Black Box Warnings

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PURPOSE

To create a system that provides standard alerts in the medical records when a high-risk medication with a black box warning is prescribed, verified, or administered. These alerts aim to support clinicians' compliance in recommended safe practices for medications with a black box warning and to prevent or minimize adverse drug events associated with use of these medications.

PERSONNEL

All Clinical Staff

DEFINITIONS

The Food and Drug Administration (FDA) "Boxed Warning" (also known as a black box warning) is the strongest labeling requirement and is intended to identify certain contraindications or serious warnings, particularly those that may lead to death or serious injury.

POLICY

The Pharmacy Department will develop alerts and guidelines approved by the Pharmacy and Therapeutics (P & T) Committee to ensure medications that carry a black box warning are controlled and distributed properly.

All medication-related adverse events associated with black box warnings will be reported to the Medication Safety and P & T Committees to review, trend, and take appropriate actions to minimize any future adverse events.

The Pharmacy Department will present all medication safety concerns to the P & T Committee upon evaluation for formulary addition. Formulary medications that contain a black box warning will be reviewed to determine the appropriate actions and/or limitations required to alert the clinicians about safe use of these drugs within the organization.

PROCEDURE

A. Identification

1. Medications approved for use in the hospital will be annually reviewed for black box warnings.
2. A "black box warning" alert will display in the medication order in the electronic health record to alert the physician or pharmacist at the time of order entry and the nurse at the point of medication administration if a drug carries a black box warning.

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B. Alerts and Guidelines

1. From a list of formulary drugs with black box warnings, the P&T Committee will establish a subset of high priority drugs for focused attention (Attachment 1). Analysis will be based on the severity risk level of the black box warning, adverse reactions history, and frequency of utilization.
2. The P&T Committee will assess the need to develop specific alerts and guidelines to be considered by physicians, nurses, and pharmacists in each medication management node as appropriate for safe use of these medications.

C. Prescribing

1. Medications that carry a black box warning will be identified on the patient's electronic medication record.
2. The physicians should assess and weigh the risk versus benefit of the medications they prescribe.
3. The Pharmacy Department will ensure that electronic drug information resources (e.g. Lexicomp, Micromedex) are available to all clinicians to provide detailed information for medications that carry black box warnings.
4. A pharmacist is available to provide information about a medication at any time, upon request.

D. Order Verification

1. The pharmacist will contact the prescribing physician when select, high-risk medications (Attachment 1) require intervention prior to order verification or require additional monitoring.

E. Dispensing

1. Select medications that require special handling will have auxiliary labels to alert clinicians about potential risks (Attachment 1).

F. Administration

1. Warnings about appropriate administration of the drug will display in the electronic medication administration record for select, high-risk medications (Attachment 1).
2. Warnings that highlight monitoring recommendations upon administration will display in the electronic medication administration record for select, high-risk medications (Attachment 1).

G. Monitoring

1. When recommended monitoring is not performed for select, high-risk medications (Attachment 1), the pharmacist will notify the prescribing physician that monitoring is recommended.

H. Education

1. Information and education about risks associated to any new black box warnings will be provided to hospital staff through P & T Committee and other communication methods (e.g. newsletters, meetings).

2. A list of all formulary-approved medications that carry a black box warning is electronically available on the Pharmacy Department's site.

REFERENCES

1. The Joint Commission Standard MM.01.01.03; MM.02.01.01
2. Centers for Medicare and Medicaid Services CMS Interpretation Guidelines CoP §482.25(a)(1)
3. www.fda.gov

Attachment 1. Table of Select Medications with Black Box Warnings and HMNH Actions or Recommendations

Black Box Warnings

Drug Class or Medication	Black Box Warning Details	HMNH Actions/Recommendations
Acetaminophen, IV	Risk of dosing errors for patients below 50kg	Pharmacists will notify physician to change to weight-based dosing for patients under 50 kg
Aminoglycosides (Amikacin, Gentamicin, Tobramycin,)	Neurotoxicity, nephrotoxicity, ototoxicity	Pharmacists will monitor peak and/or trough serum concentrations and renal function tests during therapy. See Aminoglycoside Dosing policy.
Clozapine	Severe neutropenia	Pharmacists will monitor absolute neutrophil count (ANC) prior to and during treatment. See Clozapine (Clozaril) Documentation & Dispensing policy.
Cyclosporine	Nephrotoxicity	Monitor renal function tests (serum creatinine, BUN) during therapy
Desmopressin, Intranasal or Oral	Hyponatremia	Ensure serum sodium is within normal limits prior to initiation and during therapy
Dofetilide	Induced arrhythmia upon initiation of therapy	Require ECG monitoring upon initiation per Pharmacological Cardioversion policy
Dopamine	Skin ischemia, sloughing, and necrosis upon extravasation	Monitor for signs & symptoms of extravasation. Follow Non-antineoplastic Extravasation Management policy.
Doxorubicin	Severe tissue injury and necrosis upon extravasation	Monitor for signs & symptoms of extravasation. Follow Chemotherapy Extravasation Management policy
Doxorubicin PEG-Liposomal (Doxil)	Infusion-related reactions	Monitor for flushing, shortness of breath, facial swelling, and/or hypotension.
Erythropoietin Stimulating Agents (Darbepoetin alfa, Epoetin alfa, Epoetin alfa biosimilar)	Increased risk of thrombosis, serious cardiovascular events, or death	Pharmacists will verify that hemoglobin level is 10.5 g/dL or below prior to verification and dispensing of these medications. See Epoetin Dispensing policy.
Fentanyl Patch	Serious, life-threatening, or fatal respiratory depression if used in opioid non-tolerant patients or if dosed improperly.	Pharmacists will review patient's opioid tolerance upon verification. See Fentanyl Patches policy.

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Flucytosine	Agranulocytosis, nephrotoxicity, hepatotoxicity	Pharmacists will adjust dose as appropriate for patient's renal function upon order verification. Monitor blood counts (CBC), renal and liver function tests (serum creatinine, BUN, AST, ALT, alk phos)
Ganciclovir	Granulocytopenia, anemia, thrombocytopenia, and pancytopenia	Monitor blood counts (CBC with diff) twice weekly and renal function (serum creatinine) tests weekly
Ibutilide	Potentially fatal arrhythmias	Require continuous ECG monitoring prior to initiation and during therapy. See Pharmacological Cardioversion policy.
Isoniazid	Hepatitis	Monitor liver function tests (AST, ALT) at baseline and during therapy
Ketorolac	Renal failure, cardiovascular thrombotic events, bleeding when: --Longer than 5 days of therapy --Dose exceeds 60mg/day in patients above 64 year old, below 50kg, or with renal dysfunction	Pharmacists will adjust dose as appropriate for patient's age, renal function, or weight upon order verification. Limit to no more than 5 days of therapy.
Lithium	Lithium toxicity (seizures, coma, cardiac dysrhythmia, death)	Monitor lithium levels twice weekly until clinical status and levels are stable
Metformin	Lactic acidosis	Pharmacist will review upon order verification and intervene per Renal Adjustment of Medications policy
Methadone	Life-threatening QTc prolongation	Monitor QTc interval upon admission. Consider alternative therapy for patients with QTc interval above 500 msec.
Metoclopramide	Tardive dyskinesia	Monitor for repetitive, jerking movements of face, neck and tongue. Consider alternative therapy if symptoms present.
Mitoxantrone	Severe tissue damage upon extravasation	Warning to administer slowly into freely flowing IV infusion and to avoid SC, IM, or intra-arterial routes.
Norepinephrine	Skin ischemia, sloughing, and necrosis upon extravasation	Monitor for signs & symptoms of extravasation. Follow Non-antineoplastic Extravasation Management policy.
Phenytoin	Severe hypotension & cardiac arrhythmias	Warning to administer IV at a rate not to exceed 50mg/min in adults or 1-3mg/kg/min in pediatrics. Recommend cardiac monitoring during and after administration.

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Phytonadione (Vitamin K)	Hypersensitivity, anaphylaxis, shock or cardiopulmonary arrest with IV push or IM use	Dispense as IVPB for infusion only
Promethazine	Severe skin necrosis and gangrene from any injectable form due to perivascular extravasation and intra-arterial injection	"Not for IV Push" auxiliary label upon dispensing. Warnings to give deep IM injection only. See High Alert Medications – Attachment.
Sotalol	Induced arrhythmia upon initiation of therapy	Require ECG monitoring upon initiation per Pharmacological Cardioversion policy
Tolvaptan	Osmotic demyelination upon overly rapid increase in serum sodium	Monitor serum sodium and rate of serum sodium increase closely
Valganciclovir	Leukopenia, neutropenia, anemia, thrombocytopenia	Monitor blood counts (CBC) and renal function (serum creatinine) tests
Valproic Acid	Hepatotoxicity, especially during first 6 months of therapy	Monitor liver function tests closely, if within first 6 months of therapy
Vinblastine Vincristine	Fatal if given routes other than IV	Dispense as IVPB only. See High Alert Medications – Attachment.
Warfarin	Major or fatal bleeding Severe drug interaction with capecitabine	Pharmacists will assess INR, interacting medications, and dosing history prior to prescribing. See Anticoagulation Therapy Management policy.