GUIDANCE FOR ADULT AND GENERAL HOSPITALS PARTICIPATING IN THE 2021 LEAPFROG HOSPITAL SURVEY
CLINICAL DECISION SUPPORT RELATED TO THE 2021 CPOE EVALUATION TOOL
INTRODUCTION

In 2021, to fully meet 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. Hospitals are asked to use Leapfrog’s CPOE Evaluation Tool to complete an Adult Inpatient Test to fulfill the second requirement of our standard.

SUMMARY OF CHANGES FROM THE 2020 LEAPFROG HOSPITAL SURVEY

First, based on substantial feedback received during the 2019 Survey Cycle, the CPOE Evaluation Tool developers have implemented one change to the Order Checking Categories and one change to the scoring. The Therapeutic Duplication Order Checking Category and Drug-Drug Interaction Order Checking Category have been combined into a new Order Checking Category titled Inappropriate Drug Combinations to better reflect test scenarios included in the category: medication combinations to avoid ordering together or ones to use with caution. See a list of all Order Checking Categories.

Second, medication orders that were part of the Alert Fatigue Analysis are now part of a new category titled Excessive Alerts. These test scenarios include inconsequential or low-severity medication safety problems found in some drug-drug interactions or therapeutic duplications that, if presented interruptedly, can contribute to over-alerting. This category will be used in scoring for the 2021 CPOE Evaluation Tool.

In addition, the Orders and Observation Sheet has been updated to help eliminate confusion between the answer options on the Orders and Observation Sheet and the Online Answer Form. More specifically, Leapfrog has differentiated between Single Dose and Daily Dose on the sheet because they are separate categories.

Lastly, the Test Order library has been updated to provide alternatives for medications that are commonly reported as not being available in hospitals’ formularies.

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 2021 Leapfrog Hospital Survey.

The CPOE Evaluation Tool includes both a Sample Test and an Adult Inpatient Test. All hospitals are urged to complete the Sample Test prior to the Adult Inpatient Test. Only a hospital’s score on the Adult Inpatient Test is used to determine their overall performance on Leapfrog’s CPOE Standard.

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 physician conducting the Test records the advice or information they received, if any, from their hospital’s CPOE system onto the Orders and Observation Sheet.
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 alert fatigue.

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 or medication-specific advice/information) being tested.

<table>
<thead>
<tr>
<th>Order Checking Category</th>
<th>Description</th>
<th>Example</th>
<th>Type of Clinical Decision Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate Drug Combinations</td>
<td>Medication combinations to avoid ordering together or ones to use with caution</td>
<td>Using clonazepam and lorazepam together</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td>Drug Dose (Single)</td>
<td>Specified dose of medication exceeds safe range for single dose</td>
<td>Tenfold overdose of digoxin</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td>Drug-Dose (Daily)</td>
<td>Specified frequency of administration results in daily dose that exceeds safe range for daily dose</td>
<td>Ordering ibuprofen regular dose every three hours</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td>Drug-Allergy</td>
<td>Medication (or medication class) is one for which patient allergy has been documented</td>
<td>Penicillin prescribed for patient with documented penicillin allergy</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td>Drug-Route</td>
<td>Specified route of administration is inappropriate and potentially harmful</td>
<td>Use of hydroxyzine intravenously</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
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<tr>
<td><strong>Drug-Diagnosis</strong></td>
<td>Medication dose inappropriate/contraindicated based on documented problem/diagnosis</td>
<td>Non-selective beta-blocker in patient with asthma</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td><strong>Drug-Age</strong></td>
<td>Medication dose inappropriate/contraindicated based on patient age</td>
<td>Prescribing diazepam for a patient over 65 years old</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td><strong>Drug-Laboratory</strong></td>
<td>Medication dose inappropriate/contraindicated based on documented laboratory test results (includes renal status)</td>
<td>Use of nitrofurantoin in patient with severe renal failure</td>
<td>Scenario-specific advice/information</td>
</tr>
<tr>
<td><strong>Drug Monitoring</strong></td>
<td>Medication for which the standard of care includes subsequent monitoring of the drug level or lab value to avoid harm</td>
<td>Prompt to monitor drug levels when ordering aminoglycosides or INR/PT when ordering warfarin</td>
<td>Medication-specification advice/information</td>
</tr>
<tr>
<td><strong>Excessive Alerts</strong></td>
<td>Inconsequential or low-severity medication safety problems such as certain drug-drug interactions or therapeutic duplications that, if presented interruptedly, could contribute to over-alerting</td>
<td>Concurrent use of hydrochlorothiazide and captopril</td>
<td>Scenario-specific advice/information</td>
</tr>
</tbody>
</table>

If a user reports receiving advice/information for the Test Orders in the Excessive Alerts category, these Test Orders are listed in the CPOE Results so hospitals can review them with their pharmacy committees and discuss turning these alerts off.

The CPOE Evaluation Tool 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.
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 Drug 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 Drug 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 DRUG COMBINATIONS1-7

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 Interaction and Therapeutic Duplication.

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

Examples of Level 1 DDIs 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 DDIs 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 DDIs7 include:
• Concurrent use of Levofloxacin and Warfarin
  o 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
  o Concurrent use of Sulfamethathoxazole 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)
  o Haloperidol and Citalopram or Haloperidol and Ondansetron
    ▪ Concurrent use of Haloperidol and Citalopram or Haloperidol and Ondansetron may result in prolonged QTc interval or torsades de pointes. Recommend avoiding concurrent use, but if co-therapy is warranted, recommend monitoring QTc closely.
  o Levofloxacin and Amiodarone
    ▪ Concurrent use of Levofloxacin and Amiodarone may result in an increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest).
  o Citalopram and Omeprazole
    ▪ Concurrent use of Citalopran and Omeprazole 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:
  o 2 Ace Inhibitors – Captopril and Lisinopril
  o 2 Statins – Atorvastatin and Simvastatin
  o 2 NSAID – Ibuprofen and Naprosyn
  o 2 Benzodiazepine – Diazepam and Alprazolam
  o Ibuprofen and Motrin (brand and generic name of the same drug)

DRUG-DIAGNOSIS

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
  o 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 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5270217/).

- Hepatotoxic drugs and patients with liver disease

**DRUG-AGE**

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. 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. 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.
  - 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, 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 alerts should occur when a drug is contraindicated based on a patient’s documented allergy.

**Allergy to Penicillin**

Penicillin drug-allergy alerts should be triggered when a first-generation cephalosporin is ordered for a patient 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, should be sent for skin testing to determine if they have a true allergic reaction. This can apply to patients whose preferred medications are penicillin or a first- or second-generation cephalosporin.

**Allergy to Opioids**

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 to16:

- Omeprazole and benzodiazepines
- NSAIDs and thiazide-type diuretics
REFERENCES


16. Phansalkar S, van der Sijs H, Tucker AD, et al. Drug-drug interactions that should be non-interruptive in