Doctors should disclose off-label prescribing to their patients

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Doctors should be required to disclose when they are prescribing drugs off-label, argues a new article in this week's *PLoS Medicine*. Michael Wilkes and Margaret Johns from the University of California Davis argue that the ethics related to informed consent and shared decision-making provide an imperative for doctors to inform patients about the risks of a medical treatment when their use has not been approved by regulators.

Off-label prescriptions are those that do not comply with the use approved by the Food and Drug Administration (FDA) for the drug. While off-label prescribing is legal and accounts for roughly half of all prescriptions currently written in the US, it is often not supported by sound scientific evidence. Worse, say the authors, off-label prescribing can put patients at risk and drive up healthcare costs.

The public often assumes that all common uses of prescription drugs have been approved by the FDA, say the authors. But current law does not prevent doctors from prescribing a drug to any patient for any use whether it was approved for this use or not.

And while off-label prescribing is common and sometimes necessary (as in the area of paediatrics where many drugs have not been tested on children), Wilkes and Johns argue that off-label prescribing can also pose potentially serious risks. By definition no governmental body has conducted a review of the effectiveness or safety of the drug for the off-label use, they say. As a result, an off-label prescription may be ineffective or detrimental, and could be more costly than existing drugs.

Wilkes and Johns argue that the strict requirement that doctors obtain informed consent from patients before enrolling in a research study means they should obtain the same consent when a drug is being prescribed off-label as each such prescription is just like a mini research study. The contemporary expectation for shared decision-making between doctors and patients also supports full disclosure about off-label prescribing, leaving the option open for patients to opt for a drug which has received FDA approval for the condition in question.

"From an ethical perspective," say Wilkes and Johns, "[what is required is] open, honest discussions where doctors tell their patients that the use of the drug will be off-label and thus not approved for this indication, explain the risks, potential benefits, and alternatives, and then ask patients for their permission to proceed."

A recent *PLoS Medicine* paper (http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050210) described techniques by which drug companies covertly promote off-label use. Adriane Fugh-Berman (Georgetown University Medical Center, Washington DC) and Douglas Melnick (a preventive medicine physician working in North Hollywood, California) discussed the use of "decoy indications" and drug representatives to engage in illegal pharmaceutical marketing. Pharmaceutical marketing, they say, has "distorted the discourse on off-label uses and encouraged the unmonitored, potentially dangerous use of drugs by patients for whom risks and benefits are unknown."

"Companies that engage in off-label promotion should be heavily fined and their future marketing practices subject to increased scrutiny by regulatory agencies," say Fugh-Berman and Melnick.

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