***Detail-Document#*: 260704 - CHART**

PHARMACIST'S LETTER

Evidence and Advice You Can Trust...

Recommended Lab Monitoring for Common Medications

Full update June 2010

Table is not all-inclusive. Information provided 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 or symptoms may be better indication of adverse effects than laboratory test results. Recommendations may differ from product labeling. Underlined text denotes laboratory monitoring recommended in FDA-approved labeling (i.e., package insert). Product labeling recommendations are U.S. unless otherwise referenced (i.e., Canadian monograph recommendations included if more conservative).

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

Abbreviations: ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; BUN - blood urea nitrogen; CCS - Canadian Cardiovascular Society; CrCl - creatinine clearance, GFR - glomerular filtration rate, NSAID - nonsteroidal anti-inflammatory drug; SCr - serum creatinine; T4 - thyroxine; TSH - thyroid stimulating hormone; ULN - upper limit of normal

Drug	Test	Frequency or Indication for Test	Rationale	Comments
Aldosterone antagonists [i.e., spironolactone, eplerenone (*Inspra*)]	Potassium and renal function (e.g., serum creatinine)	• Guidelines: check potassium and renal function baseline, three and seven days after initiation, monthly for three months, then quarterly. Restart monitoring cycle if ACE inhibitor or ARB added or their dose increased.[1] • Eplerenone labeling: check potassium within the first week and one month after dose adjustment.[2] • Eplerenone labeling: check potassium and renal function three to seven days after starting a moderate CYP3A4 inhibitor (e.g., verapamil, fluconazole). Contraindicated with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole).[2]	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] • Eplerenone labeling: if potassium reaches 5.5 mEq/L, hold or reduce dose.[2,3] Per U.S. labeling, do not start if potassium >5.5 mEq/L.[2] 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.[2] Per Canadian labelling, do not start if CrCl <50 mL/min.[3] • Spironolactone labeling: if potassium >5 mEq/L or SCr > 4 mg/dL, hold or discontinue.[4]
ACEI or ARB	Potassium and serum creatinine	• Check potassium and SCr within 1 to 2 weeks of initiation (within 1 week in elderly) and after dosage increases, then in 3 to 4 weeks if	Kidney perfusion in some patients is highly dependent on angiotensin[6,8]	• Discontinue if potassium >5.5 mEq/L.[6] • Discontinue if serum creatinine increases >30%

		stable.[1,6,8,37] If SCr increased, check again in 2 to 3 weeks, and again in 3 to 4 weeks.[6] Then check once or twice yearly, and when patient condition or medications change.[6-8] • Low-risk patients (see comments) with serum potassium 4.5 mEq/L or less could wait 3 to 4 weeks before initial assessment.[9] • Product labeling generally recommends monitoring potassium frequently if co-administered with potassium or potassium-sparing diuretics. • Routinely monitor renal function and electrolytes when used with aliskiren (*Tekturna* [U.S.], *Rasilez* [Canada]) in patients with diabetes.[98]		within 1st two months of starting drug despite dose reduction.[6] • 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; heart failure; sodium depletion; low albumin; atherosclerosis; dehydration; hypo- or hypertension.[8-12] • No evidence ARBs safer for kidneys than ACEI.[13]
Antiarrhythmics	Liver function tests	• Amiodarone: Baseline and every six months[30]	Hepatotoxic	• Amiodarone: Liver enzyme elevation may be asymptomatic, may decrease despite continued amiodarone use, or may progress to hepatitis, which may be fatal.[30] • Amiodarone: If LFTs are >3 times the ULN, or double in a patient with elevated baseline LFTs, 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]
Antiarrhythmics continued	Thyroid function tests	• Amiodarone: Baseline and every six months[30]	Can cause hypothyroidism or hyperthyroidism	• Incidence of hyperthyroidism may be as high as 10%.[30] • Incidence of hypothyroidism may be as high as 22%.[30] • Management options include discontinuation; levothyroxine for hypothyroidism; or corticosteroids, antithyroid medication, or surgery for hyperthyroidism.[30]
	Antiarrhythmic level	• Flecainide (*Tambocor*):[35,38] ● routine care (checking trough periodically may be useful) ● heart failure (goal trough < 0.7 to 1 mcg/mL recommended) ● liver impairment (early and frequent monitoring required to guide dose) ● severe renal impairment (CrCl 35 mL/min/1.73m^2 or lower) (frequent monitoring [daily trough, per Canadian labelling] required to guide dose)	Narrow therapeutic index drug	• Flecainide therapeutic range 0.2 to 1 mcg/mL.[35] • Increase flecainide dose only when steady-state achieved (about four days; longer in renal and hepatic impairment).[35] • Mexiletine: therapeutic range 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]

		• moderate renal impairment (may be helpful during dosage adjustment) • use with amiodarone (strongly recommended to guide dose) • use in elderly (daily trough recommended during dose adjustment, per Canadian labelling) • Mexiletine: in the event of potential drug interactions (phenytoin, rifampin, phenobarbital, cimetidine)[36]		
Anticonvulsants	Anticonvulsant level	Reasons to check level: • Loading, or dosage change[15-17,19,20] • To establish target level in patient with good control and few side effects[14,16,18] • Suspected toxicity[14-16,18] • Large variation in levels (phenytoin)[16] • Starting/stopping interacting drug[14,16,18-20,29] (See our charts, *"Cytochrome P450 Drug Interactions,"* and *"Comparison of Antiepileptic Drugs"* [based on U.S. product information] for help identifying potential interactions.) • Diseases or physiologic changes (e.g., pregnancy, renal failure)[14,15,21-23,26] • Poor control[14,18] • Suspected noncompliance[14-16,18] • Change in how administered (e.g., with or without food) (valproate)[19,20] • Potential malabsorption (phenytoin, carbamazepine)[16,18,21] • Switching dosage form (phenytoin, valproate)[16,19,20] • 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] • Unclear benefit of routine blood/serum level monitoring without clinical indication.[14] • Level usually checked in morning immediately prior to dose (trough).[17] • 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].[16-18,31] • Levels usually checked after at least 4 to 5 half-lives (i.e., steady-state).[17] • Valproate[a], phenytoin: free (unbound) level more accurate than total level in renal or liver disease, elderly, and hyperlipidemia.[16,19]
	Liver function tests	See our chart, *"Liver Function Test Scheduling"*	For agents associated with liver damage	• Carbamazepine, ethosuximide, felbamate, and valproate require routine liver function monitoring. • Most anticonvulsants require dosing adjustments or cautious dosing for hepatic impairment.
Anticonvulsants, continued	Complete blood count	• Carbamazepine: baseline, monthly for 2 or 3 months, then at least every-other-year[17] • Felbamate: baseline, frequently during therapy, and for a significant time after discontinuation[28]	Can cause bone marrow suppression	

	Renal function	• Carbamazepine: baseline and periodic urinalysis and BUN[18] • Zonisamide (*Zonegran*): periodically[27]	Can cause renal dysfunction	Most anticonvulsants require dosing adjustments or cautious dosing for renal impairment.
	HLA-B*1502 genotyping	Carbamazepine: baseline in high-risk patients (i.e., those of Asian ancestry)[18]	HLA-B*1502 allele associated with serious skin reactions	High prevalence (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 baseline, periodically, prior to planned surgery.[19,20] Monitor clotting parameters in pregnancy.[19,20]	Can cause thrombocytopenia	
	Ammonia level	• Valproate[a]: in event of lethargy, vomiting, mental status change, hypothermia[19,20] • Topiramate (*Topamax*): if encephalopathic symptoms occur[24]	Can cause hyperammonemia	Concomitant valproate/topiramate use increases risk.[19,20]
	Bicarbonate	• Topiramate (*Topamax*): baseline and periodically[24] • Zonisamide (*Zonegran*): baseline and periodically[27]	Can cause metabolic acidosis	
Anticonvulsants, continued	Thyroid function	Oxcarbazepine (*Trileptal*): Consider evaluation of thyroid hormone status (frequency not specified).[26]	May decrease total and/or free T4 (thyroxine) levels	T3 and TSH usually unaffected.[26]
	Sodium	Oxcarbazepine (*Trileptal*): • Consider periodic monitoring, especially if hyponatremia symptoms occur (e.g., nausea, headache, malaise, lethargy, mental status change, seizures).[25] • In heart failure, check in the event of worsening disease or fluid retention.[26] • 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] • In patients taking sodium-lowering meds (e.g., diuretics), consider checking periodically (per Canadian labelling, check at baseline, in two weeks, monthly for three months) and as clinically indicated (e.g., in the event of symptoms).[25,26]	Can cause hyponatremia	Hyponatremia usually occurs within the first three months of treatment. If it occurs, consider dose reduction, fluid-restriction, or discontinuation.[25] Canadian labelling recommends fluid restriction in heart failure patients with hyponatremia.[26]
Antipsychotics, Atypical (aripiprazole [*Abilify*],	Glucose, fasting	• Baseline, at 12 weeks to four months, then annually.[52,53] Check more frequently if high diabetes risk. Some clinicians check every	Increase risk of hyperglycemia and diabetes[52]	• In U.S., prescribers, patients, and pharmacies must register with the *Clozaril* National Registry (800-448-5938;

asenapine [*Saphris* (U.S.)], clozapine [*Clozaril*], iloperidone [*Fanapt* (U.S.)], olanzapine [*Zyprexa*], paliperidone [*Invega*], quetiapine [*Seroquel*], risperidone [*Risperdal*], ziprasidone [*Geodon* (U.S.), *Zeldox* (Canada)])		three to six months, with more frequent initial checks in high-risk patients.[52] • Monitor patients with diabetes regularly for worsening glucose control.[54]		www.clozarilregistry.com). Manufacturer-specific registry and distribution systems have been established for generic manufacturers. • In Canada, prescribers, patients, and pharmacies must register with the CSAN distribution system for *Clozaril* (1-800-267-2726). Manufacturer-specific registry and distribution systems have been established for generic manufacturers. • Some agents require caution, dose adjustment, or avoidance in renal or hepatic impairment. • Diabetes and hyperlipidemia risk varies among agents (see *"Comparison of Atypical Antipsychotic Agents"* charts: U.S. subscribers; Canadian subscribers).
	Lipids	• Baseline, at 12 weeks, then every two to every five years if normal.[52,53] Check more frequently if clinically indicated. Some clinicians check every three months to yearly. Checking every three months during the first year has been suggested.[52]	Can increase total cholesterol, LDL, and triglycerides[52]	
	White blood cell count, absolute, neutrophil count	*Clozaril* (clozapine): See product labeling for schedule.	Can cause agranulocytosis[55]	
Digoxin (e.g., *Lanoxin*)	Digoxin level	Reasons to check digoxin level: • Suspected toxicity[32,33] • Confirm level is therapeutic[33] • Suspected non-adherence[32] • Diseases or physiologic changes (e.g., renal impairment, thyroid disease)[32,34] • Starting or stopping an interacting drug[32,34] • Change in dose: check after 5 to 7 days (steady-state)[32]	Narrow therapeutic index drug	Therapeutic level: • heart failure: 0.5 to 1 ng/mL • atrial fibrillation: 2 ng/mL or lower[33] • Check level at least 6 to 8 hours after dose[33] • May take 15 to 20 days to reach steady-state in severe renal impairment.[32]
	Electrolytes	Periodically[33]	Hypokalemia, hypomagnesemia, and hypercalcemia enhance toxicity[32]	Closely monitor patients on diuretics or amphotericin due to potential for electrolyte changes.[32]
	Serum creatinine	Periodically[33]	Renally eliminated	Requires dose adjustment in renal impairment.[33]
Diuretics (thiazides, loops)	Electrolytes (e.g., potassium, sodium, magnesium, calcium, bicarbonate)	Within one week of initiation, frequently during the first few months (loops), then periodically (at least yearly).[37,39] Repeat potassium within four weeks of 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 may cause hypokalemia, hyponatremia, hypomagnesemia, and metabolic alkalosis[39,40] • 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] • Diuretic-associated hypokalemia (dose-dependent) is apparent within the first week and reaches a plateau within a month.[41,44] • Correction of hypomagnesemia can make hypokalemia easier to correct.[41]
	Glucose	Baseline and at least once a year.[41,43] Glucose periodically in diabetes and suspected latent	May increase glucose levels	Magnitude of increase is variable and dose-dependent. Increase is greatest in patients

		diabetes.[39]		with diabetes or prediabetes.[41]
	Renal function (BUN, SCr)	Baseline, frequently during the first few months (loops), then periodically (once or twice yearly).[39,43]	Can cause decreased renal blood flow and allergic interstitial nephritis[40,44,45]	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	Two to six weeks after initiation, and routinely.[42]	May increase uric acid levels	Usually small and clinically insignificant in patients without a history of gout.[41] Hydrochlorothiazide: uncommon with 50 mg daily or less.[43] Loops: not common.[41]
Fibric acid derivatives [e.g., gemfibrozil (*Lopid*), fenofibrate (e.g., *TriCor*, *Lipidil EZ* [Canada])	Liver Function[47,50]	See our chart, *Liver Function Test Scheduling*	Increased liver enzymes, bilirubin, and gallstones have been seen[47,50]	• Decreases in hemoglobin, hematocrit, and white blood usually stabilize, but anemia, leukopenia, thrombocytopenia, and bone marrow hypoplasia have been reported.[47,50] • Myositis risk factors include gemfibrozil use, statin use, and renal insufficiency.[47-49] • 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.[47,50,51]
	Creatine kinase	If symptoms (muscle weakness, tenderness, or pain) occur[47,50]	Risk of myositis and rhabdo-myolitis[47,48,50]	
	Complete blood count	Gemfibrozil (*Lopid*): Periodically during the first 12 months[47,50]	May decrease hemoglobin, hematocrit, and white blood cell count[47,50]	
Glitazones (pioglitazone [*Actos*], rosiglitazone [*Avandia*])	Liver function test (ALT)	• 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).[56,57] • Some experts monitor every 3 to 6 months.	Rarely associated with toxic hepatitis and liver failure	• Discontinue if ALT > 3 times the ULN despite recheck, or patient jaundiced.[56,57] • For *Actoplus Met* (pioglitazone/metformin) and *Avandamet* (rosiglitazone/metformin) also see metformin, below.
Lithium	Thyroid Function	• TSH and T4 at baseline and yearly[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 decreases levels.[95,97] • Monitor trough level (8 to 12 hours post-dose).[95] • Therapeutic range: 0.6 to 1.2 mEq/L.[95]
	Complete blood count	• Baseline and if symptoms arise[97]	Can cause leucocytosis[97]	
	Electrolytes	• Baseline, yearly, and if symptoms arise[97]	Avoid in dehydrated or sodium-depleted patients[95]	
	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] • Check more frequently if used with ACEI/ARB or diuretic (avoid concomitant use if possible).[95,100] • Monitor closely if used with metronidazole of fluoxetine.[95] • Check when patients initiate or	Narrow therapeutic index drug	

		discontinue NSAIDs.[95]		
	Pregnancy test	• In women of childbearing potential, at baseline and if suspected.[97]	May be teratogenic during first trimester[97]	
	Renal function	• Serum creatinine, BUN, urinalysis, and urine specific gravity or osmolality baseline, yearly, and if symptoms arise.[96,97]	Renal function can affect lithium levels; lithium can affect renal function[97]	
Metformin	Hemoglobin, hematocrit, red blood cell indices	Baseline and at least annually[58]	Metformin can 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 labelling: 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; [Canadian labelling recommends every six months][58,59]	Renal impairment can cause metformin accumulation and lactic acidosis	
Niacin (*Niaspan* [U.S.], *Niaspan FCT* [Canada], *Niacor* [U.S.])	Liver function tests (AST, ALT)	Baseline, then every six to 12 weeks for a year, then periodically (e.g., every six months)[60,61]	Dose-dependent hepatotoxicity[60]	Discontinue if liver function elevations persist at 3 times the ULN, or are associated with nausea, fever, and/or malaise.[60]
	Uric acid	Baseline, 6 to 8 weeks later, then annually, or as clinically indicated[60]	Dose-dependent risk of hyperuricemia[60]	Use with caution in patients predisposed to gout.[61,62]
	Glucose, fasting	Baseline, 6 to 8 weeks later, then annually, or as clinically indicated[60]	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]
	Creatine kinase	Periodically [U.S. labeling specifies in the event of muscle pain, tenderness, or weakness][61,63]	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 [U.S. labeling specifies in the event of muscle pain, tenderness, or weakness][61,63]	Risk of rhabdo-myolysis[61]	Hypokalemia predisposes to rhabdomyolitis, and rhabdomyolysis can cause hyperkalemia.
	Phosphorus	Periodically in patients at risk of hypophosphatemia[61]	Dose-dependent risk of decrease in phosphorus level[61]	Usually small and transient.[61]
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Serum creatinine	Periodically.[65] High-risk patients (see comments): check weekly for the first several weeks.[66]	Prostaglandin inhibition reduces renal blood flow; other renal injury[65]	• Discontinue if signs and symptoms consistent with renal disease develop.[65] • High risk: heart failure, ascites, renal impairment (use with caution), diuretic or ACEI/ARB use, age over 60 years with comorbidity, hypertension, sodium or volume depletion, long-term use.[65-68] • Some NSAIDs are contraindicated (e.g.,

				diclofenac [Canada], naproxen [Canada], ketorolac), or not recommended (e.g., naproxen, diclofenac) in advanced renal impairment.[65,69,70,82,93,94] • Also, monitor patients using *Flector* patch, *Pennsaid* liquid, and *Voltaren* gel per product labeling.[83-85]
	Complete blood count	• Periodically[65] • 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] • Also monitor patients using *Flector* patch *Pennsaid* liquid, and *Voltaren* gel per product labeling.[83-85]
	Liver function tests (ALT)	• Periodically in all patients[65] • Check within four to eight weeks of initiation in patients taking diclofenac.[82] • Check within eight weeks of initiation in patients with pre-existing liver disease.[66] • Also see our 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] • Severe hepatotoxicity rare. Risk factors include liver disease and diclofenac use.[66] • Canadian labelling contraindicates most NSAIDs in significant liver disease.[69,93] • Also monitor patients using *Flector* patch *Pennsaid* liquid, and *Voltaren* gel per product labeling.[83-85]
Psoriasis medications	Calcium	Calcipotriol (*Dovonex*, *Dovobet*): baseline and regularly [Canada].[71] *Dovobet* labelling specifies monitoring in patients receiving >100 g weekly [Canada].[76] In clinical trials of *Taclonex* (betamethasone/calcipotriene), calcium was checked at week four of treatment.[72]	Vitamin D analog; can increase calcium levels	• If calcium level exceeds normal, discontinue use and check weekly until levels normalize.[71] • Monitoring is especially important if coverage area is extensive.[71]
	Liver function tests (AST, ALT, LDH)	Acitretin (*Soriatane*): baseline, every one to two weeks until stable, and thereafter as clinically indicated.[73] [Canadian labelling recommends baseline, every one to two weeks for two months, then every three months. If abnormal, check weekly.][74]	Hepatotoxic[73]	Discontinue if liver function does not normalize or worsens.[74] Contraindicated in severe liver dysfunction.[73]
	Lipids	Acitretin (*Soriatane*): Every one to two weeks until stable (usually within four to eight weeks). Continue close monitoring in patients with diabetes, obesity, alcohol use, personal or family history of lipid metabolism disorder.[73]	May increase LDL and triglycerides, and decrease HDL[73,75]	Contraindicated in hyperlipidemia.[73]
	Glucose	Acitretin (*Soriatane*): Monitor carefully in patients with diabetes[73]	May increase or decrease blood glucose[73]	• Acitretin can enhance hypoglycemic effect of glibenclamide. New onset diabetes has been reported.[73]

				• Monitor more frequently during the early stages of treatment.[74]
Retinoids	Lipids	Isotretinoin: baseline, then until stable (usually by four weeks). Continue frequent monitoring in patients with diabetes, obesity, alcohol use, personal or family history of lipid metabolism disorder.[99] Acitretin: See psoriasis medications, above.	May increase triglycerides and LDL cholesterol and decrease HDL cholesterol[99]	
	LFTs	See our chart, *Liver Function Test Scheduling* and psoriasis medications, above.	Hepatotoxic	
	Glucose	Isotretinoin: check glucose more frequently in patients with diabetes.[99] Acitretin: See psoriasis medications, above	May cause new or worsening diabetes[99]	Educate patients to report symptoms of new onset diabetes (e.g., frequent urination, increased thirst).[99]
Rheumatoid arthritis medications	Various	See our document, *"Rheumatoid arthritis: the Role of DMARDs"* and chart, *"Liver Function Test Scheduling*	Most agents have potential for serious toxicity	Covers monitoring for biologic and nonbiologic disease-modifying antirheumatic drugs.
Statins	Liver function tests (e.g., ALT)	See our chart, *"Characteristics of the Various Statins"*	May cause dose-dependent, asymptomatic transaminase elevations	
	Creatine kinase	Baseline and when muscle symptoms (e.g., pain, weakness) occur[77]	Can cause myositis and rhabdomyolysis	• Risk factors for myopathy: elderly, small size, high statin dose, liver or renal disease, diabetes, uncontrolled hypothyroidism, interacting medications.[77] • Renal dose adjustment needed for some statins. See our chart, *"Characteristics of Various Statins."*
	Lipids	Check lipids six to eight weeks after initiating or increasing dose.[78]	To assess efficacy	Assuming compliance, maximum lipid effects occur within six weeks of initiation.[78]
	Thyroid stimulating hormone	If muscle symptoms occur[77]	Hypothyroidism predisposes to myopathy[77]	
Theophylline	Theophylline level	• Check when initiating therapy, before and after increasing dose, when toxicity suspected (e.g., tachycardia, nervousness, tremor, GI effects, headache), in the event of new or worsening illness predisposing to toxicity (see comments), after smoking cessation, after adding/stopping an interacting drug (see comments), and at least annually[80,81]	Narrow therapeutic index drug with interindividual differences in metabolism	• Therapeutic range 5 to 15 mcg/mL.[79] • Check peak at steady-state (at least 48 to 72 hours on same dosage).[79,80] • 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] • 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 CYP3A3 or CYP1A2 inhibitors).[80,81] • Charbroiled beef, low carbohydrate/high protein diet, parenteral nutrition, St. John's wort, rifampin, carbamazepine, and smoking decrease levels.[81] • See our chart, *"Cytochrome P450 Drug Interactions"* for help identifying potential interactions.
Thyroid Replacement	Sensitive TSH	• TSH at baseline, every six to eight weeks until normal, then every six to 12 months[86,87] • TSH six weeks to three months (eight to 12 weeks, per labeling) after change in dose or product[86,87] • Also check if clinically indicated, or if there is a change in patient health[87] • Patients over 50 years of age with cardiac disease: monitoring interval four to six weeks[88] • Adults <50 years of age with severe hypothyroidism: monitoring interval two to four weeks[88]	To ensure dose is appropriate	• Patients nonadherent to monitoring may have more adverse effects.[86] • 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 respond normally to anticoagulant therapy.[89] • Monitor diabetic control; insulin or antidiabetic dose may need to be increased.[87]
Warfarin	International Normalized Ratio (INR)	• Daily during initiation, until stable in the therapeutic range, weekly for several weeks once therapeutic, then every 1 to 4 weeks once stable[90,91] • CHF patients may require more frequent monitoring due to greater sensitivity[90] • Increase frequency after any dose adjustment until stable[90] • Increase monitoring after hospital discharge; if interacting drug or natural medicine is added, discontinued, or taken sporadically; or if brand is changed.[90]	Narrow therapeutic index drug with interindividual differences in metabolism	See our charts: *"Cytochrome P450 Drug Interactions,"* and *"Antibiotic/Antifungal Drug Interactions and Warfarin"* and document, *"Use of Low-dose Vitamin K Supplements to Stabilize INR,"* (includes warfarin/food interactions) for help identifying and managing potential interactions.
	CYP2C9 and VKORC1 genotype	Baseline[90]	Those with genetic variations may need lower dose and more frequent monitoring	See our document, *"Genotyping for Patients on Clopidogrel or Warfarin"* for more information.

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

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