High Priority Black Box Warning Medication Guidelines

Los Angeles County - Department of Health Services Core Formulary

Drug Name/Class	Formulary Restriction	Summary of Selected Black Box Warning	Physician Actions	RN Actions	Pharmacist Actions
Acetaminophen (Tylenol)	• No Restriction	• Hepatotoxicity	• Ensure total daily dose does not exceed 4 grams • Avoid ordering multiple acetaminophen-containing products • Check LFT of patients on chronic acetaminophen therapy	• Keep track of all acetaminophen-containing products. • Notify prescriber if daily dose will exceed 4grams.	• Review LFT for patients with multiple acetaminophen containing products • Verify safety warnings are placed on the MAR "NTE 4000mg in 24 hrs" • Counsel outpatients NTE 4000mg/24hrs • Notify prescriber if daily dose will exceed 4grams.
Amiodarone Oral (Cordarone)	• No Restriction	• Pulmonary toxicity • Hepatic injury • Patients with the indicated arrhythmias must be hospitalized while the loading dose of this drug is administered, and a response generally requires at least one week	• Check LFT every 3-6 months if patients receiving high maintenance therapy (>600mg)	• Monitor pulmonary functions • Monitor for arrhythmias	• Verify LFT is ordered every 3-6 months in outpatients with maintenance dose > 600mg/day
Antiarrhythmics (Class 1C) • **Propafenone (Rythmol SR)** • **Flecainide (Tambocor)**	• Cardiology	• Increased rate of risk of death or reversed cardiac arrest rate in previous MI patients with asymptomatic non-life-threatening ventricular arrhythmias treated with Class 1C anti-arrhythmic • Significant risk in patients with structural heart disease	• Avoid in patients with non-life-threatening ventricular arrhythmias • Perform baseline ECG monitoring prior to initiation of medication	• Monitor heart rate signs/symptoms of cardiac failure	• Verify ECG monitoring is ordered for newly initiated therapy
Carbamazepine (Tegretol)	• No Restriction	• Aplastic Anemia • Agranulocytosis • Severe and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TENS) and Stevens-Johnson syndrome (SJS), may occur during therapy. The risk is increased in patients with the variant *HLA-B*1502* allele, found almost exclusively in patients of Asian ancestry. Patients who test positive for HLA-B*1502 should not be treated with carbamazepine unless the expected benefit clearly outweighs the increased risk of SJS/TEN. Over 90% of carbamazepine treated patients who will experience SJS/TEN have this reaction within the first few months of treatment. Patients of any ethnicity or genotype (including HLA-B*1502 positive) who have been taking carbamazepine for more than a few months are at low risk of SJS/TEN from carbamazepine.	• Order CBC at baseline and every 3-6 months. • If a patient, in the course of treatment exhibits low or decreased white blood cell or platelet counts, monitor closely. • Discontinue medication if significant bone marrow depression develops • Prior to therapy, patients with ancestry in at-risk populations should be screened for the HLA-B*1502 allele. • Discontinue in patients who have a serious dermatological reaction.	• Verify that prescriber has ordered CBC with initial therapy.	• Verify CBC is performed at baseline and every 3-6 months • Counsel outpatients to notify prescriber if severe rash develops. • Counsel outpatients to be aware of early signs and symptoms of hematologic changes including fever, sore throat, mouth ulcers, infections, easy bruising and petechiel or purpuric hemorrhage. Inquire with prescriber if genetic testing was considered for patients of Asian ancestry.
Darbepoetin alfa (Aranesp)	• Restricted to initiation of therapy only when hemoglobin (Hgb) levels <10g/dL. Monitor Hgb levels: maximum Hgb of 10g/dL for chronic kidney disease (CKD) without dialysis and 11g/dL for CKD with dialysis	• Patient with chronic kidney disease have increased risk of death, serious cardiovascular events (thromboembolic events), and strokes when hemoglobin >11g/dL • ESAs shortened overall survival and/ or increased risk of tumor progression.	• Must enroll in and comply with the ESA APPRISE Oncology Program to prescribe darbepoetin to patients with cancer. • Use the lowest dose needed to avoid red blood cell transfusions. • Do not prescribe for patients receiving myelosuppressive therapy when the anticipated outcome is cure • Order and monitor Hgb • For chronic kidney disease (CKD) patients that require dialysis, withhold dose if hemoglobin exceeds 11 g/dL • For non-dialysis chronic kidney disease (CKD) patients, hold dose if hemoglobin exceeds 10 g/dL • For non-CKD patients, withhold dose if hemoglobin exceeds 12 g/dL • or rises by 1g/dL in any 2 week period.	• For chronic kidney disease (CKD) patients that require dialysis, withhold dose and notify prescriber if hemoglobin exceeds 11 g/dL • For non-dialysis chronic kidney disease (CKD) patients, hold dose and notify prescriber if hemoglobin exceeds 10 g/dL • For non-CKD patients, withhold dose and notify prescriber if hemoglobin exceeds 12 g/dL or rises by 1g/dL in any 2 week period	• For chronic kidney disease (CKD) patients that require dialysis, do not dispense dose and notify prescriber if hemoglobin exceeds 11 g/dL • For non-dialysis chronic kidney disease (CKD) patients, do not dispense dose and notify prescriber if hemoglobin exceeds 10 g/dL • For non-CKD patients, do not dispense dose and notify prescriber if hemoglobin exceeds 12 g/dL or rises by 1g/dL in any 2 week period • Validate indication and that prescriber has enrolled in APPRISE program in order to prescribe Darbepoetin to patients with cancer.
Divalproex Sodium and Derivatives	• No Restriction	• Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid and its derivatives. Children under the age of two years are at a considerably increased risk of developing fatal hepatotoxicity	• Check LFTs 3-6 months with initial therapy or dosing change • Exercise increased caution when prescribing valproate to patients with a	• Verify indication and pregnancy status, prior to administration. • If patient is pregnant, notify prescriber prior to administration.	• Verify LFTs are ordered 3-6 months with initial therapy or dosing change • Verify indication and pregnancy status prior to dispensing.

*Refer to DHS Formulary for detailed restriction(s).

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Approved By: Ben Ando

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		• Increased risk of pancreatitis • Teratogenicity	prior history of hepatic disease. • Check amylase and triglyceride if symptoms of possible pancreatitis • Order Pregnancy test for women of childbearing age. • Do not use for migraine if pregnant • When treating a pregnant woman or a woman of childbearing potential, carefully consider both the potential risks and benefits of treatment and provide appropriate counseling.		
Dopamine	• No Restriction	• Vesicant. Antidote for peripheral ischemia provided as boxed warning.	• Ensure proper needle or catheter placement prior to and during infusion. • Watch I.V. site closely.	• Ensure proper needle or catheter placement prior to and during infusion. • Avoid extravasation; infuse into a large vein if possible. Avoid infusion into leg veins. Watch I.V. site closely. • As soon as possible after extravasation is noted, infiltrate the area with 10 to 15 mL of 0.9% Sodium Chloride Injection containing from 5 to 10 mg phentolamine. A syringe with a fine hypodermic needle should be used and the solution liberally infiltrated throughout the ischemic area. • Notify prescriber of extravasation.	• Recommend to give phentolamine as soon as possible after extravasation is noted.
Fentanyl Transdermal (Duragesic)	• Management of pain in opioid-tolerant patients (dose 60mg/day of ORAL morphine or equivalent for 7 days). Do not use for acute, intermittent, or mild pain • Prior Authorization required for outpatient use.	• Respiratory depression and death may occur when used as recommended as well as when misused or abused. Proper dosing and titration are essential. and should only be prescribed by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain. Contraindicated for use in conditions in which the risk of life-threatening respiratory depression is significantly increased, including use as an as-needed analgesic, use in non-opioid tolerant patients, acute pain, and postoperative pain. • High abuse potential. • Application of heat, damaged, or cut patches may increase the release of fentanyl Accidental exposure may result in death and other serious medical problems. Strict adherence to the recommended handling and disposal instructions may prevent accidental exposure. • Drug interaction with CYP450 3A4 drugs may increase fentanyl plasma concentration	• Assess patients for their clinical risks for opioid abuse or addiction prior to prescribing and routinely monitor all patients for signs of misuse, abuse and addiction during treatment. • Do not use in opioid-naive patients • Do not use for break through pain • Do not use for acute post-op pain. • Use facility fentanyl patch order form for all fentanyl patch prescriptions. • Order only if all dosing criteria are met. • Ensure you have completed all required training prior to prescribing. • Review patient's profile for drug-drug interactions and consider implications.	• Do not apply heat to patch area. Notify prescriber if patient develops fever while wearing the transdermal system. • Monitor respiratory function while on medication • Ensure prescriber has completed fentanyl patch order form for prescriptions. • Remove old patch before applying new patch. • Document application site on MAR	• Verify prescriber has completed Fentanyl Patch Order Form before order entry and dispensing. • Validate dosing criteria prior to processing/dispensing. • Review profile for drug-drug interactions and notify prescriber if warranted. • Counsel outpatients to strictly adhere to the recommended handling and disposal instructions to prevent accidental exposure to themselves or others.
Haloperidol (Haldol)	• Haloperidol IV administration to be monitored by continuous and/or 12-lead ECG. If not possible in combative patients, initiate ECG as soon as possible	• Sudden death, QT prolongation and Torsades de Pointes (TdP) with haloperidol, especially when given intravenously, or at doses higher than recommended. FDA approved for IM. • Considerable evidence that the IV use of haloperidol is a relatively common off-label clinical practice. • Increase mortality in elderly patients with dementia-related psychosis	• Order ECG monitoring prior and during IV administration • If not possible in combative patient, initiate ECG as soon as possible.	• ECG monitoring prior and during IV administration. If not possible in combative patient, monitor ECG as soon as possible. • Monitor heart rate, signs/symptoms of cardiac failure.	• Verify ECG monitoring for intravenous administration. • Review profile for concomitant medications known to produce Torsades de Pointes/ QTc elongation.
Hydromorphone Injection (Dilaudid-HP)	• No Restriction	• Do not confuse hydromorphone hydrochloride high potency injection with standard parenteral formulations of hydromorphone hydrochloride or other opioids. Overdose and death could result. • Risk of respiratory depression with abuse • Sedative effect are potentiated with alcohol and other CNS depressants	• Morphine and hydromorphone doses are not interchangeable. Hydromorphone is 5-6 times more potent that parenteral morphine.	• Monitor respiratory function while on medication.	• Review appropriateness of narcotic order change, especially dosing change from morphine to hydromorphone.
Immune Globulins	• Pediatric	• Renal dysfunction, acute renal failure, osmotic nephrosis, and	• Check renal function (BUN, Scr, I/O's)	• Verify pharmacist review of	• Review concentration and infusion rate

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(human, equine, rabbit)	• Hematology	death • Risk of thrombosis with or without risk factors. • For patients at risk of thrombosis, administer at the minimum concentration available and at the minimum rate of infusion practicable. • Ensure adequate hydration in patients before administration. • Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.	and review profile for other concurrent nephrotoxic agents. • Carefully consider the following risk factors: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity and cardiovascular risk factors.	infusion rate prior to administration. • Monitor patients carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion and encourage patients to report any signs or symptoms.	and follow manufacturer's recommended infusion rate. • Review profile for other concurrent nephrotoxic agents.
Ketorolac (Toradol)	Restricted to a maximum of 5 days of therapy	• Indicated for short term management (up to 5 days) of moderate to severe acute pain. • Maximum total daily dose of oral ketorolac (40mg) • Maximum total daily dose for injectable (120mg) • Ketorolac injection is contraindicated for intrathecal and epidural administration due to its alcohol content. • Hypersensitivity reactions, ranging from bronchospasm to anaphylactic shock, have occurred. • Dosage should be adjusted for patients 65 years or older, for patients under 50 kg (110 lbs) of body weight, and for patients with moderately elevated serum creatinine. • Increased risk of bleeding; Inhibits platelet function. Reports of acute renal failure, nephritis, and nephrotic syndrome. • Increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which may be fatal. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. • Increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach and intestines, which may be fatal. • May inhibit uterine contractions and adversely affect fetal circulation. • Potential for adverse effects due to prostaglandin-inhibiting drugs on neonates. • Ketorolac tromethamine is CONTRAINDICATED in patients currently receiving ASA or NSAIDs because of the cumulative risk of inducing serious NSAID-related side effects.	• Check renal function (BUN, Scr, I/O's) • Do not order for more than 5 days • Adjust dose to renal function, age, and weight. Do not exceed 60 mg (total dose per day) of ketorolac injection in patients 65 years or older, under 50 kg (110 lbs) of body weight, and/or for patients with moderately elevated serum creatinine. • Do not use in patients with advanced renal impairment and in patients at risk for renal failure due to volume depletion. • Do not administer ketorolac via epidural or intrathecal route. • Do not use in patients who have previously demonstrated hypersensitivity to ketorolac or allergic manifestations to aspirin or other (NSAIDs). Appropriate counteractive measures must be available when administering first dose. • Do not use in labor and delivery and in nursing mothers. • Do not use in patients with active peptic ulcer disease, recent GI bleeding or perforation, and in patients with a history of peptic ulcer disease or gastrointestinal bleeding. Exercise increased caution for elderly patients, as they are at increased risk, • Do not use for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery • Do not use in patients with suspected or confirmed cerebrovascular bleeding, patients with hemorrhagic diathesis, incomplete hemostasis, and those at high risk of bleeding • Do not use as a prophylactic analgesic before any major surgery, or intra-operatively when hemostasis is critical.	• Notify prescriber if ketorolac treatment is expected to exceed 5 days. • Do not exceed total daily dose, oral (40mg), injectable (120mg) • Contact prescriber if order written for intrathecal or epidural route. • Notify prescriber of any decline in renal function prior to administering next dose. • Alert prescriber of bleeding. • Notify prescriber if patient is nursing.	• Treatment not to exceed 5 days • Check Age (≥65), Weight (<50kg) and renal function and recommend appropriate dose. • Calculate maximum daily dose for oral and injectable forms. • Assess profile and notify prescriber if concurrent use of NSAIDs is detected. • Contact prescriber if order written for intrathecal or epidural route.
Lithium	• No Restriction	Lithium toxicity is closely related to serum lithium levels, and can occur at doses close to therapeutic levels. Facilities for prompt and accurate serum lithium determinations should be available before initiating therapy.	• Determine serum concentrations twice per week during the acute phase of treatment and until serum level and clinical condition of the patient have stabilized. • Serum concentrations in uncomplicated cases receiving	• Monitor for signs and symptoms of lithium toxicity: diarrhea, vomiting, tremor, mild ataxia, drowsiness, muscular weakness, lack of coordination	• Interpret lithium levels and maintain drug levels within therapeutic range. • Counsel outpatients and their families to discontinue lithium and contact the physician if clinical signs of lithium toxicity appear.

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			maintenance therapy during remission are to be monitored at least once every 2 months. • Exercise increased caution when dosing geriatric patients.		
Long Acting Beta Agonists	• Pediatrics • Adult Allergy/Immunology • Pulmonology • Not to be used as monotherapy for treatment of asthma • Salmeterol – PA required for outpatient use (LA care patients only) • Formoterol – PA required for outpatient use	• Increased risk of asthma-related death. When treating patients with asthma, long acting beta agonists (LABAs) should only be used as additional therapy for patients not adequately controlled on other asthma-controller medications (e.g. inhaled corticosteroids) • May increase the risk of asthma-related hospitalization in pediatric and adolescent patients.	• Do not initiate in patients with acutely deteriorating asthma • Do not use a LABA alone without the use of a long-term asthma control medication, such as an inhaled corticosteroid • For pediatric and adolescent patients, if adherence cannot be assured, a fixed-dose combination product containing both an inhaled corticosteroid and LABA is recommended and must be considered. • Counsel patients to notify physician with signs/symptoms of deteriorating asthma control and seek medical attention promptly if warranted. • As LABAs do not relieve sudden-onset asthma symptoms. A rescue inhaler, such as an albuterol inhaler, should be prescribed to treat sudden asthma symptoms.	• Counsel discharged patients to notify physician with signs/symptoms of deteriorating asthma control and seek medical attention promptly if warranted • Monitor respiratory function while on medication.	• Counsel discharged patients to notify physician with signs/symptoms of deteriorating asthma control and seek medical attention promptly if warranted. • Review patient's medication profile for LABA as mono-therapy for asthma • Encourage patients, families, and caregivers to read the *Medication Guide* that accompanies LABA prescriptions.
Lamotrigine (Lamictal)	• No restriction	• May cause severe and potentially life-threatening skin rashes requiring hospitalization (including Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis and Angioedema). • Incidence of serious rash is higher in pediatric patients than adults. • Risk may be increased by co-administration with valproic acid, higher than recommended starting doses, and exceeding recommended dose titration.	• Monitor for signs/symptoms of rash or skin disorder. • Discontinue at first sign of rash, unless the rash is not drug related	• Monitor for signs/symptoms of rash or skin disorder. • Withhold dose and notify physician at first sign of rash.	• Counsel outpatients to notify physician and discontinue at first sign of rash, unless the rash is not drug related.
LMWH (Enoxaparin) **Fondaparinux (Arixtra)**	• Enoxaparin- No restriction • Fondaparinux- Restricted to Orthopedics or patients requiring anticoagulation that have suspected acute Heparin-Induced-Thrombocytopenia (HIT) or a confirmed history of HIT. Prior Authorization required for Outpatient Use.	• Risk of spinal/epidural hematoma with neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture, which can result in long-term or permanent paralysis.	• If neurologic compromise is noted, urgent treatment is necessary. • For enoxaparin, placement or removal of a spinal catheter should be delayed for at least 12 hours after administration of prophylactic doses and 24 hours for patients receiving therapeutic doses. • For fondaparinux, delay needle placement of a spinal catheter for a minimum of 72 hours and removal for at least 48 hours after previous dose. • Do not give post-procedure doses of either enoxaparin or fondaparinux for at least 4 hours after catheter removal. • A benefit-risk assessment should consider both the risk for thrombosis and the risk for bleeding in the context of the procedure and patient risk factors.	• Verify with physician the holding parameters for patients on or with a pending epidural • Monitor for signs/symptoms of neurological impairment.	• Verify safety warning is placed on MAR • If spinal catheter orders in the presence of LMWH or fondaparinux is brought to the attention of the pharmacist, the pharmacist is to verify timing recommendations with clinicians.
Metformin containing products	• No Restriction	• Lactic acidosis is a rare, but serious, metabolic complication that	• Check serum creatinine,	• Ensure metformin is held for 48	• Check serum creatinine, contreindicated

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		may occur due to metformin accumulation during treatment. When it occurs, it is fatal in approximately 50% of cases.	contreindicated Scr>1.5 (male), Scr>1.4 (female) • Hold medication for 48 hours after IV contrast administration • Discontinue Metformin immediately if acidosis is suspected.	hours after IV contrast administration	Scr>1.5 (male), Scr>1.4 (female) • Advise physicians to hold metformin 48 hours after IV contrast administration
Methadone (Dolophine)	• Injectable for inpatient use • Management of pain for opioid-tolerant patients. Do not use for acute, intermittent, or mild pain	• Deaths, cardiac and respiratory, have been reported during initiation and conversion of pain patients to methadone treatment from treatment with other opioids • Respiratory depression is the chief hazard associated with methadone hydrochloride • QT elongation and serious arrhythmias have been reported. • Abuse potential.	• Avoid use in opioid-naïve patients. • Do not use for acute, intermittent pain, or "PRN" use • Titrate dose slowly. Adverse effects may have delayed manifestation due to accumulation and long half-life • Monitor ECG for patient on long term (≥6 months) use or when concomitantly used with pro-arrhythmic medications (e.g. propafenone, flecainide, procainamide). • Use caution when prescribing concomitantly with medications known to cause respiratory depression • Evaluate patient for any history of structural heart disease, arrhythmia, syncope, and for existence of potential drug interactions. • Closely monitor patients for changes in cardiac rhythm during initiation and titration. • Assess patients for their clinical risks for opioid abuse or addiction prior to prescribing and routinely monitor all patients for signs of misuse, abuse and addiction during treatment.	• For hospitalized patients monitor cardiac and respiratory functions and alert prescriber for excessive sedation, lethargy and/or changes in cardiac rhythm.	• Review patient's medication profile for potential interaction with pro-arrhythmic medications and/or medications associated with QT changes. • Review appropriateness of methadone dose, frequency and indication. • Do not dispense for as needed (PRN) use
Methotrexate	• Hematology/Oncology • Rheumatology • Dermatology* • OB/GYN	• Bone marrow suppression • Hepatotoxicity • Pulmonary toxicity • Malignant lymphomas • Tumor lysis syndrome	• Check CBC, LFT, chest X-ray at baseline and every 3-6 months, consider more frequent monitoring with high doses, especially in oncology patients. • NSAIDs may increase risk of ulcerative stomatitis • Monitor pulmonary function	• Monitor signs/symptoms of diarrhea, ulcerative stomatitis, and notify physician if patient exhibits these symptoms • Monitor pulmonary functions and notify physicians of decrease in function	• Verify dose is appropriate for indication. • Review medication profile for NSAIDs, increase risk of ulcerative stomatitis, and notify physician of risk • Dispense preservative free formulation for intrathecal or high-dose use • Check CBC, LFT with new orders and all oncology orders.
Metoclopramide (Reglan)	• No restriction	• Chronic treatment can cause tardive dyskinesia, a serious movement disorder that is often irreversible • Risk is increased with duration of treatment and total cumulative dose • Prolonged treatment with metoclopramide (greater than 12 weeks) should be avoided in all but rare cases where therapeutic benefit outweighs the risk	• Discontinue metoclopramide therapy in patients who develop signs or symptoms of tardive dyskinesia	• Monitor signs of tardive dyskinesia (jerky muscle movements, tongue thrusting, facial grimacing/ticks, random movements of extremities) extrapyramidal side effects, parkinsonian-like symptoms	• Patients on prolonged therapy or a high-dose regimen are at greater risk for these adverse effects • Notify prescriber if therapy duration is expected to exceed 12 weeks. • Counsel patients to notify physician of signs/symptoms of tardive dyskinesia (jerky muscle movements, tongue thrusting, facial grimacing/ticks, random movements of extremities), extrapyramidal effects, or parkinsonian symptoms.
Midazolam (Versed)	• Anesthesiology • Emergency Medicine • Specialties/ area approved per facility moderate sedation	• May cause severe respiratory depression, respiratory arrest, or apnea. Use with extreme caution, particularly in noncritical care settings. For deeply sedated pediatric patients, a dedicated individual, other than the practitioner performing the procedure,	• Ensure immediate availability of flumazenil before administration • Utilize lower doses for older (over 60 years) or debilitated patients and in	• Ensure immediate availability of flumazenil before administration. • Closely monitor respiratory and cardiovascular status.	• Ensure that flumazenil is readily available • Verify dose is appropriate based on patient population. • Verify initial pediatric doses for

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	policies	should monitor the patient throughout the procedure. • Initial doses in debilitated patients should be conservative; start at the lower end of dosing range. • Do not administer by rapid I.V. injection in neonates; severe hypotension and seizures have been reported; particularly with concomitant fentanyl use.	patients receiving concomitant narcotics or other central nervous system depressants. No more than 1.5 mg is to be given over a period of no less than 2 minutes in the above patient population. • Initial doses and subsequent doses are to be titrated slowly. • Pediatric doses are to be calculated on a mg/kg basis.	• Verify IV rate prior to administration in neonates.	sedation/anxiolysis/amnesia is age, procedure and route dependent.
Midodrine	• No Restriction	• Can cause supine hypertension. Systolic pressure of about 200 mmHg were seen overall in about 13.4% of patients given 10 mg. Systolic elevations of this degree were most likely to be observed in patients with relatively elevated pre-treatment systolic blood pressures (mean 170 mmHg). Not recommended in patients with initial supine systolic pressure above 180 mmHg. It is essential to monitor supine and sitting blood pressures in patients while on midodrine.	• Carefully consider the risks and benefits of midodrine use in inpatients. • Prescribe only for patients whose lives are considerably impaired despite standard clinical care for symptomatic orthostatic hypotension (OH). • Assess potential for supine and sitting hypertension, renal function and hepatic function prior to prescribing. • In the presence of renal dysfunction, exercise caution. Starting dose is not to exceed 2.5mg. • Do not prescribe for patients with initial supine systolic pressure above 180mmHg. • May only continue treatment in those patients who report significant symptomatic improvement. • Although doses may be given in 3 hour intervals, if required, to control symptoms, do not prescribe more frequently. • Closely monitor hepatic function, renal function and blood pressure.	• Check blood pressure every shift. For ambulatory patients, check standing blood pressure with every shift. • Withhold dose and notify prescriber if signs or symptoms of supine hypertension.	• Verify initial supine systolic pressure. • Counsel outpatients not to take their last dose of the day after the evening meal or less than 4 hours before bedtime to minimize nighttime supine hypertension. • Counsel outpatients about blood pressure recording. • Counsel outpatients to immediately report symptoms of supine hypertension to the prescriber.
Morphine Extended-release (e.g. Kadian, MS Contin)	• Kadian-Restricted to G-tube or J-tube patients who are unable to swallow pills • MS Contin- No restriction.	• Abuse potential • Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. • Indicated for opioid tolerant patients for management of moderate to severe pain when continuous around the clock opioid is needed. Not to be used for "as needed" (PRN) analgesic • Opioid-naive patients are NOT to receive ≥ 100 mg single dose • Capsule beads that are chewed, crushed, or dissolved may increase the risk of rapid release and absorption resulting in a fatal dose • Accidental ingestion can result in a fatal overdose of morphine, especially in children.	• Do not prescribe partial doses - Only full capsule dosages are to be used • Extended-release capsules are indicated for once daily administration for moderate to severe pain requiring continuous, around the clock therapy for a period of time • Do not use as a PRN analgesic • Review patient's history with opioid tolerance • Do not order ≥ 100 mg single dose for opioid-naive patients • Assess patients for their clinical risks for opioid abuse or addiction prior to prescribing and routinely monitor all patients for signs of misuse, abuse and addiction during treatment.	• Capsules must be swallowed whole or the contents of the capsules sprinkled on applesauce. • Should not be administered as PRN analgesic. Notify prescriber if written as PRN. • Do not administer ≥ 100 mg single dose for opioid-naïve patients and notify prescriber.	• Educate patient that alcohol consumption may result in rapid release and potential fatal dose of morphine • If written as PRN, notify prescriber that medication is to be used on a scheduled basis only. • Review patients history to determine opioid tolerance • Notify prescriber if ≥100mg single dose is ordered for an opioid-naive patient • Counsel outpatients not to crush, dissolve, or chew extended release formulations to prevent rapid release and absorption of a potentially fatal dose of morphine. • Counsel outpatients to take precautionary measures to prevent accidental exposure
Mycophenolate (CellCept)	• Transplant Patients • Nephrology • Dermatology • Rheumatology • Prior Authorization required for outpatient use	• Increased susceptibility to infection and possible development of lymphoma. • Increased risk of pregnancy loss and congenital malformations	• Complete Mycophenolate REMS training prior to prescribing. • Verify pregnancy status prior to administration. Perform repeat pregnancy tests during routine follow-up visits. • Order initial and periodic WBC panel • Check initial and periodic renal	• Notify physician if patient informs of pregnancy or suspected pregnancy	• Verify pregnancy status prior to administration • Verify WBC and renal function are checked initially and at periodic intervals. • Counsel Females of Reproductive Potential about pregnancy prevention and planning.

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			function		
Oxycodone Controlled Release (OxyContin)	• Pain Service • Hematology/Oncology • Prior Authorization required for outpatient use.	→ Abuse potential → Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. → Indicated for opioid tolerant patients for management of moderate to severe pain when continuous around the clock opioid is needed. Not to be used for "as needed" (PRN) analgesic → Opioid-naive patients are NOT to receive > 40 mg single dose or total daily dose > 80 mg → Tablets should not be crushed, cut, broken, dissolved, or chewed as this may lead to rapid release of oxycodone → Accidental exposure may result in fatal overdose of oxycodone, especially in children.	• Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy. • Not intended for PRN use. Do not prescribe for PRN use. • Prescribe full dosage forms (no partial dosages) • Prescribe an alternate agent if patient requires oral dosages to be crushed or chewed (e.g. NG tube) • Review patients history with opioid tolerance • Do NOT order > 40 mg single dose or total daily dose > 80 mg for Opioid-naive patients • Assess patients for their clinical risks for opioid abuse or addiction prior to prescribing and routinely monitor all patients for signs of misuse, abuse and addiction during treatment.	• Do not crush, chew, or break as release • Controlled release oxycodone (Oxycontin) 10mg is not interchangeable with oxycodone 10mg • Do NOT administer > 40 mg single dose or total daily dose > 80 mg to Opioid-naive patients. Notify prescriber of concern. • Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy.	→ Be alert for orders that involve the need to crush, chew, or break this dosage form → Controlled release oxycodone (Oxycontin) 10mg is not interchangeable with oxycodone 10mg → Do not dispense for PRN use and notify prescriber that medication is not intended for PRN use → Review patients history with opioid tolerance → Do NOT dispense > 40 mg single dose or total daily dose > 80 mg to Opioid-naive patients and notify prescriber. → Counsel patients to swallow tablets intact. The tablets are not to be crushed, dissolved, or chewed to prevent a potentially fatal overdose, especially in opioid-naive individuals. → Counsel outpatients to take precautionary measures to prevent accidental exposure
Pioglitazone (Actos)	• Restricted to documented failure/intolerance to metformin OR sulfonylurea.	→ Pioglitazone hydrochloride may cause or exacerbate congestive heart failure in some patients → After initiation and dose increases, monitor patients carefully for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care and discontinuation or dose reduction of must be considered. → ACTOS is not recommended in patients with symptomatic heart failure. → Initiation of ACTOS in patients with established New York Heart Association (NYHA) Class III or IV heart failure is contraindicated.	• Prescribe with caution in patients with history of CHF or previous MI • Counsel discharged patient to contact physician immediately for signs of edema, dyspnea and rapid weight gain.	• Check daily weights • Counsel discharged patient to contact physician immediately for signs of edema, dyspnea and rapid weight gain.	→ Counsel discharged patient or outpatient to contact physician immediately for signs of edema, dyspnea, and rapid weight gain.
Procainamide (Pronestyl)	• No Restriction	→ Agranulocytosis → Bone marrow depression → Neutropenia → Hypoplastic anemia → Thrombocytopenia. → Prolonged administration may lead to a positive anti-nuclear antibody (ANA) test	• Order CBC, basic metabolic panel, and anti-nuclear antibody test promptly if the patient develops any signs of infection, bruising, or bleeding • Perform CBC, including white cell, differential and platelet counts at weekly intervals for the first three months of therapy, and periodically thereafter. • If any of these hematologic disorders are identified, discontinue procainamide therapy.	• Monitor for signs/symptoms of bleeding, bruising, or fever while on medication • Counsel discharged patient to contact physician immediately with signs/symptoms of bruising or bleeding	→ Counsel discharged patient to contact physician immediately with signs/symptoms of bruising or bleeding
Rituximab (Rituxan)	• Hematology/Oncology. - Restricted to Rheumatology patients who have failed traditional DMARDs and at least 1 TNF inhibitor. - Restricted to Nephrology for patients who have failed traditional immunosuppressant therapy. - Restricted to Dermatology for patients with Pemphigus Vulgaris that have failed 2 systemic standard immunosuppressant agents.	→ Fatal Infusion Reactions within 24 hours of infusion → Severe Mucocutaneous Reactions, some with fatal outcomes → Hepatitis B Virus Reactivation in some cases resulting in fulminant hepatitis, hepatic failure, and death. → FDA recommends discontinuing all chemotherapy until HBV infection is controlled or resolved. → Progressive Multifocal Leukoencephalopathy resulting in death	• Pre-medicate patients with acetaminophen and an antihistamine (if patient has RA, use recommended dose of methylprednisolone or equivalent. • Discontinue in patients experiencing severe mucocutaneous skin reactions • Screen for HBV using HBsAG and anti-HBc prior to initiating treatment. • For patients at risk of HBV reactivation, consult with local facility experts regarding monitoring and use of HBV anti-viral therapy. • During therapy and for several months	• Closely monitor for reactions during infusion. • Notify prescriber if patient presents with severe Mucocutaneous skin reaction	→ If new start, verify if HBV screening has occurred and been reviewed

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High Priority Black Box Warning Medication Guidelines

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Drug Name/Class	Formulary Restriction	Summary of Selected Black Box Warning	Physician Actions	RN Actions	Pharmacist Actions
			thereafter, monitor patients with past history of HBV infection for clinical and laboratory signs of HBV reactivation. • If reactivation occurs, immediately discontinue rituximab and initiate HBV anti-viral therapy.		
Rivaroxaban (Xarelto)	• Restricted to Orthopedics for Total Knee or Hip Arthroplasty Postoperative Thromboprophylaxis per Rivaroxaban (Xarelto) PA Form	• Spinal/Epidural Hematomas have occurred in patients who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Optimal timing between the administration of rivaroxaban and neuraxial procedures is not known.	• Prior to scheduling patients for spinal procedures consider risk of developing epidural or spinal hematoma which can result in long-term or permanent paralysis. • Prior to scheduling a spinal procedure evaluate patient for age, renal and hepatic impairment and make necessary adjustments to regimen. • Wait at least 18 hours after last dose before removing epidural catheter. • Wait at least 6 hours after catheter removal prior to administering next dose. • If traumatic puncture occurs, administration is to be delayed for 24 hours. • Monitor for signs/symptoms of neurological impairment. • If neurologic compromise is noted, urgent treatment is necessary.	• Verify with physician the holding parameters for patients on or with a pending epidural • Monitor for signs/symptoms of neurological impairment.	• Verify safety warning is placed on MAR • If spinal catheter orders in the presence of rivaroxaban is brought to the attention of the pharmacist, the pharmacist is to verify timing recommendations and warnings with clinicians. • Evaluate profile for concomitant use of drugs that affect hemostasis.
Tumor Necrosis Factor (TNF) Blockers	• Rheumatology* • Dermatology* • GI Services	• Increased risk for developing serious infections involving multiple organ systems and sites that may lead to hospitalization or death due to bacterial, mycobacterial, fungal, viral, parasitic, and other opportunistic pathogens, including *Legionella* and *Listeria*. • Cases of active TB have developed in patients receiving adalimumab whose screening for latent TB infection was negative. • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients. Hepatosplenic T-cell lymphoma has been reported in patients with Crohn's disease or ulcerative colitis treated with infliximab and concurrent or prior azathioprine or mercaptopurine use, usually reported in adolescent and young adult males.	• Consider the risks and benefits prior to initiating therapy in patients with chronic or recurrent infection, patients with underlying conditions that may predispose them to infection, patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing a TNF blocker in patients who develop a malignancy. • Prior to initiating treatment, test for latent TB. If positive, start treatment for TB prior to starting TNF Blocker. Monitor all patients for active TB during treatment, even if initial latent TB test is negative. • During treatment, monitor for signs and symptoms of serious infections. • Consider empiric antifungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness. • Discontinue if a patient develops a	• Ensure TB skin test or CXR has been ordered and reviewed by prescriber • Notify prescriber if patient presents with signs or symptoms of serious infection.	• If new start, inquire with clinician to verify TB skin test or CXR has been ordered and reviewed by prescriber. • Encourage patients to read the Medication Guide that accompanies their prescription for a TNFα blocker. • Notify prescriber to discontinue if a patient develops a serious infection or sepsis.

High Priority Black Box Warning Medication Guidelines

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Drug Name/Class	Formulary Restriction	Summary of Selected Black Box Warning	Physician Actions	RN Actions	Pharmacist Actions
			serious infection or sepsis.		
Warfarin (Coumadin)	• No Restriction	• Risk of major or fatal bleeding	• Check Hb/Hct and PT/INR at initiation of therapy and at regular intervals thereafter, per facility protocol • Ensure that dietician reviews patient diet • Instruct patient to report bleeding.	• Monitor for signs and symptoms of bleeding or excessive bruising • Ensure that dietician reviews patient diet • Instruct patient to report bleeding.	• Review profile for severe drug-drug interaction. • Check PT/INR • Advise dietician of warfarin order • Follow facility anticoagulation protocol • Instruct patient to report bleeding

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