohol and other medicines, and buying online only from a licensed pharmacy located in the United States.

On your next refill, place the new container beside the previous one and bring a written medicines list. Ask the pharmacist or prescriber to confirm the medicine and whether the change needs clinical monitoring-especially if it is an immunosuppressant. Do not alter or stop it while you wait for reassurance.

That step takes two things you can hold: your medicine containers and a written medicines list. They turn a foggy worry about "generics" into a precise question about the medicine in front of you.

Where this comes from

- Drug Safety

  MedlinePlus, U.S. National Library of Medicine · https://medlineplus.gov/drugsafety.html
- Medicines

  MedlinePlus, U.S. National Library of Medicine · https://medlineplus.gov/medicines.html

- The Association Between Patient Sociodemographic Characteristics and Generic Drug Use: A Systematic Review and Meta-analysis.

  Journal of managed care & specialty pharmacy, 2018 · https://pubmed.ncbi.nlm.nih.gov/29485953/
- Are Generic Drugs Used in Cardiology as Effective and Safe as their Brand-name Counterparts? A Systematic Review and Meta-analysis.

  Drugs, 2020 · https://pubmed.ncbi.nlm.nih.gov/32279239/
- Immunosuppression with generic tacrolimus in liver and kidney transplantation-systematic review and meta-analysis on biopsy-proven acute rejection and bioequivalence.

  Transplant international : official journal of the European Society for Organ Transplantation, 2021 · https://pubmed.ncbi.nlm.nih.gov/31971288/
- Bioavailability, Efficacy and Safety of Generic Immunosuppressive Drugs for Kidney Transplantation: A Systematic Review and Meta-Analysis.

  American journal of nephrology, 2018 · https://pubmed.ncbi.nlm.nih.gov/27576318/
- First line antiretroviral treatment failure and its association with drug substitution and sex among children in Ethiopia: systematic review and meta-analysis.

  Scientific reports, 2022 · https://pubmed.ncbi.nlm.nih.gov/36316358/