Micromedex® Solutions
Drug Interactions Policy

Background

A drug interaction is defined as a clinically meaningful alteration in the exposure and/or response to a drug that has occurred as a result of the co-administration of another drug. [xiv] Monitoring and alerting for drug interactions is an important role of clinicians.

The use of clinical decision support (CDS) systems in health systems can improve medical documentation, reduce errors, and improve patient safety.[i] An important part of CDS systems is drug interaction information. The Centers for Medicare and Medicaid Services (CMS) include drug interaction CDS alerts in their meaningful use guidelines for electronic health records.[ii] Research shows that both prescribers and pharmacists are often unable to recognize potential drug interactions when presented outside a CDS tool, making the use of CDS systems a significant part of the workflow for clinicians. [i,iii] Unfortunately, the use of CDS systems does not show consistent reductions in drug interaction interventions, based on reviewing the number of alerts generated and acted on by prescribers.[iv,v]

In an effort to be all-inclusive, current systems alert for drug interactions with limited clinical relevance and may extrapolate drug interactions to other drugs in the same therapeutic and pharmacologic class.[vi] Current systems also include theoretical drug interactions which are not supported by current medical evidence but are based solely on theoretical lists from manufacturers or other sources. Excess alerts may lead to alert fatigue and inappropriate drug interaction overrides by the clinician.[vii] Clinically important drug interactions may be missed in the "noise" of many non-clinically relevant interactions. Research shows clinicians have high override rates for drug interactions. A recent study showed physicians override of drug interaction alerts 95% of the time.[viii] Past estimates range from 33% to 96%.[ix,x] Experts recommend reducing alert fatigue by lowering the number of alerts presented to clinicians and by increasing alert specificity. [vii,xi,xii,xiii,xiv] A recent expert group also recommended drug compendia and CDS systems do not necessarily need to align with product labeling if the labeling is not consistent with existing evidence in order to prevent excess noise and alert fatigue. [xiv] It is critical that busy clinicians are provided with only clinically relevant, evidence-based drug interaction information.

Action

As the industry leader in providing clinically relevant, evidence-based drug information for clinical users, Truven Health Micromedex is committed to helping solve the problem of drug interactions. Micromedex Solutions is aligning with the recommendations of the drug interaction experts.[xiv] Going forward, drug interactions in Micromedex will meet specific criteria for inclusion. These criteria are:

1. Contraindicated drug interactions
2. Specifically named substances from the source document that have a clinically actionable recommendation or where a clinically important effect occurs
3. Drug interactions supported by evidence-based published medical literature:
   a. Human study of 6 or more subjects
   b. In vivo study with validated substrates, inhibitors, or inducers
   c. Case reports with Drug Interaction Probability Scale (DIPS) score of 5 or greater (Probable), using the DRug Interaction eVidence Evaluation Instrument (DRIVE).[xiv]
4. Pharmacodynamic drug interactions: Pharmacodynamic drug interactions are also called additive adverse effects. These drug interactions are created if they fulfill another rule above (eg are contraindicated) or are one of the following types that commonly result in patient harm:
   a. Anticoagulants
   b. Hypoglycemic Agents
   c. Respiratory depressants
   d. QT Prolongation
   e. Serotonin syndrome-producing agents

The following drug interactions will not be created in Micromedex Solutions content:
1. Negative drug interactions
2. Moderate or weak inhibitors/inducers unless meet other criteria
3. Based solely on in vitro or animal data
4. Occur outside of therapeutic dosages
5. The stated effect is not clinically relevant (e.g., when clinical relevance is not supported by additional literature or when a causal relationship between drug interaction and effect is poorly established)
6. Interactions caused by disease states

Drugs are often inhibitors, inducers, or substrates of specific enzymes or transporters that may affect drug interactions. Micromedex Solutions has developed clinically sound, evidence-based criteria to determine which drugs belong on which enzyme and transporter lists. Lists are available in the Micromedex Solutions product by going to Drug Interactions in the Drug Consults list. Clinicians also may use the lists to verify if alternative agents are also affected by a drug interaction, helping the clinician make informed decisions for their patients.

Micromedex drug interactions will continue to be classified by Severity, Onset, and Documentation. In addition, Micromedex Solutions provides an Interaction Effect, Clinical Management, and Probable Mechanism along with Literature Reports for each drug interaction. The new, streamlined alerts will minimize noise and decrease the risk of alert fatigue, providing clinicians with the evidence-based material needed to make clinically sound decisions for every patient, every time.

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[iii] Ko Y, Malone D, Skrepnek G. Prescribers' knowledge of and sources of information for potential drug–drug interactions; a postal survey of US prescribers. Drug Saf 2008; 31: 525–536.

[iv] Smithburger PL, Buckley MS, Bejian S, et al. A critical evaluation of clinical decision support for the detection of drug–drug interactions (expert opinion). Drug Saf 2011; 10 (6): 871–882.

[v] Duke JD, Li X, Dexter P. Adherence to drug–drug interaction alerts in high-risk patients: a trial of context-enhanced alerting. J Am Med Inform Assoc 2013; 20 (3): 494–498.

[vi] Hansten PD, Horn JR, Hazlet TK. ORCA: OpeRational ClassificAtion of drug interactions. J Am Pharm Assoc (Wash). 2001 Mar-Apr;41(2):161-5.

[vii] van der Sijs H, Aarts J, Vulto A, et al. Overriding of drug safety alerts in computerized physician order entry. J Am Med Inform Assoc 2006;13:138e47.

[viii] Bryant AD, Fletcher GS, Payne TH. Drug interaction alert override rates in the Meaningful Use era: no evidence of progress. Appl Clin Inform. 2014 Sep 3;5(3):802-13. doi: 10.4338/ACI-2013-12-RA-0103. eCollection 2014.

[ix] Taylor LK, Tamblyn R. Reasons for physician non-adherence to electronic drug alerts. Stud Health Technol Inform 2004;107:1101e15.

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[xi] Kuperman GJ, Bobb A, Payne TH, et al. Medication-related clinical decision support in computerized provider order entry systems: a review. J Am Med Inform Assoc 2007;14: 29e40.

[xii] Paterno MD, Maviglia SM, Gorman PN, et al. Tiering drug-drug interaction alerts by severity increases compliance rates. J Am Med Inform Assoc 2009;16:40e6.

[xiii] Weingart SN, Toth M, Sands DZ, Aronson MD, Davis RB, Phillips RS. Physicians' decisions to override computerized drug alerts in primary care. Arch Intern Med. 2003 Nov 24;163(21):2625-31.

[xiv] Scheife RT, Hines LE, Boyce RD, Chung SP, Momper JD, Sommer CD, et al. Consensus recommendations for systematic evaluation of drug-drug interaction evidence for clinical decision support. Drug Saf. 2015 Feb;38(2):197-206.