*PL Detail-Document* **#300610**
*−This PL Detail-Document gives subscribers*
*additional insight related to the Recommendations published in−*
***PHARMACIST'S LETTER / PRESCRIBER'S LETTER***
June 2014

# Lab Monitoring for Common Medications

Table not all-inclusive. Information applies to adults. Emphasis is on routine monitoring, as opposed to symptom-triggered monitoring (e.g., checking amylase in event of pancreatitis symptoms). In some situations, signs/symptoms may be a better indication of adverse effects than lab test results. Recommendations may differ from product labeling. **Underlined text denotes lab monitoring recommended in FDA-approved labeling** (i.e., package insert). Product labeling recommendations are U.S. unless otherwise referenced. Label recommendations may differ among brands or drugs within a class. Canadian monograph recommendations included if more conservative than referenced FDA-approved labeling.

**Please note potassium conversion for Canada: mEq/L=mmol/L**

**Abbreviations**: ACEI - angiotensin-converting enzyme inhibitor; ALT - alanine aminotransferase; ARB - angiotensin receptor blocker; AST - aspartate aminotransferase; BUN - blood urea nitrogen; CCS - Canadian Cardiovascular Society; CPhA - Canadian Pharmacists Association; CrCl - creatinine clearance; GFR - glomerular filtration rate; LDH - lactate dehydrogenase; NSAID - nonsteroidal anti-inflammatory drug; SBP - systolic blood pressure; SCr - serum creatinine; T4 - thyroxine; TSH - thyroid stimulating hormone; ULN - upper limit of normal

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Aldosterone antagonists [i.e., spironolactone, eplerenone (*Inspra*)] | Potassium and renal function | • Guidelines: check potassium and renal function at baseline, three and seven days after initiation, monthly for three months, then quarterly. Restart monitoring cycle if ACEI or ARB added or their dose increased.[1]<br>• Eplerenone labeling: check potassium at baseline, within the first week, one month after initiation or dose adjustment, then periodically.[2] Also check potassium and serum creatinine three to seven days after starting a moderate CYP3A4 inhibitor (e.g., verapamil, fluconazole). Contraindicated with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole).[2]<br>• Spironolactone labeling: check potassium and creatinine one week after initiation or dose increase, monthly for three months, quarterly for a year, then every six months.[4] | Antagonism of aldosterone can cause hyperkalemia and worsening renal function.[1] | • Guidelines: do not start if serum creatinine >2.5 mg/dL (221 umol/L) in men or >2 mg/dL (176.8 umol/L) in women (for spironolactone, ≥200 umol/L per CCS), **or** CrCl ≤30 mL/min., **or** potassium ≥5 mEq/L (≥5.2 mmol/L for spironolactone, per CCS).[1,5] Reduce dose or discontinue if serum potassium >5.5 mEq/L.[1]<br>• Eplerenone labeling: if potassium reaches 5.5 mEq/L, hold or reduce dose.[2] Do not start if potassium >5.5 mEq/L (Canada: >5 mmol/L).[2,3] Per U.S. hypertension indication, do not start if SCr >2 mg/dL in men or >1.8 mg/dL in women, or CrCl <50 mL/min (for other indications, do not start if CrCl ≤30 mL/min).[2] Per Canadian labeling, do not start if GFR <30 mL/min/1.73m$^2$ in any patient.[3]<br>• Spironolactone labeling: if potassium >5 mEq/L or SCr > 4 mg/dL, hold or stop.[4] |

*More. . .*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| ACEI or ARB | Potassium and renal function | • Check potassium and SCr within 1 to 2 weeks of initiation and after dosage increases, then in 3 to 4 weeks if stable.[1,6,8,37] If SCr increased, check again in 2 to 3 weeks, and again in 3 to 4 weeks (at minimum).[6,9] Then check once or twice yearly, and when patient condition or medications change.[6-8,37]<br>• Low-risk patients (see comments) with serum potassium 4.5 mEq/L or less could wait 4 weeks before initial assessment.[9]<br>• Product labeling generally recommends monitoring potassium frequently if co-administered with potassium or potassium-sparing diuretics. | Kidney filtration in some patients is highly dependent on angiotensin.[6,8] | • Discontinue if potassium ≥5.5 mEq/L.[6]<br>• Discontinue if SCr increases >30% within 1st two months of starting drug despite dose reduction.[6]<br>• Discontinue if SCr increases by >1 g/dL or by ≥50%.[6,8]<br>• Risk factors for adverse renal effects: diabetes; use of NSAID, cyclosporine, or diuretic; renal artery stenosis (risks: elderly, female, smoking, high cholesterol); GFR <60 mL/min; chronic kidney disease; heart failure; sodium depletion; low albumin; atherosclerosis; dehydration; hypo- or hypertension.[8-12]<br>• No evidence ARBs safer for kidneys than ACEI.[10] |
| | White blood cell counts | • ACEI: consider checking periodically in patients with renal impairment or collagen vascular disease.[132] (e.g., lupus). Canada: can consider for all patients.[133] | May cause bone marrow suppression. | |
| Aliskiren (*Tekturna* [U.S.], *Rasilez* [Canada]) | Potassium and renal function | • Periodically[9] | Can impair renal function and increase potassium.[98] | • Do not use with ARBs or ACEIs in patients with diabetes.[98]<br>• Per Canadian labeling, do not use with ARB or ACEI if GFR <60 mL/min/1.73m$^2$.[101] |
| Antiarrhythmics | Liver function | • Amiodarone: Baseline and every six months[30] | Drug is metabolized in the liver, and is hepatotoxic.[30] | • Transaminase >2 times normal occurs in in 15% to 30% of patients, but hepatitis/cirrhosis occurs in <3%.[30]<br>• If hepatotoxicity suspected, consider discontinuation, liver scan, and/or biopsy.[30,102]<br>• If transaminases >3 times the ULN, or double in a patient with elevated baseline, consider dosage decrease or discontinuation.[92] |
| | Potassium level | • Flecainide (*Tambocor*): baseline[35] | Potassium disturbances may alter drug effects. | • Correct hypo- or hyperkalemia before administration.[35] |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Antiarrhythmics continued | Thyroid function | • Amiodarone: baseline and every six months[30] | Can cause hypothyroidism or hyperthyroidism. | • Incidence of hyperthyroidism may be as high as 12%.[30]<br>• Incidence of hypothyroidism may be as high as 22%.[30]<br>• Management options include discontinuation; levothyroxine for hypothyroidism; or corticosteroids, antithyroid medication, or surgery for hyperthyroidism.[30] |
| | Drug level | • Flecainide (*Tambocor*). Check trough periodically:<br>• in routine care (may be useful)[35]<br>• in heart failure (recommended; goal trough <0.7 to 1 mcg/mL)[35]<br>• in severe liver impairment (early and frequent monitoring required)[35]<br>• in severe renal impairment (CrCl 35 mL/min/1.73m$^2$ or less; frequent monitoring required [daily trough, per Canadian labeling])[35,38]<br>• moderate renal impairment (may be helpful [recommended, Canada])[35,38]<br>• if used with amiodarone (strongly recommended)[35]<br>• in elderly (recommended; check daily during dose adjustment, Canada)[38]<br>•Mexiletine: when taken with enzyme inducers (phenytoin, rifampin, phenobarbital)[36] | Narrow therapeutic index drug. | • Flecainide therapeutic range: trough 0.2 to 1 mcg/mL.[35]<br>• Increase flecainide dose only when steady-state achieved (about four days; longer in renal and hepatic impairment).[35]<br>• Mexiletine: therapeutic range approximately 0.5 to 2 mcg/mL. Peak occurs two to three hours post-dose. Assess peak when toxicity (e.g., central nervous system adverse effects) is of concern; assess trough when efficacy (arrhythmic control) is of concern.[36] |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Anticoagulants, oral | Renal function | Apixaban (*Eliquis*): baseline, yearly, and when clinically indicated[23]<br><br>Dabigatran (*Pradaxa*): baseline, yearly (Canada), and when clinically indicated[31,103]<br><br>Rivaroxaban (*Xarelto*): at baseline, yearly (Canada), and when clinically indicated.[104,105] Monitor closely if CrCl close to 30 mL/min.[105] | Renal dose adjustment required. | See our *PL Chart, Comparison of Oral Anticoagulants*, for renal dosing information. |
| | International Normalized Ratio (INR) | Warfarin:<br>• Daily until stable in the therapeutic range, then every 1 to 4 weeks. Check frequently in patients with high bleeding risk[90] or heart failure.[106]<br>• Guidelines: for stable patients, suggested frequency 12 weeks.[91]<br>• In elderly, check at least every six weeks.[37]<br>• Increase monitoring if interacting drug or natural medicine is added, discontinued, or taken sporadically; if brand is changed;[90] and after hospital discharge.[106]<br>• If single measurement ≤0.5 above or below therapeutic range, repeat in 1 to 2 weeks.[91] | Narrow therapeutic index drug with interindividual differences in metabolism. | • See our *PL Charts, Cytochrome P450 Drug Interactions* and *Antimicrobial Drug Interactions and Warfarin*, and *PL Algorithm, How to Manage High INRs in Warfarin Patients*, for help managing drug interactions and INR excursions.<br>• Patients with heart failure may be more sensitive to warfarin's effect, and may need more frequent monitoring.[106] |
| | CYP2C9 and VKORC1 genotype | Warfarin: baseline[90] | Those with genetic variant may need lower dose or more frequent monitoring.[90,106] | • Guidelines recommend against routine genotyping.[91] |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Anticonvulsants | Drug level | Reasons to check level:<br>• Loading, or dosage change[15-17,19,20]<br>• To establish target level in patient with good control and few side effects[14,16,18]<br>• Suspected toxicity[14-16,18]<br>• Large variation in levels (phenytoin)[16]<br>• Starting/stopping interacting drug[14,16,18-20,29] (See our *PL Charts, Cytochrome P450 Drug Interactions,* and *Comparison of Antiepileptic Drugs* [based on U.S. product information] for help identifying potential interactions.)<br>• Diseases or physiologic changes (e.g., pregnancy, renal failure)[14-16,21,26]<br>• Poor control[14,18-20]<br>• Suspected noncompliance[14-16,18]<br>• Change in how administered (e.g., with or without food) (valproate)[19,20]<br>• Potential malabsorption (phenytoin, carbamazepine, valproate)[16,19,21]<br>• Switching dosage form, salt form, or product (phenytoin, valproate)[16,19,20]<br>• Switching brand (phenytoin)[16] | Narrow therapeutic index drugs. | • Therapeutic level not well-established for most agents (e.g., valproate[a], newer agents [e.g., lamotrigine, etc]).[17]<br>• Unclear benefit of routine blood/serum level monitoring without clinical indication.[14]<br>• Level usually checked in morning immediately prior to dose (trough).[17]<br>• Checking peak may help assess toxicity for some agents (e.g., carbamazepine [tablets 4 to 5 hrs post-dose; suspension 1.5 hrs post-dose; extended-release tablets 3 to 12 hrs post-dose], phenytoin extended-release [4 to 12 hrs post-dose], divalproex [about 4 hrs post-dose, fasting]).[13,16,18,19,22]<br>• Levels usually checked after at least 4 to 5 half-lives (i.e., steady-state).[17]<br>• Valproate[a], phenytoin: free (unbound) level more accurate than total level in renal or liver disease, elderly, and hyperlipidemia (valproate).[16,19] |
| | Liver function | See our *PL Chart, Liver Function Test Scheduling.* | For agents associated with liver damage. | • Carbamazepine, eslicarbazepine, ethosuximide, felbamate, and valproate require routine liver function monitoring.<br>• Most anticonvulsants require dosing adjustments or cautious dosing for hepatic impairment. |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Anticonvulsants, continued | Complete blood count | • Carbamazepine: baseline, monthly for 2 or 3 months, then at least every other year[17,18]<br><br>• Felbamate: baseline, frequently during therapy, and for a significant time after discontinuation[28] | Can cause bone marrow suppression.[18] | |
| | Renal function | • Carbamazepine: baseline and periodic urinalysis and BUN[18]<br><br>• Zonisamide (*Zonegran*): periodically[27] | Can cause renal dysfunction. | Most anticonvulsants require dosing adjustments or cautious dosing for renal impairment. |
| | HLA genotype | Carbamazepine: HLA-B*1502 at baseline in high-risk patients (i.e., those of Asian ancestry).[18] Also consider HLA-A*3101 genotyping.[21]<br><br>Oxcarbazepine: consider HLA-B*1502 genotyping at baseline in high-risk patients (i.e., those of Asian ancestry)[26] | HLA-B*1502 and HLA-A*3101 alleles associated with serious skin reactions. | High prevalence of HLA-B*1502 (>15%) in Hong Kong, Thailand, Malaysia, and parts of the Philippines, followed by Taiwan (10%), North China (4%), and Japan and Korea (1%).[18] In South Asians, including Indians, risk is 2% to 4%, but may be higher in some groups.[18] |
| | Platelet count, coagulation tests | Valproate[a]: check platelet count and coagulation tests at baseline, periodically, and prior to planned surgery.[19,20] Monitor clotting parameters in pregnancy.[19,20] | Can cause thrombocyto-penia and low fibrinogen.[19] | |
| | Ammonia level | • Valproate[a]: in event of lethargy, vomiting, mental status change, hypothermia[19,20]<br><br>• Topiramate (*Topamax*): if encephalopathic symptoms occur[24] | Can cause hyper-ammonemia. | Concomitant valproate/topiramate use increases risk.[19,20] |
| | Bicarbonate | • Topiramate (*Topamax*): baseline and periodically[24]<br>• Zonisamide (*Zonegran*): baseline and periodically[27] | Can cause metabolic acidosis. | |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Anticonvulsants, continued | Thyroid function | Oxcarbazepine (*Trileptal*): consider evaluation of thyroid hormone status (frequency not specified)[26] | May cause hypo-thyroidism.[26] | T3 and TSH usually unaffected.[25] |
| | Sodium | Oxcarbazepine (*Trileptal*):<br>• Consider periodic monitoring, especially if hyponatremia symptoms occur (e.g., nausea, headache, malaise, lethargy, mental status change, seizures)[25]<br>• In heart failure, check in the event of worsening disease or fluid retention[26]<br>• In patients with renal disorders associated with low sodium, check at baseline, in two weeks, monthly for three months, and as clinically indicated (e.g., in event of symptoms)[26]<br>• In patients taking sodium-lowering meds (e.g., diuretics), consider checking periodically (per Canadian labeling, check at baseline, in two weeks, monthly for three months) and as clinically indicated (e.g., in the event of symptoms)[25,26]<br><br>Carbamazepine:<br>• In patients with renal conditions associated with low sodium, or taking sodium-lowering meds, check at baseline, in two weeks, monthly for three months, then as clinically indicated[21]<br><br>Eslicarbazepine (*Aptiom*):<br>• Consider periodic monitoring, especially in patients with hyponatremia risk factors (e.g., taking other sodium-lowering meds). Check in the event of hyponatremia symptoms.[138] | Can cause hyponatremia. | Oxcarbazepine: hyponatremia usually occurs within the first three months of treatment. If it occurs, consider dose reduction, fluid-restriction, or discontinuation.[25] Canadian labeling recommends fluid restriction in heart failure patients with hyponatremia.[26] |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Antipsychotics, Atypical<br><br>(aripiprazole [*Abilify*], asenapine [*Saphris*], clozapine [*Clozaril*], iloperidone (*Fanapt* (U.S.)], lurasidone (*Latuda*), olanzapine [*Zyprexa*], paliperidone [*Invega*], quetiapine [*Seroquel*], risperidone [*Risperdal*], ziprasidone [*Geodon* (U.S.), *Zeldox* (Canada)]) | Glucose, fasting | • Patients with diabetes: monitor regularly for worsening glucose control.[54]<br>• Patients with diabetes risk factors: baseline and periodically[54]<br>• Canadian labeling: baseline and periodically for all patients<br>• Guidelines: baseline, at 12 weeks, then annually.[52] (Check more frequently if high diabetes risk.[53] Some clinicians check every three to six months, with more frequent initial checks in high-risk patients).[53] | Increased risk of hyperglycemia and diabetes.[53] | • In U.S., prescribers, patients, and pharmacies must register with the *Clozaril* National Registry (800-448-5938; www.clozarilregistry.com). Manufacturer-specific registry and distribution systems have been established for generic manufacturers.<br>• In Canada, prescribers, patients, and pharmacies must register with the CSAN distribution system for *Clozaril* (800-267-2726). Manufacturer-specific registry and distribution systems have been established for generic manufacturers.<br>• Some agents require caution, dose adjustment, or avoidance in renal or hepatic impairment.<br>• Diabetes and hyperlipidemia risk varies among agents (see our *PL Charts, Comparison of Atypical Antipsychotics* (U.S. subscribers) (Canadian subscribers). |
| | Lipids | • Baseline and periodically (olanzapine, quetiapine, aripiprazole [adolescents, Canada], clozapine [Canada])[107-110]<br>• Consensus statement: baseline, at 12 weeks, then every two to every five years if normal.[52] Check more frequently if clinically indicated.[52] Some clinicians check every three months, especially during the first year, to yearly.[53] | Some agents can increase total cholesterol, LDL, and/or triglycerides. | |
| | Complete blood count | • *Clozaril* (clozapine): See product labeling for schedule.<br>• In patients with history of leucopenia or neutropenia, frequently during the first few months (aripiprazole, asenapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone)[109-115,120,134]<br>• Canada: baseline and periodically, all patients (aripiprazole, lurasidone, olanzapine, paliperidone, quetiapine, ziprasidone)[43,107,116-118,135] | Antipsychotics (particularly clozapine) have been associated with bone marrow suppression. | |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Antipsychotics, continued | Potassium and magnesium | • Baseline and periodically in patients at risk for electrolyte disturbances (iloperidone, clozapine, ziprasidone)[113,119,120] | Increased risk of QT prolongation/ arrhythmia. | |
| Digoxin (e.g., *Lanoxin*) | Digoxin level | Reasons to check digoxin level:<br>• Suspected toxicity[33]<br>• To aid in dose adjustment[33]<br>• Suspected non-adherence[32]<br>• Diseases or physiologic changes (e.g., renal or liver impairment)[32,33]<br>• Starting or stopping an interacting drug[33]<br>• Change in dose: check after at least 5 to 7 days (steady-state)[32,34] | Narrow therapeutic index drug. | • Therapeutic level:<br>• heart failure: 0.5 to 0.9 ng/mL (0.6-1.2 nmol/L)[32]<br>• atrial fibrillation: 2 ng/mL (2.6 nmol/L) or lower[32]<br>• Check level at least 6 hours after dose.[33]<br>• May take up to 21 days to reach steady-state in renal impairment.[34] |
| | Electrolytes | Periodically[33] | Hypokalemia, hypomagnes-emia, and hypercalcemia enhance toxicity.[33] | Closely monitor patients on diuretics, corticosteroids, or amphotericin due to potential for electrolyte changes.[34] |
| | Renal function | Periodically, especially in elderly[33] | Renally eliminated. | Requires dose adjustment in renal impairment.[33] |
| Diuretics (thiazides, loops) | Electrolytes (e.g., potassium, sodium, magnesium, calcium, bicarbonate) | Baseline, within two weeks of initiation (loops), frequently during the first few months (loops) (weekly may be appropriate, even for thiazides), then periodically (every three to 12 months), and after dosage increases.[7,37,39,121] Repeat potassium 2 to 4 weeks after initiation or dosage increase.[41] Check if vomiting or receiving IV fluids, or if symptomatic (see comments).[39,40,41] Careful monitoring is needed in hepatorenal syndrome.[46] | • Thiazides and loops cause hypokalemia, hyponatremia, hypo-magnesemia, and metabolic alkalosis.[39,40]<br>• Loops cause calcium loss; thiazides cause calcium retention.[39,40] | • Symptoms of fluid and electrolyte disturbances include dry mouth, thirst, weakness, lethargy, drowsiness, restlessness, myalgia, muscle cramps, hypotension, low urine output, rapid heart rate, confusion, seizures, gastrointestinal symptoms (e.g., nausea, vomiting).[40]<br>• Diuretic-associated hypokalemia (dose-dependent) reaches a plateau within one week (loops) to one month (thiazides).[41,44]<br>• Correction of hypomagnesemia can make hypokalemia easier to correct.[41] |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Diuretics, continued | Glucose | Baseline and periodically in diabetes and suspected latent diabetes (loops).[7,39,121] | May increase glucose levels. | Magnitude of increase is generally minimal and transient at daily doses of hydrochlorothiazide <50 mg.[41] |
| | Renal function (BUN, SCr) | Baseline, frequently during the first few months (loops), then periodically (loops) (once or twice yearly)[7,39,121] | May reduce renal blood flow or cause interstitial nephritis.[39,40,44] Higher risk of ototoxicity (loops) in renal impairment.[39] | Prolonged overdiuresis and dehydration may cause renal ischemia and resultant renal damage that may not be reversible, as indicated by increased serum creatinine that is not reversible with rehydration.[44] |
| | Uric acid | Baseline, two to six weeks after initiation, and routinely.[42,121] | May increase uric acid levels. | Increases are usually clinically insignificant in patients without a history of gout, and hyperuricemia is uncommon with hydrochlorothiazide at daily doses less than 50 mg.[41] Risk is lower with loops than with thiazides.[41] |
| Fibrates [e.g., gemfibrozil, fenofibric acid (U.S.)(e.g., *Trilipix*), and its prodrug fenofibrate (e.g., *TriCor*, *Lipidil EZ* [Canada]) | Liver function[45,47,49,50] | Fenofibrate, fenofibric acid: baseline and regularly.[49,50] (Canada: baseline, every three months for 12 months, then at least yearly.)[45] Gemfibrozil: periodically.[47] | Increased liver enzymes, bilirubin, and gallstones have been seen.[47,49,50] | •Decreases in hemoglobin, hematocrit, and white blood cells usually stabilize, but anemia, leukopenia, thrombocytopenia, and bone marrow hypoplasia have been reported.[47,49,50] •Myositis risk factors include gemfibrozil use, statin use, colchicine use, advanced age, diabetes, renal insufficiency, and hypothyroidism.[47,49,50] •Discontinue if creatine kinase >10 times the ULN with muscle symptoms. Recent trauma or exercise may increase creatine kinase.[48] •Requires dose adjustment or avoidance in renal or liver impairment.[45,47,49-51] |
| | Renal function | Periodically in patients with renal impairment (fenofibric acid, fenofibrate)[49,50] | May increase serum creatinine.[49,50] | |
| | Creatine kinase | If symptoms (muscle weakness, tenderness, or pain) occur[47,49,50] | Risk of myositis and rhabdomyolysis.[47-50] | |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Fibrates, continued | Complete blood count | Periodically during the first 12 months[47,49,50] | May decrease hemoglobin, hematocrit, and white blood cell count.[47,49,50] | |
| Glitazones (pioglitazone [*Actos*], rosiglitazone [*Avandia*]) | Liver function | •Pioglitazone (U.S.): baseline and in the event of symptoms.[56] Canada: baseline and periodically, per clinician judgment.[122]<br>• Rosiglitazone: baseline and periodically, per the clinician's judgment, or in the event of symptoms of hepatotoxicity (e.g., nausea, vomiting, abdominal pain, jaundice, dark urine, fatigue, loss of appetite)[57,122] | Rarely, associated with toxic hepatitis and liver failure. | •Pioglitazone (U.S.): hold drug and investigate if ALT >3 times the ULN. Do not restart unless alternate cause is found.[56]<br>• Rosiglitazone (and pioglitazone, Canada): discontinue if ALT >3 times the ULN despite recheck, or patient jaundiced.[57,122]<br>•For *Actoplus Met* (pioglitazone/metformin) and *Avandamet* (rosiglitazone/metformin) also see metformin, below. |
| Hepatitis C antivirals | See our *PL Chart, Comparison of Hepatitis C Drugs*, for information on safety monitoring. | | | |
| Lithium | Thyroid function | • TSH and T4 at baseline and at least yearly if hypothyroidism pre-existing[95-97] | Can cause hypothyroidism. | •Loop diuretics, thiazide diuretics, potassium-sparing diuretics, ACEIs/ARBs, metronidazole, and NSAIDs increase lithium levels.[95,97,100] Fluoxetine may increase or decrease levels.[95] Acetazolamide, theophylline, and caffeine decrease levels.[95,97]<br>• Dehydration and sodium depletion can increase levels.[95]<br>•Monitor trough level (8 to 12 hours post-dose).[95]<br>•Therapeutic range: 0.6 to 1.2 mEq/L.[95] Some |
| | Complete blood count | •Baseline[97] | Can cause leukocytosis.[97] | |
| | Electrolytes, calcium | •Electrolytes: baseline and yearly[97]<br>•Calcium: baseline, after six months, and yearly[96] | Can deplete sodium or potassium, or increase calcium.[96] | |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Lithium, continued | Serum lithium level | •Twice per week until serum concentrations and clinical condition have stabilized, then at least every two months and if symptomatic[95,97]<br>•Check more frequently if used with ACEI/ARB or diuretic (avoid concomitant use if possible)[95,100]<br>•Monitor closely if used with metronidazole or fluoxetine, and when patients start or stop NSAIDs[95] | Narrow therapeutic index drug. | patients (e.g., elderly) may have symptoms of toxicity within this range.[96]<br>• Hypercalcemia can occur alone or in conjunction with hyperparathyroidism.[96] Canadian subscribers, see our *PL Detail-Document, Lithium and the Risk of Hypercalcemia*. |
| | Pregnancy test | •In women of childbearing potential, at baseline[97] | May be teratogenic, especially in first trimester.[97] | |
| | Renal function | •Serum creatinine or creatinine clearance, BUN, and urinalysis (e.g., for urine specific gravity or osmolality; 24-hr urine volume) baseline and during treatment (yearly, and if symptoms arise)[95-97]<br>• Canadian labeling additionally recommends serum creatinine every two months[96] | Renal function can affect lithium levels; lithium can affect renal function.[97] | |
| Metformin | Hemo-globin, hematocrit, red blood cell indices | Baseline and at least annually[58] | Metformin may cause B12 deficiency and megaloblastic anemia. | Contraindicated in renal insufficiency (serum creatinine 1.4 mg/dL in women or 1.5 mg/dL in men or abnormal creatinine clearance).[58] [Canadian labeling: contraindicated if serum creatinine 124 umol/L in women or 136 umol/L in men or creatinine clearance <60 mL/min.][59] |
| | Serum creatinine | Baseline and at least annually (Canada: every six months)[58,59] | Renal impairment can cause metformin accumulation and lactic acidosis. | |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Niacin (*Niaspan* [U.S.], *Niaspan FCT* [Canada], *Niacor* [U.S.]) | Liver function (ALT, AST) | Baseline, then every six to 12 weeks for a year, then periodically (e.g., every six months).[61,62] Per guidelines, baseline, during up-titration, and every six months.[136] | Dose-dependent hepatotoxicity.[60] | Discontinue/do not use if transaminases exceed 2 to 3 times ULN.[136] |
| | Uric acid | Baseline, during up-titration, and every six months.[136] | Dose-dependent risk of hyperuricemia.[60] | Use with caution in patients predisposed to gout.[61,62] |
| | Glucose, fasting | Frequently.[61,62] Baseline, during up-titration, and every six months.[136] | Dose-dependent impaired glucose tolerance.[60] | Patients with diabetes or at risk of diabetes should have their glucose monitored closely during the first few months after initiation or dosage increase.[61] A1C can be used as an alternative to fasting glucose.[136] |
| | Creatine kinase | Periodically (Canada).[63] Consider during the initial months of use with a statin or after dosage increase of either drug.[61,62] Check in the event of muscle symptoms (e.g., pain, tenderness, weakness).[64] | Risk of rhabdo-myolysis.[61] | Risk factors include use of statins, especially in the elderly and patients with diabetes, renal failure, or uncontrolled hypothyroidism, and hypokalemia.[61,64] |
| | Potassium | Periodically (Canada).[63] Consider during the initial months of use with a statin or after dosage increase of either drug.[61,62] Check in the event of muscle symptoms (e.g., pain, tenderness, weakness).[64] | Risk of rhabdo-myolysis.[61] | Hypokalemia predisposes to rhabdomyolysis, and rhabdomyolysis can cause hyperkalemia.[64] |
| | Phosphorus | Periodically in patients at risk of hypophosphatemia[61] | Dose-dependent risk of decrease in phosphorus level.[61] | Usually small and transient.[61] Hypophosphatemia is a risk factor for rhabdomyolysis.[64] |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | Electrolytes and serum creatinine | Periodically.[65] Patients at high-risk of adverse renal effects (see comments): check weekly for the first several weeks.[66] | Prostaglandin inhibition reduces renal blood flow; other renal injury.[65,66] | •Discontinue if signs and symptoms consistent with renal disease develop.[65]<br>•High risk: heart failure, liver dysfunction, renal impairment, diuretic or ACEI/ARB use, elderly, hypertension, sodium or volume depletion, long-term use[10,65-68,131]<br>•Some NSAIDs are contraindicated (e.g., ketorolac), or not recommended (e.g., naproxen, ibuprofen, celecoxib, diclofenac) in advanced renal impairment.[65,69,70,82,123,124]<br>• CPhA monograph contraindicates NSAIDs if CrCl <30 mL/min.[93]<br>•Also monitor patients with advanced renal disease using *Flector* patch, *Pennsaid* liquid, and *Voltaren* gel.[83-85] |
| | Complete blood count | • Periodically[65]<br>• Check hemoglobin or hematocrit in the case of signs or symptoms of anemia[65] | Can cause anemia and rarely bone marrow suppression. | •NSAID associated anemia may be due to fluid retention, GI bleeding, or an effect on erythropoiesis.[65]<br>•Also monitor patients using *Flector* patch, *Pennsaid* liquid, and *Voltaren* gel.[83-85] |
| | Liver function (ALT) | •Periodically[65]<br>•Check within four to eight weeks of initiation in patients taking diclofenac, then periodically[69,82]<br>•Check within eight weeks of initiation in patients with pre-existing liver disease[66]<br>•Also see our *PL Chart*, *Liver Function Test Scheduling.* | NSAIDs carry varying risks of rare hepatotoxicity. | •Discontinue if signs/symptoms consistent with liver disease develop, or if abnormal liver tests persist or worsen.[65]<br>•Severe hepatotoxicity rare. Risk factors include liver disease and diclofenac use.[66]<br>•CPhA monograph contraindicates NSAIDs in severe liver disease.[93]<br>•Also monitor patients using *Flector* patch, *Pennsaid* liquid, and *Voltaren* gel.[83-85] |
| Proton Pump Inhibitors | Magnesium | Consider at baseline and periodically in patients on long-term therapy or who take digoxin or diuretics[130] | Hypo-magnesemia reported. | See our *PL Detail-Document*, *Treating Magnesium Deficiency*, for more information. |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Psoriasis medications | Calcium | • Calcipotriol/betamethasone (*Dovobet* [Canada]): baseline and periodically in patients at risk of hypercalcemia [Canada].[76,94]<br>• Calcipotriol (*Dovonex* [Canada]): baseline and periodically, especially with high doses or in patients with severe, extensive psoriasis[71] | Vitamin D analog; can increase calcium levels. | If calcium level exceeds normal, discontinue use and check weekly until levels normalize.[71,76,94] |
| | Liver function (AST, ALT, LDH) | Acitretin (*Soriatane*): baseline, every one to two weeks until stable, and thereafter as clinically indicated.[73] [Canada: baseline, every four weeks for two months, then every three months. If abnormal, check weekly.][74] | Hepatotoxic.[73] | Contraindicated in severe liver dysfunction.[73] Discontinue if hepatotoxicity is suspected,[73] or if elevated LFTs do not normalize or worsen.[74] Then continue monitoring for at least three months.[74] |
| | Lipids, fasting | Acitretin (*Soriatane*): Baseline, every one to two weeks until stable (usually within four to eight weeks). Continue close monitoring in patients with a personal or family history of diabetes, obesity, alcohol use, or abnormal lipid metabolism.[73] (Canada: every three months).[74] | May increase LDL and triglycerides, and decrease HDL.[73,75] | Contraindicated in hyperlipidemia.[73] |
| | Glucose, fasting | Acitretin (*Soriatane*): monitor closely in patients with diabetes[73] | May cause new or worsening diabetes.[73] | New onset diabetes has been reported.[73] Acitretin can enhance hypoglycemic effect of glyburide (glibenclamide).[73] Monitor more frequently during the early stages of treatment.[74] |
| | Pregnancy test | Acitretin: baseline and monthly.[73] See product labeling for details. | Teratogenic. | Prescribing of acitretin requires use of a special pregnancy prevention program (iPLEDGE [U.S.]; *Soriatane* Pregnancy Prevention Program [Canada]). |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Retinoids (For acitretin, see psoriasis medications, above). | Lipids | Isotretinoin: baseline, then weekly or biweekly until stable (usually within four weeks). Continue close monitoring in patients with diabetes, obesity, alcohol use, or personal or family history of abnormal lipid metabolism.[99,125] | May increase triglycerides and LDL, and decrease HDL cholesterol.[99,137] | Canada: contraindicated if lipids are excessively elevated.[126-128] |
| | Liver function | See our *PL Chart, Liver Function Test Scheduling*, and psoriasis medications, above. | Hepatotoxic. | |
| | Glucose | Isotretinoin: periodically in all patients, especially those with diabetes or diabetes risk factors[126-128]<br><br>Acitretin: See psoriasis medications, above | May cause new or worsening diabetes.[99] | New onset diabetes has been reported.[99] |
| | Pregnancy test | Isotretinoin: baseline and monthly.[99] See product labeling for details. | Teratogenic. | Prescribing of isotretinoin requires enrollment in special pregnancy prevention program (iPLEDGE [U.S.]). Each Canadian manufacturer has their own program. |
| Rheumatoid arthritis medications | See our *PL Detail-Document, DMARDs in the Treatment of Rheumatoid Arthritis* and *PL Chart, Liver Function Test Scheduling*, for information on safety monitoring. | | | |
| Statins | Liver function (ALT)[77] | Baseline and when clinically indicated.[129] Some Canadian products have more conservative recommendations. See our *PL Chart, Liver Function Test Scheduling.* | May cause transaminase elevations. Usually asymptomatic. | |
| | Creatine kinase | When muscle symptoms occur, and perhaps at baseline as a point of reference in high-risk patients.[77] Consider during the initial months of use with niacin or after dosage increase of either drug.[61,62] | Can cause myositis and rhabdomyolysis. | •Risk factors for myopathy: elderly, small size, high statin dose, liver or renal disease, diabetes, uncontrolled hypothyroidism, interacting medications.[72]<br>•Renal dose adjustment needed for some statins. See our *PL Chart, Characteristics of the Various Statins.* |

*Continued…*

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Statins, continued | Lipids | Check fasting lipid panel four to 12 weeks after statin initiation, then every three to 12 months[77] | To assess efficacy and adherence.[77] | Assuming compliance, maximum lipid effects occur within six weeks of initiation.[78] |
| | Thyroid stimulating hormone | If muscle symptoms occur[72] | Hypothyroidism predisposes to myopathy.[72] | |
| Theophylline | Drug level | •During titration, check before each dosage increase, which should occur not less than every three days. Check three days after dosage decrease. If stable, check at least every six months in growing children and at least yearly in adults. Check every 24 hours in acute illness. Check when adverse effects occur, in the event of physiologic changes that could affect clearance (e.g., fever), an interacting medication or supplement is started or stopped, or after smoking cessation.[81] | Narrow therapeutic index drug with interindividual differences in metabolism. | •Therapeutic range 5 to 15 mcg/mL (peak).[79,81]<br>•Check peak at steady-state (at least 48 to 72 hours on same dosage).[79,80]<br>•Peak for immediate-release (e.g., *Theolair*): one to two hours after dose; *Theo-24*: 12 hours post-dose; *Uniphyl*: 8 to 12 hours after once-daily evening dose.[80,81]<br>•Risk factors for reduced clearance: liver impairment, heart failure, cor pulmonale, septic shock, sustained fever (e.g., >102°F[39°C] for a day or more, elderly, hypothyroidism, interacting medications (e.g., ciprofloxacin, clarithromycin, other CYP3A or CYP1A2 inhibitors).[80,81]<br>•Charbroiled beef, low carbohydrate/high protein diet, parenteral nutrition, St. John's wort, rifampin, carbamazepine, and smoking decrease levels.[81]<br>•See our *PL Chart*, *Cytochrome P450 Drug Interactions* for help identifying potential interactions. |
| Thyroid Replacement<br><br>*Continued…* | Sensitive TSH | •Baseline, every six to eight weeks until normal, then after 8 to 12 weeks, then every six to 12 months[86,87]<br>•Check six weeks to three months (eight to 12 weeks, per labeling) after change in dose or product[86,87]<br>•Also check if clinically indicated, or if there | To ensure dose is appropriate. | •Patients nonadherent to monitoring may have more adverse effects.[86]<br>•Monitor INR when starting or stopping thyroid hormones in patient on anticoagulants. Anticoagulant dose may need to be adjusted to maintain desired INR. Patients stabilized on thyroid hormones and considered euthyroid will |

| Drug or Drug Class | Test | Frequency or Indication for Test | Rationale | Comments |
|---|---|---|---|---|
| Thyroid replacement, continued | | is a change in patient health.[87]<br>•Elderly patients with cardiac disease: every four to six weeks until stable[88]<br>•Severe hypothyroidism: every two to three weeks until stable[88] | | respond normally to anticoagulant therapy.[89]<br>•Monitor diabetes control; insulin or antidiabetic dose may need to be increased.[87] |

a. "Valproate" refers to products containing divalproex (e.g., *Depakote* [U.S.], *Epival* [Canada]) or valproic acid (e.g., *Depakene*).

---







*More. . .*

***Project Leader in preparation of this PL Detail-Document:*** *Melanie Cupp, Pharm.D., BCPS*

## *References*


1. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of chronic heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the International Society for Heart and Lung Transplantation. *J Am Coll Cardiol* 2009;53:e1-e90.
2. Product information for *Inspra*. Pfizer Inc. New York, NY 10017. April 2014.
3. Product monograph for *Inspra*. Pfizer Canada Inc. Kirkland, QC H9J 2M5. August 2012.
4. Product information for *Aldactone*. Pfizer Inc. New York, NY 10017. July 2013.
5. Arnold JM, Liu P, Demers C, et al. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: diagnosis and management. *Can J Cardiol* 2006;22:23-45.
6. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine: is this a cause for concern? *Arch Intern Med* 2000;160:685-93.
7. Chobanian AV, Bakris GL, Black HR. JNC 7 Express, the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. US Department of Health and Human Services 2003. http://www.nhlbi.nih.gov/guidelines/hypertension/jnci ntro.htm. (Accessed April 18, 2014).
8. Nurko S. At what level of hyperkalemia or creatinine elevation should ACE inhibitor therapy be stopped or not started? *Cleve Clin J Med* 2001;68:754, 757-8, 760.
9. National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. http://www.kidney.org/professionals/kdoqi/guidelines _bp/guide_11.htm#table123. (Accessed April 18, 2014).
10. Munar MY, Brophy DF. Acute Kidney Injury. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:743-63.
11. Singh H, Marrs JC. Heart Failure. In: Alldredge BK, Corelli RL, Ernst ME, et al, Eds. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:436-88.
12. Brigham and Women's Hospital. Renal artery stenosis. http://www.brighamandwomens.org/Departments_and_Services/surgery/services/vascularsurgery/Services/RenalArtery.aspx. (Accessed April 18, 2014).
13. Eadie MJ. Therapeutic drug monitoring-antiepileptic drugs. *Br J Clin Pharmacol* 2001;52(Suppl 1):11S-20S.
14. Welty TE. The pharmacotherapy of epilepsy. Pharmacotherapy Self-Assessment Program. Book 7, Neurology, Psychiatry. 4th ed. Kansas City, MO: American College of Clinical Pharmacy, 2002.
15. Malaty W, Stigleman S, Smith PC. FPIN's clinical inquiries. Antiepileptic drug level monitoring. *Am Fam Physician* 2008;78:385-6.
16. Product information for *Dilantin*. Pfizer Inc. New York, NY 10017. September 2013.
17. McAuley JW, Lott RS, Alldredge BK. Seizure Disorders. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:1387-1418.
18. Product information for *Tegretol*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. January 2014.
19. Product information for *Depakote*. AbbVie Inc. North Chicago, IL 60064. May 2013.
20. Product information for *Depakene*. AbbVie Inc. North Chicago, IL 60064. April 2014.
21. Product monograph for *Tegretol*. Novartis Pharmaceuticals Canada Inc. Dorval, QC H9S 1A9. March 2014.
22. Product monograph for *Epival*. Abbott Laboratories, Limited. St. Laurent, QC H4S 1Z1. November 2013.
23. Product monograph for *Eliquis*. Pfizer Canada Inc. Kirkland, QC H9J 2M5. November 2012.
24. Product information for *Topamax*. Ortho-McNeil-Janssen Pharmaceuticals, Inc. Titusville, NJ 08560. April 2014.
25. Product information for *Trileptal*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. March 2013.
26. Product monograph for *Trileptal*. Novartis Pharmaceuticals Canada Inc. Dorval, QC H9S 1A9. July 2013.
27. Product information for *Zonegran*. Eisai Inc. Woodcliff Lake, NJ 07677. January 2012.
28. Product information for *Felbatol*. MEDA Pharmaceuticals Inc. Somerset, NJ 08873. July 2011.
29. Product information for *Gabitril*. Cephalon, Inc. Frazer, PA 19355. September 2010.
30. Goldschlager N, Epstein AE, Naccarelli GV, et al. A practical guide for clinicians who treat patients with amiodarone: 2007. *Heart Rhythm* 2007;4:1250-9.
31. Product information for *Pradaxa*. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT 06877. April 2014.
32. *PL Detail-Document*, Digoxin for Atrial Fibrillation. *Pharmacist's Letter/Prescriber's Letter*. February 2013.
33. Product information for *Lanoxin*. Covis Pharmaceuticals, Inc. Cary, NC 27511. October 2013.


*More. . .*

34. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Toloxin* (June 2012). http://www.e-therapeutics.ca. (Accessed May 15, 2014).
35. Product information for *Tambocor*. Medicis. Scottsdale, AZ 85256. December 2011.
36. Product information for mexiletine. Teva Pharmaceuticals USA. Sellersville, PA 18960. August 2012.
37. Shrank WH, Polinski JM, Avorn J. Quality indicators for medication use in vulnerable elders. *J Am Geriatr Soc* 2007;55 (Suppl 2):S373-82.
38. Product monograph for *Tambocor*. Valeant Canada LP. Montreal, QC H4R 2P9. February 2013.
39. Product information for *Lasix*. Sanofi-aventis U.S. LLC. Bridgewater, NJ 08807. November 2012.
40. Product information for hydrochlorothiazide. Heritage Pharmaceuticals Inc. Eatontown, NJ 07724. October 2013.
41. Saseen JJ. Essential Hypertension. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:291-330.
42. Carter BL. Management of essential hypertension. Pharmacotherapy Self-Assessment Program. Book 1, Cardiovascular. 4th ed. Kansas City, MO: American College of Clinical Pharmacy, 2001.
43. Product monograph for *Zeldox*. Pfizer Canada, Inc. Kirkland, QC H9J 2M5. May 2013.
44. Singh H, Marrs JC. Heart Failure. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:436-88.
45. Product monograph for *Lipidil EZ*. Fournier Pharma Inc. Saint-Laurent, QC H4S 1Z1. September 2013.
46. Product monograph for *Lasix*. Sanofi-aventis Canada Inc. Laval, QC H7L 4A8. December 2013.
47. Product information for *Lopid*. Pfizer Inc. New York, NY 10017. November 2013.
48. Ito MK. Dyslipidemia, Atherosclerosis, and Coronary Heart Disease. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:252-90.
49. Product information for *Trilipix*. AbbVie Inc. North Chicago, IL 60064. March 2013.
50. Product information for *TriCor*. AbbVie Inc. North Chicago, IL 60064. February 2013.
51. Product monograph for gemfibrozil. Pro Doc Ltee. Laval, QC H7L 3W9. August 2013.
52. Barrett E, Blonde L, Clement S, et al. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004;27:596-601.
53. *PL Detail-Document*. Monitoring the Metabolic Effects of Atypical Antipsychotics. *Pharmacist's Letter/Prescriber's Letter*. March 2004.
54. AstraZeneca Pharmaceuticals LP. Dear health care provider letter. April 22, 2004. http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM166523.pdf. (Accessed April 24, 2014).
55. Product information for *Clozaril*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. January 2010.
56. Product information for *Actos*. Takeda Pharmaceuticals America, Inc. Deerfield, IL 60015. November 2013.
57. Product information for *Avandia*. GlaxoSmithKline. Research Triangle Park, NC 27709. September 2013.
58. Product information for *Glucophage* and *Glucophage XR*. Bristol-Myers Squibb. Princeton, NJ 08543. January 2009.
59. Product monograph for *Glucophage*. Sanofi-aventis Canada, Inc. Laval, QC H7L 4A8. October 2009.
60. *PL Detail-Document*, Niacin use: an update. *Pharmacist's Letter/Prescriber's Letter.* December 2005.
61. Product information for *Niaspan*. AbbVie Inc. North Chicago, IL 60064. March 2013.
62. Product information for *Niacor*. Upsher-Smith Laboratories, Inc. Minneapolis, MN 55447. December 2002.
63. Product monograph for *Niaspan FCT*. Sunovion Pharmaceuticals Canada Inc. Mississauga, ON L5N 2V8. December 2011.
64. Keltz E, Khan FY, Mann G. Rhabdomyolysis. The role of diagnostic and prognostic factors. *Muscles Ligaments Tendons J* 2014;3:303-12.
65. Product information for *EC-Naprosyn, Naprosyn*, *Anaprox*, *Anaprox DS*. Genentech USA Inc. South San Francisco, CA 94080. March 2013.
66. Chen SW. Rheumatoid Arthritis. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:1002-38.
67. Loboz KK, Shenfield GM. Drug combinations and impaired renal function-the "triple whammy." *Br J Clin Pharmacol* 2005;59:239-43.
68. Beebe FA, Barkin RL, Barkin S. A clinical and pharmacologic review of skeletal muscle relaxants for musculoskeletal conditions. *Am J Ther* 2005;12:151-71.
69. Product information for *Voltaren XR*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. February 2011.
70. Product information for ketorolac. Teva Pharmaceuticals. Sellersville, PA 18960. April 2013.
71. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Dovonex* (January 2012). http://www.e-therapeutics.ca. (Accessed May 15, 2014).
72. *PL Detail-Document*, Statin-Associated Muscle Symptoms. *Pharmacist's Letter/Prescriber's Letter*. June 2012.
73. Product information for *Soriatane*. Stiefel Laboratories, Inc. Coral Gables, FL 33134. February 2014.


*More. . .*

74. Product monograph for *Soriatane*. Tribute Pharmaceuticals Canada, Inc. London, ON N5W 3Z8. May 2014.
75. Geiger JM. Efficacy of acitretin in severe psoriasis. *Skin Therapy Lett* 2003;8:1-3,7.
76. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Dovobet* ointment (August 2013). http://www.e-therapeutics.ca. (Accessed May 15, 2014).
77. *PL Detail-Document*, 2013 ACC/AHA Cholesterol Guidelines. *Pharmacist's Letter/Prescriber's Letter*. January 2014.
78. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
79. Kallstrom TJ. Evidence-based asthma management. *Respir Care* 2004;49:783-92.
80. Weinberger M, Hendeles L. Theophylline in asthma. *N Engl J Med* 1996;334:1380-8.
81. Product information for *Theo-24*. UCB Pharma, Inc. Smyrna, GA 30080. August 2012.
82. Product information for *Cataflam*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. February 2011.
83. Product information for *Flector*. King Pharmaceuticals, Inc. Bristol, TN 37620. November 2011.
84. Product information for *Pennsaid*. Mallinckrodt Brand Pharmaceuticals, Inc. Hazelwood, MO 63042. October 2013.
85. Product information for *Voltaren* gel. Endo Pharmaceuticals Inc. Chadds Ford, PA 19317. September 2009.
86. Stelfox HT, Ahmed SB, Fiskio J, Bates DW. An evaluation of the adequacy of outpatient monitoring of thyroid replacement therapy. *J Eval Clin Pract* 2004;10:525-30.
87. Product information for *Synthroid*. AbbVie Inc. North Chicago, IL 60064. September 2012.
88. Product monograph for *Synthroid*. Abbott Laboratories, Limited. Saint-Laurent, QC H4S 1Z1. April 2011.
89. *PL Detail-Document,* Clinically Important Drug Interactions. *Pharmacist's Letter/Prescriber's Letter*. June 2004.
90. Product information for *Coumadin*. Bristol-Myers Squibb Company. Princeton, NJ 08543. October 2011.
91. Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;4(Suppl 2):e152S-84S.
92. Product information for *Cordarone*. Wyeth Pharmaceuticals Inc. Philadelphia, PA 19101. October 2011.
93. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Nonsteroidal anti-inflammatory drugs (NSAID)* CPhA monograph (October 2013). http://www.e-therapeutics.ca. (Accessed April 26, 2014).
94. Product monograph for *Dovobet* gel. LEO Pharma Inc. Thornhill, ON L3T 7W8. February 2013.
95. Product information for *Lithobid.* Noven Therapeutics, LLC. Miami, FL 33186. October 2011.
96. Product monograph for *Carbolith*. Laval, QC H7L 4A8. September 2013.
97. Gasper JJ. Mood Disorders II: Bipolar Disorders. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:1983-98.
98. Product information for *Tekturna*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. March 2014.
99. Product information for *Zenatane.* Dr. Reddy's Laboratories Limited. Bachupally, India 500 090. February 2013.
100. Aruna AS. Lithium toxicity secondary to lithium-losartan interaction. *J Pharm Technol* 2009;25:89-93.
101. Product monograph for *Rasilez*. Novartis Pharmaceuticals Canada Inc. Dorval, QC H9S 1A9. September 2013.
102. Product monograph for *Cordarone*. Pfizer Canada, Inc. Kirkland, QC H9J 2M5. April 2013.
103. Product monograph for *Pradaxa*. Boehringer Ingelheim Canada Ltd. Burlington, ON L7L 5H4. May 2013.
104. Product information for *Xarelto*. Janssen Pharmaceuticals, Inc. Titusville, NJ 08560. March 2014.
105. Product monograph for *Xarelto*. Bayer Inc. Toronto, ON M9W 1G6. August 2013.
106. Product monograph for *Coumadin*. Bristol-Myers Squibb Canada. Montreal, QC H4S 0A4. March 2011.
107. Product monograph for *Abilify*. Bristol-Myers Squibb Canada. Montreal, QC H4S 0A4. May 2013.
108. Product monograph for *Clozaril*. Novartis Pharmaceuticals Canada Inc. Dorval, QC H9S 1A9. May 2013.
109. Product information for *Zyprexa*. Lilly USA, LLC. Indianapolis, IN 46285. July 2013.
110. Product information for *Seroquel*. AstraZeneca Pharmaceuticals LP. Wilmington, DE 19850. October 2013.
111. Product information for *Abilify*. Bristol-Myers Squibb Company. Princeton, NJ 08543. August 2013.
112. Product information for *Saphris*. Merck & Co., Inc. Whitehouse Station, NJ 08889. March 2013.
113. Product information for *Fanapt*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. January 2013.
114. Product information for *Invega*. Janssen Pharmaceuticals, Inc. Titusville, NJ 08560. January 2014.


*More. . .*

115. Product information for *Risperdal*. Janssen Pharmaceuticals, Inc. Titusville, NJ 08560. November 2013.
116. Product monograph for *Zyprexa*. Eli Lilly Canada Inc. Toronto, ON M1N 2E8. February 2013.
117. Product monograph for *Invega*. Janssen Inc. Toronto, ON M3C 1L9. October 2013.
118. Product monograph for *Seroquel*. AstraZeneca Canada Inc. Mississauga, ON L4Y 1M4. December 2013.
119. Product information for *Clozaril*. Novartis Pharmaceuticals Corporation. East Hanover, NJ 07936. November 2013.
120. Product information for *Geodon.* Pfizer Inc. New York, NY 10017. January 2014.
121. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Thiazide diuretics* CPhA monograph (May 2012). http://www.e-therapeutics.ca. (Accessed April 25, 2014).
122. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Actos* (May 2012). http://www.e-therapeutics.ca. (Accessed May 15, 2014).
123. Product information for ibuprofen. Amneal Pharmaceuticals. Glasgow, KY 42141. September 2009.
124. Product information for *Celebrex*. Pfizer Inc. New York, NY 10017. February 2011.
125. Product information for *Absorica*. Ranbaxy Laboratories Inc. Jacksonville, FL 32257. May 2012.
126. Product monograph for *Clarus*. Mylan Pharmaceuticals ULC. Etobicoke, ON M8Z 2S6. November 2013
127. Product monograph for *Accutane*. Hoffmann-La Roche Limited. Mississauga, ON L5N 6L7. August 2013.
128. Product monograph for *Epuris*. Cipher Pharmaceuticals Inc. Mississauga, ON L4W 4P1. March 2013.
129. FDA. FDA drug safety communication: important safety label changes to cholesterol-lowering statin drugs. February 28, 2012. http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm. (Accessed April 27, 2014).
130. FDA. FDA drug safety communication: low magnesium levels can be associated with long-term use of proton pump inhibitors (PPIs). March 2, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm245011.htm. (Accessed April 27, 2014).
131. Choosing Wisely. American Society of Nephrology. Five things physicians and patients should question. http://www.choosingwisely.org/doctor-patient-lists/american-society-of-nephrology/. (Accessed April 27, 2014).
132. Product information for *Prinivil*. Merck & Co., Inc. Whitehouse Station, NJ 08889. December 2012.
133. Product monograph for *Prinivil*. Merck Canada Inc. Kirkland, QC H9H 4M7. June 2013.
134. Product information for *Latuda*. Sunovion Pharmaceuticals, Inc. Marlborough, MA 01752. October 2010.
135. Product monograph for *Latuda*. Sunovion Pharmaceuticals, Inc. Mississauga, ON L5N 2V8. March 2014.
136. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013 Nov 12 [epub ahead of print].
137. DeGrasse ER, Cavanaugh JJ. Acne. In: Alldredge BK, Corelli RL, Ernst ME, et al, editors. Koda-Kimble & Young's Applied Therapeutics: the Clinical Use of Drugs. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013:944-55.
138. Product information for *Aptiom*. Sunovion Pharmaceuticals, Inc. Marlborough, MA 01752. November 2013.

***Cite this Detail-Document as follows: Pl Detail-Document, Lab Monitoring for Common Medications. Pharmacist's Letter/Prescriber's Letter. June 2014.***

PHARMACIST'S LETTER *Evidence and Recommendations You Can Trust…* PRESCRIBER'S LETTER

3120 West March Lane, Stockton, CA 95219 ~ TEL (209) 472-2240 ~ FAX (209) 472-2249