Off-Label Use of Drugs

Questions and answers about the off-label use of drugs

What does off-label mean?

The term "off-label" refers to any use of a drug beyond what Health Canada has reviewed and authorized to be marketed in Canada and as indicated on the product label. Usually, this means using a drug for an illness or disease other than the authorized reasons for use — in other words, an "off-label indication." However, drug doses, when and how often to take a drug, and the type of patient (e.g., children, pregnant women, and elderly) uses may be considered "off-label," as well. Off-label use is also sometimes called expanded use.

What is an indication?

An indication for a drug is the reason the drug is used, usually to treat an illness or disease.

For example, insulin is indicated for the treatment of diabetes. This does not mean that every person with diabetes should be treated with insulin. It means that insulin *can* be used for this purpose, and that diabetes is an acceptable reason for using insulin.

Many drugs have more than one indication. In other words, they can be used for several reasons. When Health Canada authorizes a drug for sale in Canada, this authorization is for a specific indication or indications. These specific uses of the drug are known as Health Canada indications or authorized indications.

What is a label?

When a drug is authorized for sale in Canada, Health Canada allows specific reasons for a drug to be used, how much and when to use it, what might make it not safe to take a drug, and directions for use. This information is then included in the labels affixed to the container or packaging of the drug and in any separate Health Canada-authorized documents, such as the prescribing information, product monographs, package inserts, etc., that are collectively referred to as the "label" for that drug.[1]

What are off-label drugs used for?

The off-label uses for a drug include (but are not limited to) using the drug to treat an illness other than the authorized indication (e.g., using a beta blocker to prevent migraines), using the drug in a different population than authorized (e.g., use in children when authorized only for patients 12 years of age or older), prescribing a drug with different dose and administration instructions (e.g., taking the drug twice daily instead of the authorized three times a day), and using the drug in a different authorized route of administration (e.g., taking as an oral solution instead of the authorized capsule format).

How does a drug get an authorized indication?

In Canada, the authorization of an indication for a drug can only be obtained if a manufacturer files an application that is reviewed and granted authorization by Health Canada to market that drug. A manufacturer cannot promote any off-label uses of their products, as Health Canada has only verified and authorized the drug for the indication applied for.

Why are common uses of drugs sometimes still considered off-label?

A drug may be useful for other indications as well as the approved ones, but a manufacturer may choose not to apply for an indication if there is unlikely to be a good return on investment, as seeking approval for a medication can be costly and time-consuming. One example of this is an older drug that no longer has patent protection that could be used for another treatment in a very small population of patients. In this case, there is little financial incentive for the manufacturer to apply to Health Canada for new marketable indications.

Are there rules around off-label use?

Yes. Drug manufacturers are only allowed to market their drugs in Canada for indications authorized by Health Canada. Drug manufacturers can be fined heavily if they are found to be promoting off-label uses for a product.

Your clinician, however, is not bound by these same rules and may prescribe you a drug for an off-label purpose.

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How common is off-label prescribing?

It's pretty common, especially for children, mostly because children are often not included in the clinical trials while a new drug is being developed.

Why would my clinician prescribe something off-label?

If a drug has not been authorized for a certain indication, this does not mean it doesn't work. There are many reasons your clinician might prescribe a drug off-label:

- When manufacturers get to the stage of testing a drug on patients (clinical trial), they do not often include elderly patients, children, and pregnant or nursing women, so prescribing in these groups is often off-label by necessity.
- The illness or disease being treated may be similar to the actual authorized indication. For example, a drug may be authorized for a certain stage of breast cancer but used off-label for bone cancer or a different stage of breast cancer.
- A clinician may have run out of all "on-label" (authorized) options for treating your illness or disease.
- In the treatment of rare diseases, there may be few or no other treatment options.
- New uses may be discovered for drugs that are already on the market but Health Canada has not yet authorized the new use (e.g., no manufacturers have submitted an application to Health Canada for authorization of the "new uses").

Is off-label prescribing safe?

Yes, provided there is strong scientific evidence to support it, including the balancing of risks and benefits.

Example of off-label prescribing without strong evidence

Health Canada issued a warning regarding off-label use of quinine, a drug used to prevent or treat malaria, in 2011. It is prescribed off-label 99.5% of the time for night time leg pain but lacks strong evidence to support this. Quinine is also associated with serious side effects. So why is it prescribed? There are currently no effective drugs to treat night-time leg pain, but quinine has a long history of being prescribed for this. Therefore, clinicians may feel comfortable prescribing it, although it is not advisable to do so due to risks outweighing any benefit.

Example of off-label prescribing with strong evidence

Metoprolol is not indicated for the treatment of patients with atrial fibrillation (irregular heart rhythm), but it is actually part of the first drug class (beta blockers) that clinicians prescribe to control their patients' heart rates. This practice is supported by evidence-based clinical guidelines.

Bottom Line:

- "Off-label" use means that a drug is being used in a way that has not been reviewed and authorized by Health Canada.
- A Health Canada review occurs when a manufacturer submits an application to Health Canada. Authorization allows the manufacturer to market the product for the approved use.
- Marketing of off-label uses is prohibited for drug products sold in Canada. Off-label prescribing is allowed, and necessary in some cases.
- Off-label use may or may not be supported by strong scientific evidence.

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References

1. Government of Canada [Internet]. Ottawa: Government of Canada; 2017 Jun 28. Guidance document: labelling of pharmaceutical drugs for human use; 2015 [cited 2017 Jun 28]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/labelling-pharmaceutical-drugs-human-use-2014-guidance-document.html

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