

Adverse Drug Events, Adverse Drug Reactions and Medication Errors *Frequently Asked Questions*

VA Center for Medication Safety
And
VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel
November 2006

DEFINITIONS

1. What is an adverse drug event (ADE)?

An *adverse drug event* is “an injury resulting from the use of a drug. Under this definition, the term ADE includes harm caused by the drug (adverse drug reactions and overdoses) and harm from the use of the drug (including dose reductions and discontinuations of drug therapy).”¹ Adverse Drug Events may result from medication errors but most do not.

2. What is an adverse drug reaction (ADR)?

An *adverse drug reaction* is a “response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function.” Note that there is a causal link between a drug and an adverse drug reaction.

In sum, an *adverse drug reaction* is harm **directly caused by the drug at normal doses, during normal use.**

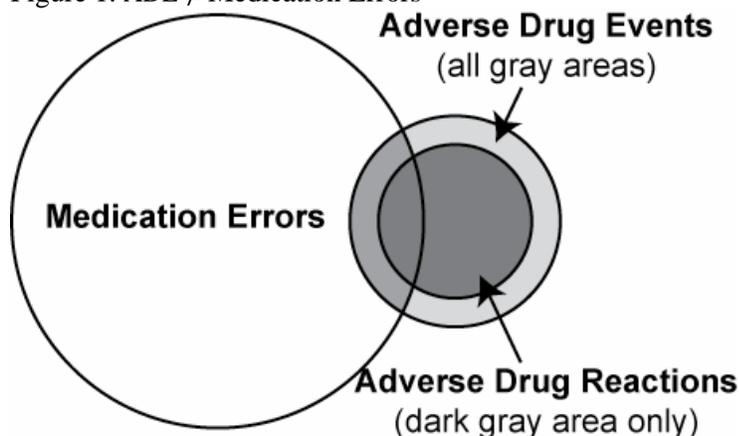
3. How does an ADR differ from a side effect or allergy?

An *allergy* is an *adverse drug reaction* mediated by an immune response (e.g., rash, hives). A *side effect* is an expected and known effect of a drug that is not the intended therapeutic outcome. The term “side effect” tends to normalize the concept of injury from drugs. It has been recommended that this term should generally be avoided in favor of *adverse drug reaction*.

4. What is a medication error?

Medication errors are mishaps that occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug. Examples of medication errors include misreading or miswriting a prescription. Medication errors that are stopped before harm can occur are sometimes called “near misses” or “close calls” or more formally, a *potential adverse drug event*. Not all prescribing errors lead to adverse outcomes. Some do not cause harm, while others are caught before harm can occur (“near-misses”).

Figure 1. ADE ≠ Medication Errors



Medication errors are more common than adverse drug events, but result in harm less than 1% of the time. About 25% of adverse drug events are due to medication errors.

Nebecker et al. Ann Intern Med 2004; 140: 795-801.

DOCUMENTING AND REPORTING ADVERSE DRUG REACTIONS:

5. Should we document adverse drug reactions?

Yes, the purpose of documenting is to **prevent future injuries** for your patients and for others.

New adverse drug reactions are often discovered when drugs are used in larger or in different populations than studied during initial clinical trials. This typically occurs within 3 years of entering the market. Therefore, documentation and reporting becomes a crucial element in clarifying the side effect profile of a drug (see below).

6. Which types of adverse drug reaction should be documented?

Of particular importance to the Food and Drug Administration (FDA) are **suspected adverse drug reactions** for a new drug (i.e., within 3 years of entry to market) and **suspected severe adverse drug reactions** for any drug, no matter when the drug entered the market (see below).

In practice, a good rule of thumb is to document adverse drug reactions that have caused harm or altered therapeutic care and/or where future use of the drug might cause danger or harm to a patient.

7. Where should adverse drug reactions be documented?

Document should take place in your clinic note and in the allergies/adverse reactions data field in CPRS. The latter allows for highlighting the adverse reaction on the cover sheet so others can view the information and allows for triggering alerts for you or other providers. You or a clinical pharmacist can do this.

8. How are adverse drug reactions entered into the allergy/adverse reactions datafield in CPRS?

This simple process takes about 30 seconds. Use the Order menu in CPRS, click on Allergies, enter the drug name and complete the form. For details see,

<http://vaww.pbm.va.gov/vamedsafe/How%20To%20Enter%20an%20Allergy%20or%20Adverse%20Drug%20.pdf>

The presentation is also available as a video/audio tutorial. See

http://vaww.hines.med.va.gov/cprs/Presentations/ADR_WMV/ADR.html

9. What is the difference between an “Observed” and “Historical” Adverse Drug Reaction?

When you enter the allergies/adverse reactions into CPRS, there is a choice of stating whether the event was “Observed or “Historical”.

Observed reaction is defined in the CPRS system as a reaction that is “directly observed or occurring while the patient was on the suspected causative agent.” For example, “Observed” would be appropriate if a new allergy or adverse reaction occurs while the patient was on a drug prescribed by you or a colleague.

“Observed” refers to a newly noted adverse outcome, typically within the past 3 months. Although the term implies that the clinician of record made the diagnosis, the fact that a clinician does not visually “observe” an adverse drug reaction does not preclude reporting it as “Observed.” For example, if you prescribe an ACE Inhibitor to a patient, who then is seen at an outside facility, or by another VA provider, for angioedema, you may record it as “Observed” in CPRS.

“Historical” generally refers to events in the past (i.e., more than 3 months old) or that reportedly occurred in the past at another healthcare setting. It is defined in the CPRS system as “reported by the patient as occurring in the past; no longer requires intervention.”

10. Should any other information be provided?

It is important to consider and document severity of the allergies/adverse reactions in the field provided in CPRS template. The pull down menu lists “mild”, “moderate” or “severe” These may be thought of as follows:

MILD - Requires minimal therapeutic intervention such as discontinuation of drug(s)

MODERATE - Requires active treatment of adverse reaction, or further testing or evaluation to assess extent of non-serious outcome (see below for definition of serious).

SEVERE - Includes any serious outcome, resulting in life- or organ-threatening situation or death, significant or permanent disability, requiring intervention to prevent permanent impairment or damage, or requiring/prolonging hospitalization.

Any additional information on the cause(s) of reaction may assist another reader in understanding the reaction and the likelihood that the drug caused the reaction. For example, for a case of myositis caused by a fibric acid-HMG CoA Reductase combination, the following would be helpful, "Statin titrated to 40 mgs and then fibrates added, with subsequent muscle pain 1 month later. A suspected contributor to this interaction was underlying renal insufficiency."

11. What is done with the information?

Information that you provide on observed reactions is reviewed by a pharmacist and is reported to your Pharmacy & Therapeutics (P&T) Committee. This committee helps guide medication safety efforts and may modify the medication use system subsequent to ADE reporting from practitioners. Serious reactions (defined above) are reported to the FDA's MedWatch program. In addition, any untoward reactions on newly-marketed drugs, typically within 3 years of release, are reported to the FDA. Reports are generally sent by your facility's pharmacy service. The FDA's draft guidance entitled, "Post-Approval Safety Data Management: Definitions And Standards For Expedited Reporting" can be found at <http://www.fda.gov/cber/gdlns/ichexrep.pdf>. In addition to reporting ADEs via CPRS (see #7, #8), clinicians may report reactions to the FDA. (see #12)

12. May an individual provider report a problem to the FDA?

Absolutely. Clinicians may report serious events to the FDA. MedWatch forms are on the FDA website <http://www.fda.gov/medwatch/report/hcp.htm>. Note that it is important to report the information to your P&T Committees at your facility and/or enter the information into CPRS as well. If you report on your own, please inform your facility's pharmacy service to avoid duplication in the reporting process.

13. What does the FDA do with MedWatch reports?

Adverse drug reactions reported through MedWatch can act as "signals" which are then investigated to determine their clinical significance and potential public health impact. This may lead to regulatory action, including mandatory warnings and labeling changes, manufacturer-sponsored post-marketing studies, journal publications, "Dear Health Professional" letters warning clinicians of possible drug-associated events, modified indications, and/or dosing schedules, or rarely, product withdrawal.

14. How should significant medication errors be reported?

Medication errors that are stopped before harm can occur are sometimes called "near misses" or "close calls" or more formally, a "potential adverse drug event." Significant medication errors should be reported through the patient incident reporting system at your healthcare facility through the Patient Safety Manager. They are analyzed quarterly by the facility and reported to the VA National Center for Patient Safety. Alternatively, it may be done confidentially via the Patient Safety Reporting System (PSRS) at <http://psrs.arc.nasa.gov/>.

15. Is there anything else that should be done for VA patients who suffer a serious adverse drug reaction?

It is always best to inform the patient on what happened and on what drug(s) to avoid in the future. Since the VA's electronic medical record does not transmit allergy/adverse reaction data automatically from site to site, or outside of VA, it is prudent for the patient to be advised to wear a MedicAlert bracelet or necklace when (s)he has a life or organ threatening reaction to a drug. (<http://www.medicalert.org>)

16. Is there any time that previously documented Allergies/Adverse Reactions may be removed from CPRS?

The following criteria should be considered guidance in that process and any removal should follow policy and protocols developed by an institution's Pharmacy & Therapeutics Committee. When removing

an allergies/adverse reactions some rationale should be entered into a progress note. Possible reasons to remove an adverse reaction or allergy include but are not necessarily limited to:

1. The ADR represents a clerical error such as entry on the wrong patient or drug.
2. The initial ADR was based on a suspected temporal relation between a drug and subsequent clinical event but no further ADR has occurred upon re-challenge to the drug.
3. The initial entry was based on or due to a comorbid condition that no longer exists or is no longer clinically relevant (e.g., lab value normalization; disease or condition resolution).

Reference:

1. Nebeker JR, Barach P, Samore MH. Clarifying Adverse Drug Events: A Clinician's Guide to Terminology, Documentation, and Reporting. *Ann Intern Med.* 2004; 140:795-801.