THE LEAPFROG GROUP
Giant Leaps for Patient Safety

GUIDANCE FOR ADULT AND GENERAL HOSPITALS PARTICIPATING IN THE 2022 LEAPFROG HOSPITAL SURVEY

CLINICAL DECISION SUPPORT RELATED TO THE 2022 CPOE EVALUATION TOOL

INTRODUCTION

To achieve Leapfrog's Computerized Physician Order Entry (CPOE) Standard, each adult and general hospital must (1) ensure that licensed prescribers enter at least 85% of inpatient medication orders via a computer system that includes decision support software to reduce prescribing errors, and (2) demonstrate, via a test, that its inpatient CPOE system can alert physicians to at least 60% of frequent serious medication errors known to cause harm to patients. To fulfill the second requirement of our standard, hospitals use Leapfrog's CPOE Evaluation Tool to complete an Adult Inpatient Test.

Upon successful completion of an Adult Inpatient Test, a hospital's responses are immediately scored and available to be viewed and printed. Results from the test are also archived and can be accessed anytime by logging back into the CPOE Evaluation Tool from the Survey Dashboard. For a copy of previous CPOE Test results from August 2022 or earlier, contact the Leapfrog Help Desk by submitting a ticket at https://leapfroghelpdesk.zendesk.com or an email to helpdesk@leapfrog-group.org.

SUMMARY OF CHANGES FROM THE 2022 LEAPFROG HOSPITAL SURVEY

Leapfrog is once again requiring adult and general hospitals to complete the CPOE Evaluation Tool to achieve the CPOE standard. The CPOE Evaluation Tool is accessible from the Survey Dashboard once Section 2 CPOE is completed and affirmed. The Survey cannot be submitted, including the results from the Adult Inpatient Test, until all five required sections (1 Basic Hospital Information, 2 CPOE, 4 Maternity Care, 5 ICU Physician Staffing, and 6 Patient Safety Practices) are completed and affirmed. See the CPOE scoring algorithm for adult and general hospitals on the Scoring and Results webpage.

Questions about various aspects of a hospital's EHR formerly included in the CPOE Evaluation Tool are moving to Section 2: Medication Safety – CPOE of the Online Survey Tool. As in previous years, Leapfrog does not score or publicly report responses to these questions.

DESCRIPTION OF THE CPOE EVALUATION TOOL

The CPOE Evaluation Tool was designed by medication safety experts and researchers at Brigham and Women's Hospital and the University of Utah to test the ability of inpatient CPOE systems to alert licensed prescribers to frequent serious medication errors known to cause harm to patients. In addition, the Tool was designed to help hospitals improve on their use of clinical decision support to reduce adverse drug events and improve medication safety. The Tool was first included in the Leapfrog Hospital Survey in 2008. The fifth release of the tool (version 4.0) is available for the 2022 Leapfrog Hospital Survey.

The timed Test provides users with a set of Test Patients, along with a corresponding set of Test Orders, that users enter into their hospital's CPOE and related clinical systems. The prescriber conducting the Test records the advice or information they received, if any, from their hospital's CPOE system onto the Orders and Observation Sheet, and then completes the Online Answer Form. Users receive immediate feedback summarizing the results of the Test. The Tool includes ten Order Checking Categories described in the next section.

ORDER CHECKING CATEGORIES

Nine of the ten order checking categories included in the CPOE Evaluation Tool represent an area where a serious adverse drug event (ADE) could occur if the CPOE system's clinical decision support fails to alert the prescriber. The tenth order checking category includes Test Orders that, if presented interruptedly, could contribute to over-alerting.

The CPOE Evaluation Tool is designed to test for two types of clinical decision support:

1. **Scenario-Specific Advice/Information**: Information related to the Test Order, which may include the medication's specific dose, route, and frequency, and the Test Patient, which includes specific patient demographics (e.g., age, gender) and clinical information such as problems/diagnoses, lab values, and allergies, as applicable. The scenario-specific advice/information may also involve the *combination* of two specific medication orders.

2. **Medication-Specific Advice/Information**: General information that might appear any time the medication is ordered for any patient and is not specifically related to the Test Patient (see the Drug Monitoring Order Checking Category).

The table below includes descriptions of each Order Checking Category included in the CPOE Evaluation Tool, as well as examples and the type of clinical decision support (i.e., scenario-specific advice/information or medication-specific advice/information) being tested.

Order Checking Category	Description	Example	Type of Clinical Decision Support
Inappropriate Drug Combinations	Medication combinations to avoid ordering together or ones to use with caution	Using clonazepam and lorazepam together	Scenario-specific advice/information
Drug Dose (Single)	Specified dose of medication exceeds safe range for single dose	Tenfold overdose of digoxin	Scenario-specific advice/information
Drug Dose (Daily)	Specified frequency of administration results in daily dose that exceeds safe range for daily dose	Ordering ibuprofen regular dose every three hours	Scenario-specific advice/information
Drug Allergy	Medication (or medication class) is one for which patient allergy has been documented	Penicillin prescribed for patient with documented penicillin allergy	Scenario-specific advice/information
Drug Route	Specified route of administration is inappropriate and potentially harmful	Use of hydroxyzine intravenously	Scenario-specific advice/information
Drug Diagnosis	Medication dose inappropriate/contraindicated based on documented problem/diagnosis	Non-selective beta-blocker in patient with asthma	Scenario-specific advice/information
Drug Age	Medication dose inappropriate/contraindicated based on patient age	Prescribing diazepam for a patient over 65 years old	Scenario-specific advice/information
Drug Laboratory	Medication dose inappropriate/contraindicated based on documented laboratory test results (includes renal status)	Use of nitrofurantoin in patient with severe renal failure	Scenario-specific advice/information
Drug Monitoring	Medication for which the standard of care includes subsequent monitoring of the drug level or lab value to avoid harm	Prompt to monitor drug levels when ordering aminoglycosides or INR/PT when ordering warfarin	Medication-specification advice/information
Excessive Alerts	Low-priority medication combinations, such as drug interactions or therapeutic duplications, that should not trigger decision support warnings.	Concurrent use of hydrochlorothiazide and captopril	Scenario-specific advice/information

The Adult Inpatient Test also includes a “Deception Analysis,” which checks for “false positives” (e.g., hospitals reporting advice/information for Test Orders that should not generate any warning in the hospital’s CPOE

system). Hospital's that "fail" the Deception Analysis are scored as "Incomplete Evaluation" and will not be able to retake an Adult Inpatient Test for 120 days.

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GENERAL GUIDANCE

HARD STOPS VS. DISRUPTIVE ALERTS

Both hard stops and disruptive alerts can be effective in preventing potentially unsafe orders from reaching the patient.

The CPOE Evaluation Tool developers recommend a "hard stop" when a medication order is absolutely contraindicated because a "hard stop" prevents the licensed prescriber from entering the unsafe order and prevents manual overrides. However, "hard stops" should be used judiciously and infrequently as there are very few contraindications that warrant a hard stop. Some examples include:

- Inappropriate Medication Combinations where there is no benefit of the drug combination that outweighs the risk (i.e., Monoamine Oxidase Inhibitors and Sumatriptan).
- Drug Route combinations where there has been documented harm or death (i.e., Vincristine given intrathecally).

Other Inappropriate Medication Combinations might not warrant a hard stop. For example, sildenafil and nitroglycerin should trigger an alert, but would not warrant a hard stop.

GUIDANCE FOR SPECIFIC ORDER CHECKING CATEGORIES

INAPPROPRIATE MEDICATION COMBINATIONS[1–7]

Inappropriate Drug Combination alerts should appear when prescribers order medications that should not be ordered together, or when prescribers order medications together that require caution. The CPOE Evaluation Tool tests for two specific types of inappropriate drug combination alerts: Drug-Drug Interactions and Therapeutic Duplication.

Drug Interactions
Level 1 Drug Interactions are drug combinations that are contraindicated for concurrent use. These Drug Interactions have a high potential for patient harm where the risk outweighs the benefit.

Examples of Level 1 Drug Interactions include:

- Concurrent use of simvastatin and itraconazole, which may result in increased exposure to Simvastatin and an increased risk of myopathy or rhabdomyolysis.
- Concurrent use of tizanidine and ciprofloxacin, which may result in increased Tizanidine plasma concentrations resulting in increased hypotensive and sedative effects.
- Concurrent use of monoamine oxidase inhibitors and sumatriptan, which may result in increased risk of serotonin syndrome (hypertension, hyperthermia, myoclonus, and mental status changes).

Level 2 Drug Interactions have a high potential for patient harm if action is not taken by a licensed prescriber. These actions may include monitoring drug levels and/or making dose adjustments as needed.

Examples of Level 2 Drug Interactions[7] include:

- Concurrent use of levofloxacin and warfarin
    - Concomitant use has been associated with increases in INR or prothrombin time and clinical episodes of bleeding. If concomitant use is required, early and more frequent monitoring of the patient's INR is recommended.
- Bactrim DS (sulfamethoxazole 800 mg and trimethoprim 160 mg) and warfarin sodium
    - Concurrent use of sulfamethoxazole and warfarin may result in increased warfarin exposure. If co-administration is required, monitor prothrombin time and INR early and closely, especially during initiation. Discontinuation of SMX is recommended. Preemptive warfarin dose reductions may be considered to prevent INR prolongation during co-administration.
- Drugs that both cause QT prolongation (see http://www.torsades.org for list of known risk drugs)
    - haloperidol and citalopram or haloperidol and ondansetron
        Concurrent use of either of these drug combinations may result in prolonged QTc interval or torsades de pointes. It is recommended to avoid concurrent use, however if co-therapy is warranted, monitoring QTc closely is recommended.
    - levofloxacin and amiodarone
        - Concurrent use may result in an increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest).
    - citalopram and omeprazole
        - Concurrent use may result in increased citalopram exposure and risk of QT interval prolongation. If co-administration of citalopram with omeprazole is required, do not exceed citalopram doses of 20 mg/day and discontinue citalopram in patients who have persistent QTc measurements greater than 500 milliseconds.

Therapeutic Duplication
Therapeutic Duplication are drug combinations that overlap therapeutically (same agent or same class).

Examples of Therapeutic Duplication include:
- 2 Ace Inhibitors – captopril and lisinopril
- 2 Statins – atorvastatin and simvastatin
- 2 NSAIDs – ibuprofen and naprosyn
- 2 Benzodiazepines – diazepam and alprazolam
- ibuprofen and motrin (brand and generic name of the same drug)

DRUG DIAGNOSIS[17]

Drug Diagnosis alerts should occur when the medication that is ordered is contraindicated based on a patient's documented problem or diagnosis.

Examples of Drug Diagnosis contraindications include:
- ketorolac and patients with GI Bleeds
    - Black Box warning: Contraindicated in active or history of peptic ulcer disease, recent gastrointestinal bleeding or perforation, or history of gastrointestinal bleeding
- prasugrel and stroke patients
    - Black Box warning: prasugrel can cause significant and sometimes fatal bleeding. Do not use prasugrel in patients with active pathological bleeding or a history of transient ischemic attack or stroke

- propranolol and carvedilol and asthma patients
    - Non-cardio selective beta-blockers were associated with a significantly increased risk of moderate asthma exacerbations when initiated at low to moderate doses and both moderate and severe exacerbations when prescribed chronically at high dose.[17]
- Hepatotoxic drugs and patients with liver disease

DRUG AGE[8–11]

Drug Age alerts should occur when the medication is contraindicated based on a patient's age. The CPOE Evaluation Tool focuses on medications that are contraindicated for geriatric patients. There are two resources that provide important examples of drug-age contraindications.

- 2019 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[8] Hospitals should focus on those recommendations where the quality of evidence and strength of the recommendation is **high**, which includes the following:
    - dronedarone – Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure
    - nifedipine, immediate release – Avoid
    - amiodarone – Avoid amiodarone as first-line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy
    - Antidepressants, alone or in combination (amitriptyline, amoxapine, clomipramine, desipramine, doxepin >6 mg/d, imipramine, nortriptyline, paroxetine, protriptyline, trimipramine) – Avoid
    - Barbiturates (amobarbital, butobarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, secobarbital) – Avoid
    - Ergoloid mesylates (dehydrogenated ergot alkaloids, Isoxsuprine) – Avoid
    - Growth hormone – Avoid, except as hormone replacement after pituitary gland removal
    - Sulfonylureas, long-duration (chlorpropamide) – Avoid
    - Proton-pump inhibitors – Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (e.g., due to failure of drug discontinuation trial or H2 blockers

- Screening Tool of Older Persons' Prescriptions (STOPP) version 2.[9] Potentially inappropriate medications listed in STOPP criteria, like some of those listed in Beers criteria, are significantly associated with avoidable ADEs in older people that cause or contribute to urgent hospitalization.[10]
    - Use of benzodiazepines, opiates or neuroleptics that lead to falls
    - Use of NSAID that lead to gastritis /peptic ulcer disease
    - Use of diuretics that lead to acute kidney injury and symptomatic orthostasis

Hospitals should also focus on drugs that are known to induce a patient's risk of falling such as: Antihypertensive agents, diuretics, sedatives and hypnotics, neuroleptics and antipsychotics, benzodiazepines, and narcotics.[11]

STOPP criteria and Beers criteria have several areas of overlap. Both sets of criteria emphasize the higher risk of adverse drug reactions and events in older people with use of long-acting benzodiazepines, tricyclic

antidepressants, anticholinergic drugs, and non–cyclooxygenase 2–selective nonsteroidal anti-inflammatory drugs.[10]

DRUG LABORATORY AND DRUG MONITORING[12]

Drug Laboratory alerts should occur when drug combinations are contraindicated based on documented laboratory test results, which includes renal status.

Examples of contraindicated drug lab combinations include:

- Ordering potassium chloride (KCl) or a potassium sparing diuretic (spironolactone) in a patient with a high potassium level
- Ordering digoxin in a patient with a high digoxin level
- Ordering nephrotoxic and/or renally cleared medications in a patient with a high Creatinine level

Drug Monitoring alerts should occur for drug combinations where the standard of care includes subsequent monitoring of the drug level or lab value to avoid harm. Hospitals should focus on drugs with a narrow therapeutic range, such as aminoglycosides, carbamazepine, digoxin, lithium, phenytoin, phenobarbital, theophylline, and warfarin. Hospitals should ensure that when ordering these medications, their systems directly alert the licensed prescriber at the point of ordering or provide a laboratory order to monitor the patient's labs that are needed for that medication. Examples of these include potassium levels, creatinine level, INR, and therapeutic drug levels.[12]

DRUG DOSE

Drug Dose alerts should occur when the specified dose or frequency of a medication or administration exceeds the safe range for a single dose or daily dose.

Hospitals should focus on drugs with a narrow therapeutic range, such as digoxin, as well as drugs that can cause serious or immediate toxicity if given in excessive amounts, such as narcotics and benzos. Hospitals should consult the Institute for Safe Medication Practices High-Alert Medications to ensure their clinical decision support alerts their prescribers to drugs that are known to cause harm if given in excessive doses, including:

- Hypoglycemic agents
- Anticoagulants
- Neuromuscular blockers
- Narcotics / Opioids

DRUG ALLERGY[13–15]

Drug Allergy alerts should occur when a drug is contraindicated based on a patient's documented allergy.

Allergy to Penicillin
Drug allergy alerts should not be triggered when a cephalosporin that is not structurally similar to penicillin is ordered for a patient with a documented anaphylaxis reaction to penicillin. Cephalosporins like cefazolin, cefdinir, ceftriaxone, cefpodoxime, and cefepime, do not have side chain structures similar to commonly

prescribed penicillins (e.g., penicillin, amoxicillin and ampicillin). Therefore, these specific cephalosporins are safe to use in patients with a documented anaphylaxis reaction to penicillin. For hospitals focused on improving their antibiotic stewardship practices, it is recommended that patients with a documented anaphylaxis reaction to penicillin be sent for skin testing to determine if they have a true allergic reaction. This can apply to patients whose preferred medications are penicillins or structurally similar cephalosporins.

Allergy to Opioids[13–15]
Patient reports of opioid "allergies" are common, most often due to symptoms of nausea, vomiting, itching, hypotension, or constipation. However, many healthcare providers struggle with distinguishing true allergic reactions from these reported adverse effects/intolerances.

Generally, allergies to one opioid agent does not mean the patient is allergic to other opioids so switching to an agent in another opioid chemical class (see list below) may be effective. A patient who is "allergic" to an opioid from one class (e.g., morphine, a phenanthrene) may be treated with an agent from another class (e.g., methadone, a phenylheptane) without allergy cross-sensitivity.

Chemical Classes of Opioid Medications
Phenanthrenes
codeine
hydrocodone
hydromorphone
levorphanol
morphine
oxycodone
Diphenyleptanes
methadone
propoxyphene
Phenylpiperidine
fentanyl
meperidine
Other
tramadol

Even though the risk of cross-sensitivity is extremely low, patients who exhibit a true allergic reaction to one of the opioid analgesics should be monitored carefully if an agent from another class is substituted. Hospitals should focus on opioid-related drug allergy alerts when the reaction is unknown, not documented, or a true allergic reaction (this excludes intolerances such as GI upset, nausea, constipation, etc.).

EXCESSIVE ALERTS

Medication orders in the Excessive Alerts category include low-priority medication combinations that should not trigger decision support warnings. By presenting these orders uninterruptedly, the number of alerts prescribers see is reduced, which can help reduce alert fatigue.

Examples of these inconsequential medication combinations include, but not limited to[16]:

- omeprazole and benzodiazepines
- NSAIDs and thiazide-type diuretics

REFERENCES

1. Hug BL, Witkowski DJ, Sox CM, et al. Adverse Drug Event Rates in Six Community Hospitals and the Potential Impact of Computerized Physician Order Entry for Prevention. *J Gen Intern Med*. 2010;25(1):31-38. doi:10.1007/s11606-009-1141-3
2. Phansalkar S, Desai AA, Bell D, et al. High-priority drug–drug interactions for use in electronic health records. *J Am Med Informatics Assoc*. 2012;19(5):735-743. doi:10.1136/amiajnl-2011-000612
3. Payne TH, Hines LE, Chan RC, et al. Recommendations to improve the usability of drug-drug interaction clinical decision support alerts. *J Am Med Informatics Assoc*. 2015;22(6):1243-1250. doi:10.1093/jamia/ocv011
4. Tilson H, Hines LE, McEvoy G, et al. Recommendations for selecting drug–drug interactions for clinical decision support. *Am J Heal Pharm*. 2016;73(8):576-585. doi:10.2146/ajhp150565
5. McEvoy DS, Sittig DF, Hickman T-T, et al. Variation in high-priority drug-drug interaction alerts across institutions and electronic health records. *J Am Med Inform Assoc*. 2017;24(2):331-338. doi:10.1093/jamia/ocw114
6. Phansalkar S, van der Sijs H, Tucker AD, et al. Drug—drug interactions that should be non-interruptive in order to reduce alert fatigue in electronic health records. *J Am Med Informatics Assoc*. 2013;20(3):489-493. doi:10.1136/amiajnl-2012-001089
7. Classen DC, Phansalkar S, Bates DW. Critical Drug-Drug Interactions for Use in Electronic Health Records Systems With Computerized Physician Order Entry. *J Patient Saf*. 2011;7(2):61-65. doi:10.1097/PTS.0b013e31821d6f6e
8. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2019;67(4):674-694. doi:10.1111/jgs.15767
9. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing*. 2014;44(2):213-218. doi:10.1093/ageing/afu145
10. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially Inappropriate Medications Defined by STOPP Criteria and the Risk of Adverse Drug Events in Older Hospitalized Patients. *Arch Intern Med*. 2011;171(11):1013-1019. doi:10.1001/archinternmed.2011.215
11. de Jong MR, Van der Elst M, Hartholt KA. Drug-related falls in older patients: implicated drugs, consequences, and possible prevention strategies. *Ther Adv Drug Saf*. 2013;4(4):147-154. doi:10.1177/2042098613486829
12. Touw DJ, Neef C, Thomson AH, Vinks AA, Cost-Effectiveness of Therapeutic Drug Monitoring Committee of the International Association for Therapeutic Drug Monitoring and Clinical Toxicology. Cost-effectiveness of therapeutic drug monitoring: a systematic review. *Ther Drug Monit*. 2005;27(1):10-17. http://www.ncbi.nlm.nih.gov/pubmed/15665740. Accessed August 14, 2019.
13. Topaz M, Seger DL, Lai K, et al. High Override Rate for Opioid Drug-allergy Interaction Alerts: Current Trends and Recommendations for Future. *Stud Health Technol Inform*. 2015;216:242-246. http://www.ncbi.nlm.nih.gov/pubmed/26262047. Accessed August 14, 2019.
14. Slight SP, Beeler PE, Seger DL, et al. A cross-sectional observational study of high override rates of drug allergy alerts in inpatient and outpatient settings, and opportunities for improvement. *BMJ Qual Saf*. 2017;26(3):217-225. doi:10.1136/bmjqs-2015-004851

15. Saljoughian M. Opioids: Allergy vs. Pseudoallergy. US Pharm. https://www.uspharmacist.com/article/opioids-allergy-vs-pseudoallergy. Published 2006. Accessed August 14, 2019.
16. Phansalkar S, van der Sijs H, Tucker AD, et al. Drug-drug interactions that should be non-interruptive in order to reduce alert fatigue in electronic health records. *J Am Med Inform Assoc*. 2013;20(3):489–493. doi:10.1136/amiajnl-2012-001089
17. Morales D, Lipworth B, Donnan P, Jackson C, Guthrie B. Respiratory effect of beta-blockers in people with asthma and cardiovascular disease: population-based nested case control study. *BMC Med*. 2017; 15: 18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5270217/. Accessed March 21, 2022.