Guidelines for off-label medicines use

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The off-label prescribing and dispensing of medicine is the use of a registered medicine in a manner that is different from that approved by the Therapeutic Goods Administration (TGA).

Information about off-label or unregistered use of a medicine is therefore not included in the product information (PI) which has a summary of the scientific information relevant to the safe and effective use of a registered medicine. Examples of off-label use include the use of a medicine:

- For a different clinical indication,
- In unapproved subpopulations (for example: patient age range e.g. paediatric or geriatric patients, and pregnant women), and
- By varying the dosage or the method of administration.

There are various explanations as to why pharmaceutical companies may choose not to submit an application for a new indication after a product has registration with the TGA. One reason is that there may be little motivation to undertake studies for registering the medicine for a new or an uncommon indication considering the financial costs involved with the clinical trials and TGA registration processes.

Off-label use of medicines is legal and allows prescribers to use their professional clinical judgement to prescribe medicines outside the TGA approved conditions. Indeed, off-label use of medicines is common practice with research indicating rates of up to 40% in adults and up to 90% in pediatric patients. The high percentage of off-label medicine use in pediatric patients is due to the fact that most medicines are registered on the basis of pre-marketing clinical trials involving adults.

Clinical evidence

Clinical trials are usually carried out in restricted groups of patients and trials often exclude people who are older and in general poor health. It is therefore often only after a medicine has been registered and is being used by large numbers of patients that new indications are revealed. Knowledge about a medicine's benefits and side-effects subsequently increases over time as new evidence becomes available after the medicine has been registered. Prescribers' freedom to prescribe medicines off-label allows adopting new practices based on the new evidence. Off-label prescribing encourages innovation in clinical practice.

However, as independent health professionals pharmacists should take appropriate precautionary measures before dispensing a medicine for off-label use. Pharmacists should be familiar with the clinical evidence to support off-label use when dispensing off-label medicine. The evidence to support off-label medicine use could be high-quality or in some cases there may be little evidence but a need to innovate. For example, when there are no alternatives and the potential benefits outweighs the risks.

Gazarian et al. defined three broad categories of off-label use, namely:

- Use justified by high-quality evidence,
- Use within the context of a formal research proposal, and
- Exceptional use, justified by individual clinical circumstances.

These categories could be used to guide decisions about the appropriateness of off-label medicine use. It is also important to collaborate with the prescriber in order to establish the reason for the off-label prescribing. This information is required to be able to determine whether there is appropriate evidence to support the off-label use. Additionally, the dispensing process should involve checking whether there is not another registered medicine that could be used.

Pharmacists should consult evidence based medicine information resources to guide decision-making such as the Australian Medicines Handbook (AMH) or the Therapeutic Guidelines. The AMH signposts the off-label indications by the designation 'accepted indication'.

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Informed consent

It is best for a patient or carer to know that a medicine is being prescribed and dispensed for off-label use and the reasoning behind the decision. Patients or carers may want the level of supporting evidence to be disclosed and indeed have a right to receive relevant information in order to make an informed decision. It is also important to explain that information about the indication will not be covered in the Consumer Medicines Information (CMI) leaflet as CMIs only cover the registered indications and other details from the approved PI.

Clinical judgement

Off-label use of medicines is widespread and often is clinically appropriate. However, it is a grey area with little guidance for prescribers and dispensers. Pharmacist need to be aware of the risk involved as it challenges claims and expectations that medicine safety and efficacy have been fully evaluated. It raises particular concerns when medicines have high potential for toxicity.

Pharmacists should use their independent clinical judgement, based on the relevant information and evidence, to determine whether the off-label medicine will be safe and appropriate for the patient.

References