Hyperlipidemia Management Protocol
STANFORD COORDINATED CARE

PURPOSE: To enhance collaborative patient care by referral of patients with a diagnosis of dyslipidemia, coronary artery disease (CAD), diabetes (DM) or is at high risk for coronary heart disease to be co-managed by the clinical pharmacist, pharmacy resident or RN following this protocol.

SUPPORTIVE DATA: There is a strong link between serum cholesterol and cardiovascular mortality. Reductions in LDL cholesterol are followed by reductions in mortality. In general, each 1% fall in LDL cholesterol confers a 2 % reduction in cardiovascular events. The goal of therapy is to decrease cardiovascular morbidity and mortality by lowering cholesterol to a target level. The target LDL cholesterol is determined by the number of patient risk factors. The goal is achieved through diet, lifestyle modification, and drug therapy.

ACKNOWLEDGEMENT: This protocol is adapted from one developed at Santa Clara Valley Medical Center in San Jose, CA by Tyler Aguinaldo, MD, Director of Diabetes & Metabolism Center; Dorleen Von Raesfeld, MSN, RN, CDE, Assistant Nurse Manager and Susan Yu, Clinical Pharmacist, CDE, Chronic Care Management. We gratefully acknowledge their willingness to share this protocol.

Please feel free to utilize these protocols and please credit Stanford Coordinated Care.

I. CONTENT

A. LIPID MANAGEMENT IN ADULTS

1. INCLUSION CRITERIA (must fulfill all)
   a. Adult >35 years of age.
   b. Non-pregnant adult.
   c. Hyperlipidemia with LDL above goal.

2. EXCLUSION CRITERIA
   a. Heavy alcohol abuse (>3 drinks/day).
   b. History of pancreatitis.
   c. Active liver disease or elevated liver enzymes (persistent, unexplained) or baseline ALT $\geq$ 3 times upper limit of normal (ULN) or clinical evidence of cirrhosis (eg., GIB, ascites, hepatic encephalopathy INR > 1.3, albumin < 3, radiographic or pathological findings consistent with cirrhosis).
   d. Active adjustment of glucocorticoid (e.g., prednisone, dexamethasone, hydrocortisone, triamcinolone) doses.
   e. Active vascular disease (e.g., unstable angina, stroke-like symptoms).
   f. Active systemic infection.
   g. HIV-positive patients.
   h. Serum creatinine level $\geq$ 2 mg/dL, dialysis patients, OR patients with treatable etiology for nephrotic syndrome.
   i. TSH > 5 μIU/mL.
   j. Previous hemorrhagic stroke.

3. ASSESSMENT OF LDL-C GOAL
   a. If no history of CHD, count the number of major risk factors and estimate 10-year risk for men and women using Framingham Risk Score (see Attachment B).
   b. Major Risk Factors for CHD
      1) Cigarette smoking
      2) Hypertension (BP ≥ 140/90 mmHg or on antihypertensive medication)
      3) Low HDL (< 40 mg/dL)
      4) Family history of premature CHD (CHD in male first degree relative < 55 yrs; CHD in female first degree relative < 65 yrs)
      5) Age (men ≥ 45 yrs; women ≥ 55 yrs)
      6) Diabetes is regarded as CHD risk equivalent in ATPIII

Risk Category	LDL Goal (mg/dL)	LDL level at which to initiate Therapeutic Lifestyle Changes (mg/dL)	LDL level at which to consider drug therapy[f]
CHD[a] or CHD Risk Equivalents[b]; High risk (10-year risk > 20%)	< 100 (optional goal < 70 mg/dL)[c]	≥ 100[d]	≥ 100 mg/dL[e] (< 100 mg/dl: consider drug options)[f]
2+ Risk Factors[g]; Moderately high risk (10-year risk 10%-20%)[h]	< 130[i]	≥ 130[d]	≥ 130 (100-129; consider drug therapy options)[j]
2+ Risk Factors[g]; moderate risk (10-year risk <10%)[h]	< 130	≥ 130	≥ 160
0-1 Risk Factor; Lower risk[k]	< 160	≥ 160	≥ 190mg/dL (160-189: LDL-lowering drug therapy optional)

[a]CHD includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia

[b]CHD risk equivalents include clinical manifestations of non-coronary forms of atherosclerotic disease, abdominal aortic aneurysm, and carotid artery disease (transient ischemic attacks or stroke of carotid origin or > 50% obstruction of a carotid artery), peripheral vascular disease, diabetes, and 2+ risk factors with 10-year risk for hard CHD > 20%

[c]Very high risk favors the optional LDL-C goal of < 70 mg/dL. **Very high-risk** patients are those who have had a recent heart attack, or those who have cardiovascular disease combined with either diabetes, or severe or poorly controlled risk factors (such as continued smoking), or metabolic syndrome (a cluster of risk factors associated with obesity that includes high triglycerides and low HDL cholesterol).

[d]Any person at high risk or moderately high risk who has lifestyle-related risk factors (eg, obesity, physical inactivity, elevated trigylceride, low HDL-C, or metabolic syndrome) is a candidate for therapeutic lifestyle changes to modify these risk factors regardless of LDL-C level

[e]If baseline LDL-C < 100 mg/dL, institution of an LDL-lowering drug is a therapeutic option on the basis of available clinical trial results. If a high-risk person has high triglycerides or low HDL-C, combining a fibrate or nicotinic acid with an LDL-lowering drug can be considered.

[f]When LDL-lowering drug therapy is employed, it is advised that intensity of therapy be sufficient to achieve at least a 30% to 40% reduction in LDL-C levels

[g]Risk factors include cigarette smoking, hypertension (BP ≥ 140/90 mm Hg or on antihypertensive medication), low HDL cholesterol (<40 mg/dl), family history of premature CHD (CHD in male first-degree relative < 55 years of age; CHD in female first-degree relative < 65 years of age), and age (men ≥ 45 years of age, women ≥ 55 years of age)

[h]Electronic 10-year calculators are available at www.nhlbi.nih.gov/guidelines/cholesterol
[i]Optional LDL-C < 100 mg/dl
[j]For moderately high-risk persons, when LDL-C level is 100-129 mg/dl, at baseline or on lifestyle therapy, initiation of an LDL-lowering drug to achieve an LDL-C level < 100 mg/dl is a therapeutic option on the basis of available clinical trial results
[k]Almost all people with zero or 1 risk factor have a 10-year risk < 10%, and a 10-year risk assessment in people with zero or 1 risk factor is thus not necessary.

B. ASSESSMENT

1. Subjective
   a. Review contraindications for treatment, patient's medical history, drug history, and drug interactions.
   b. Review medication list (including Rx, OTC, and herbal supplements) and dietary compliance and adherence.
   c. Assess the occurrence of any adverse reactions, including symptoms of hepatotoxicity and myopathy/ rhabdomyolysis.
   d. Set individualized goals for LDL.
   e. Medical nutrition therapy.
   f. Weight management.
   g. Physical activity.
   h. Access adherence/compliance.

2. Objective
   a. Vital signs
   b. Fasting lipid panel (FLP)
   c. BMP
   d. Hepatic function panel
   e. TSH

C. INSTRUCTIONS FOR PROTOCOLS

1. Ascertain patient meets criteria for lipid protocol and determine LDL goal.

   A. Patients with **DIABETES without known CVD**:
   Target LDL goal < 100 mg/dL

   B. **DIABETES with known CVD**:
   Target LDL < 70 mg/dL is an option after consultation with MD.
   Please note other factors to consider when consulting with MD for target LDL < 70mg/dL: persistent cigarette smoking, MI within past 2 years, ACS, elements of metabolic syndrome (a cluster of risk factors associated with obesity that includes high triglyceride and low HDL cholesterol), and other atherosclerotic disease (PAD, TIA, stroke of carotid origin).

   C. Patients with **previous TIA or ISCHEMIC STROKE**:
   In patients with an LDL $\geq$ 100 mg/dL, target a reduction of at least 50% in LDL or a LDL goal < 70 mg/dL.

2. Obtain baseline evaluation parameters and baseline FLP, BMP, hepatic function panel, and TSH prior to initiation of therapy. Monitor necessary laboratory tests according to each protocol.
3. Interview and evaluate patient, review goals, and reinforce lifestyle therapies at all visits.
4. Start Protocol (see ATTACHMENT D for lipid algorithm).
5. Address adherence to therapy
6. To address patient adherence to diet, exercise, and drug therapy.
   a. Patients should be questioned about adherence to treatment at each visit. A minimum of three to six months of intensive diet and exercise is recommended before medications are initiated for primary prevention. Shorter trials of medical nutritional therapy (MNT) and exercise are appropriate for patients with severe hyperlipidemia or atherosclerotic cardiovascular disease (ASCVD), since aggressive drug therapy is of demonstrated efficacy in these high risk groups. Reasons for diet and exercise noncompliance include the following:

1) Incomplete patient effort and self-motivation: Some patients are unable or unwilling to comply with strict dietary changes, such as a Step II diet, and a regular exercise regimen.
2) Nadir values of LDL cholesterol and triglycerides may not be achieved until after three to six months following lifestyle modification. Wait at least 6 to 8 weeks to retest for therapeutic lifestyle change (TLC) effect. Pharmacotherapy likewise may not result in lower lipid values until after at least one month of treatment. Re-measurement of serum lipids after at least one month of drug therapy, or after at least three months of dietary therapy, allows for the documentation of efficacy, the identification of unfavorable effects of treatment, and the dose titration of medication.
3) Suboptimal social support: Family and lifestyle may not be conducive to strict dietary changes. Patients may not have access to exercise facilities or safe environment (e.g., safe neighborhood in which to walk).
4) Incomplete patient education: Some patients may not have received adequate information because of missed visits or inadequate time for counseling.
5) Cost: Patients may perceive that dietary interventions increase costs, though this is generally not the case. Patients unable to walk may not have access to other exercise options (swimming, stationary bike/machines, etc.).

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PROTOCOL A SIMVASTATIN / ATORVASTATIN THERAPY

INCLUSION SUB-CRITERIA
1. Need to meet Adult Treatment Panel (ATP) III goals

ADDITIONAL EXCLUSION SUB-CRITERIA
1. Hypersensitivity to simvastatin and/or atorvastatin
2. Caution:
   a. history of myopathy
   b. renal failure (serum creatinine level ≥ 2 mg/dL)
   c. significant drug interactions (see Attachment A Appendix D)

ALGORITHM
1. For simvastatin:
   a. Assess the initial dose of simvastatin.
   b. Usual starting dose is 20 mg at bedtime. If patient has diabetes or CHD equivalent or needs LDL-C reduction of > 45%, usual starting dose is 40 mg at bedtime.
   c. Measure fasting lipid panel a six to eight weeks after initiation of simvastatin.
   d. If the patient is not at LDL goal, double the dose of simvastatin. Confirm patient shows no sign of myopathy, liver function abnormalities, or drug-drug interaction with simvastatin.
   e. Measure patient's fasting lipid panel six to eight weeks after doubling dose of simvastatin.
   f. Continue steps c-e until the maximum dose of simvastatin (40 mg/day) is achieved.
   g. If the patient is not at LDL goal, stop simvastatin and may go to maximum dose of atorvastatin (start with atorvastatin 40 mg for 1 month to verify tolerability and then increase to 80 mg).
2. For atorvastatin:
   a. Assess the initial dose of atorvastatin.
   b. Usual starting dose is 10 mg daily. If patient has diabetes or CHD equivalent or needs LDL reduction of > 45%, usual starting dose is 20 mg daily.
   c. Measure fasting lipid panel eight to twelve weeks after initiation of atorvastatin
   d. If patient is not at LDL goal, double the dose of atorvastatin. Confirm patient shows no signs of myopathy or liver function abnormalities.
   e. Measure patient's fasting lipid panel eight to twelve weeks after doubling dose of atorvastatin.
   f. Continue steps c-e until the maximum dose of atorvastatin (80 mg/day) is achieved.
   g. If the patient is not at LDL goal with atorvastatin 80 mg, consider adding second agent.
   h. If patient is intolerant of combination therapies, then contact MD.
3. Notify MD or referring physician if any of the following:
   a. Unexplainable muscle weakness, tenderness, general malaise, or dark urine. Obtain CPK and notify MD of result.
   b. Dark urine, pale stools, RUQ abdominal pain, nausea, vomiting, yellowing of skin or eyes and/or fever. Obtain LFTs and notify MD of result.
   c. LFT ≥ 3 times upper limit of normal.
   d. Development of allergic reaction to medication.

Guide for Equivalency (LDL-C Reduction) Between HMG CoA RIs

Atorvastatin (mg)	Pravastatin (mg)	Rosuvastatin (mg)	Simvastatin (mg)
-	10	-	5
-	20	-	10
10	40	-	20
20	80	5	40
40	-	10	80
80	-	20-40	

Mean Percent Reductions in LDL-C (Primary Hypercholesterolemia Patients)

↓ LDL <25%	↓ LDL 25-35%	↓LDL 35-45%	↓LDL 45-50%	↓ LDL > 50%
Pravastatin 10mg **Simvastatin 5mg**	Pravastatin 20-40mg **Simvastatin 10-20mg**	**Atorvastatin 10-20mg** Pravastatin 80mg Rosuvastatin 5mg **Simvastatin 40mg**	**Atorvastatin 40mg** Rosuvastatin 10mg **Simvastatin 80mg**	**Atorvastatin 80mg** Rosuvastatin 20-40 mg

Note: In general, a doubling of the HMG CoA RI dose results in an additional 5-8% reduction in LDL-C levels

PROTOCOL B NIACIN (NIASPAN) THERAPY

INCLUSION SUB-CRITERIA
1. Monotherapy: tried and failed statin (e.g. contraindication to using a statin, intolerance such myopathy, etc) if fulfilled inclusion criteria for agent

ADDITIONAL EXCLUSION SUB-CRITERIA
1. Active peptic ulcer disease
2. Arterial bleeding
3. Gout
4. Hypersensitivity to niacin or any component
5. Caution:
   a. concurrent anticoagulants
   b. concurrent vasoactive agents
   c. consumption of substantial amounts of alcohol
   d. history of liver disease
   e. predisposition to gout
   f. renal disease (Creatinine >2 or GFR <30)
   g. unstable angina
   h. may worsen blood glucose (monitor)
   i. concurrent statins
   j. significant drug interactions (see Attachment B)

ALGORITHM
1. Prior to starting niacin, baseline chemistry panel, uric acid and TSH should be measured.
2. Start 500 mg PO QHS x 4 weeks, then increase 500 mg/day every 4 weeks based on effect/tolerance. Maximum dose is 2000 mg/day
3. Measure patient's lipid panel after eight to twelve weeks of initiation or after dose adjustment.
4. If patient has no contraindications to aspirin, may pre-medicate 30 minutes prior to niacin dose with aspirin 325 mg.
5. Notify MD if any of the following:
   a. Unexplainable muscle weakness or tenderness, general malaise, or dark urine. Obtain CPK and notify MD of result.
   b. Dark urine, pale stools, RUQ abdominal pain, nausea, vomiting, yellowing of skin or eyes and/or fever. Obtain LFTs and notify MD of result.
   c. LFT $\geq$ 2 times upper limit of normal
   d. Development of allergic reaction to medication

D. REPORTABLE CONDITIONS / INTERVENTIONS

1. Non-compliance for follow-up lab work or clinic/phone visits.
2. Any adverse side effects to medications listed above.
3. Pregnancy.
4. Patient has reached LDL goal or maximized therapy.

E. REFERRAL TO PHYSICIAN

1. Patient is pregnant.
2. Signs or symptoms of myopathy or CPK is $\geq$ 3 times upper limit of normal.
3. Signs or symptoms of hepatotoxicity (ALT/AST $\geq$ 2 times upper limit of normal).
4. LDL-C not at goal after combination therapy of two agents.
5. Triglycerides or non-HDL-C not at goal after optimal LDL-C and lifestyle modification.

F. PATIENT EDUCATION / FOLLOW-UP

1. Evaluation of current lab data (within last 3 months) to include: BMP, fasting lipid panel and hepatic function panel, TSH, uric acid and CPK if necessary.
2. Identify acute or other concerns, which need to be addressed by the referring provider.
3. Relationship among nutrition, exercise (state the need to consult with health care team before beginning an exercise program if there is any existing medical problems that would potentially prohibit such activity) and medication.
4. Medications
   a. State the brand and amount of medication to be taken
   b. Describe the use and storage of medication
   c. State the side effects of medication

G. DOCUMENTATION

1. Document the following in EPIC:

a. Patient goals and concerns
b. Laboratory parameters assessment as defined in inclusion and exclusion criteria
c. Allergy status
d. Educational opportunities/reinforcement of care issues – patient education materials available on EPIC (Lane Library, Up-to-date, MyHealth, etc.)
e. Action plan
f. Any physician notification including reason and time
g. Referral to dietician

II. CLINICAL REQUIREMENTS

A. REQUIREMENTS OF CLINICAL PHARMACIST

1.	EDUCATION / TRAINING:	Graduated from an accredited School of Pharmacy. Current licensure by the California State Board of Pharmacy required and must have either a) a PharmD degree and completion of an ASHP accredited clinical residency program OR b) completed a Board of Pharmaceutical Specialties (BPS) Certification and have three years clinical experience in direct patient care. Specialty in ambulatory care pharmacy preferred. The clinical pharmacist must also sign the Collaborative Practice Agreement with the physician(s) at Stanford Coordinated Care prior to the start of practice.
2.	EXPERIENCE:	Minimum of three years of experience as a pharmacist, with familiarity in chronic care management.
3.	INITIAL EVALUATION:	In-service/orientation and competency validation to the protocol.
4.	ON-GOING EVALUATION:	Annual review of competency.

B. REQUIREMENTS OF REGISTERED NURSE:

1.	EDUCATION / TRAINING:	Current licensure in the state of California. Completion of an RN program from an accredited school of nursing.
2.	EXPERIENCE:	Minimum of one year of experience as a registered nurse, with familiarity in disease management or chronic care management.
3.	INITIAL EVALUATION:	In-service/orientation and competency validation to the protocol.
4.	ON-GOING EVALUATION:	Annual review of competency.

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ATTACHMENT A APPENDIX A

HMG CoA Reductase Inhibitor Formulations

Generic name	Brand name	Formulation	Strengths	Color
Atorvastatin	**Lipitor®**	Film-coated, elliptical tablets	10 mg 20 mg 40 mg 80 mg	White White White White
Pravastatin	Pravachol®	Tablets	10 mg (rectangular) 20 mg (rectangular) 40 mg (rectangular) 80 mg (oval)	Pink-peach Yellow Green Yellow
Rosuvastatin	Crestor®	Tablets	5 mg (round, biconvex) 10 mg (round, biconvex) 20 mg (round, biconvex) 40 mg (oval, biconvex)	Yellow Pink Pink Pink
Simvastatin	**Zocor®**	Film-coated tablets	5 mg (shield-shaped) 10 mg (shield-shaped) 20 mg (shield-shaped) 40 mg (shield-shaped) 80 mg (capsule-shaped)	Buff Peach Tan Brick-red Brick-red

Guide for Equivalency (LDL-C Reduction) Between HMG CoA Ris

Atorvastatin (mg)	Pravastatin (mg)	Rosuvastatin (mg)	Simvastatin (mg)
-	10	-	5
-	20	-	10
10	40	-	20
20	80	5	40
40	-	10	80
80	-	20-40	

ATTACHMENT A APPENDIX B

Mean Percent Reductions in LDL cholesterol (Primary Hypercholesterolemia Patients)

↓ LDL <25%	↓ LDL 25-35%	↓LDL 35-45%	↓LDL 45-50%	↓ LDL > 50%
Pravastatin 10 mg **Simvastatin 5 mg**	Pravastatin 20-40 mg **Simvastatin 10-20 mg**	**Atorvastatin 10-20 mg** Pravastatin 80 mg Rosuvastatin 5 mg **Simvastatin 40 mg**	**Atorvastatin 40 mg** Rosuvastatin 10 mg **Simvastatin 80 mg**	**Atorvastatin 80 mg** Rosuvastatin 20-40 mg

Note: In general, a doubling of the HMG CoA Reductase Inhibitor dose results in an additional 5-8% reduction in LDL levels

Mean Percent Reductions in TGs (Primary Hypercholesterolemia Patients)

↓ TG 0-5%	↓ TG 5-10%	↓ TG 10-20%	↓ TG 20-30%
Pravastatin 10 mg	Pravastatin 20-40 mg	**Atorvastatin 10-20 mg** Pravastatin 80 mg Rosuvastatin 5 mg **Simvastatin 10-40 mg**	**Atorvastatin 40-80 mg** Rosuvastatin 10-40 mg **Simvastatin 80 mg**

Effects of HMG CoA Reductase Inhibitors on HDL levels

- Atorvastatin 10-80 mg/d, fluvastatin 20-80 mg/d, lovastatin 10-80 mg/d, pravastatin 10-80 mg/d, rosuvastatin 5-40 mg/d, simvastatin 5-80 mg/d, and Vytorin® 10/40 – 10/80mg increase the HDL cholesterol level by 3-12%

ATTACHMENT A APPENDIX C

Usual Dosage and Administration

Drug (generic name)	Brand name	FDA-Approved Daily Dosage	Timing of dose
Atorvastatin	**Lipitor®** (Pfizer)	Initial: 10 mg once daily. Start 20 mg daily if patient has diabetes, CHD equivalent, or needs LDL-C reduction > 35%. Maximum: 80 mg once daily	Any time of the day
Pravastatin	Pravachol® (Bristol-Myers-Squibb)	Initial: 40 mg once daily Maximum: 80 mg once daily (FDA-approval for 80 mg dose this year)	Any time of the day
Rosuvastatin	Crestor® (AstraZeneca)	Initial: 10 mg once daily Maximum: 40 mg once daily	Any time of the day
Simvastatin	**Zocor®** (Merck)	Initial: 20 mg once daily. Start 40 mg daily if patient has diabetes, CHD equivalent, or needs LDL-C reduction > 35%. Maximum: 80 mg once daily	Take at bedtime

Recommended Doses in Patients with Impaired Renal Function and/or Taking Certain Medications

HMG CoA Reductase Inhibitor	Impaired renal function dosage adjustment	Concomitant medication/food
Atorvastatin	No dose adjustment	≥ 1g/d niacin: do not exceed 10 mg/d Fibric acid derivatives: do not exceed 10 mg/d
Pravastatin	Patients with significant renal dysfunction should receive an initial dose of 10 mg/d	
Rosuvastatin	If CrCl < 30ml/min/1.73m^2, patients should receive an initial dose of 5 mg/d; 10 mg once daily dose should not be exceeded	Cyclosporine: do not exceed 5 mg/d Gemfibrozil: do not exceed 10 mg/d
Simvastatin	Patients with significant renal dysfunction should receive an initial dose of 5 mg/d	Cyclosporine: do not exceed 10 mg/d ≥ 1g/d niacin: do not exceed 10 mg/d Fibric acid derivatives: do not exceed 10 mg/d Amiodarone: do not exceed 20 mg/d Verapamil: do not exceed 20 mg/d

CPK Monitoring (per ACC/AHA/NHLBI Clinical Advisory)

- CK measurement should be obtained if the patient reports muscle soreness, tenderness or pain; rule out common causes such as exercise or strenuous work and obtain a thyroid-stimulating hormone level.
- If the CK level is moderately elevated (3-10 times ULN), follow the patient's symptoms and CK levels weekly until there is no longer any medical concern. Contact the primary care physician to inform him/her of the patient's laboratory abnormalities. Discontinue HMG CoA RI therapy if a CK level greater than 10 times ULN is seen in a patient with suggestive muscle symptoms.

ATTACHMENT A APPENDIX D

Drug Interactions with HMG CoA Reductase Inhibitors

Precipitant drug/food	Object drug	Comments
Amiodarone	Lovastatin, simvastatin	Risk of myopathy increased. **Do not exceed a dose of 20 mg for simvastatin when taking amiodarone.**
Atorvastatin	Digoxin	Coadministration may increase risk for digoxin toxicity.
Azole antifungals **Itraconazole** **Ketoconazole**	Atorvastatin, simvastatin	Risk of myopathy increased. *Do not take simvastatin if the patient is on itraconazole or ketoconazole.*
Cyclosporine	Atorvastatin, rosuvastatin, simvastatin	Risk of myopathy increased. **Do not exceed a dose of 5 mg and 10 mg, rosuvastatin and simvastatin, respectively, when taking cyclosporine.**
Danazol	Simvastatin	Do not exceed a dose of simvastatin 10mg
Erythromycin **Clarithromycin** **Telithromycin**	Atorvastatin, lovastatin, simvastatin	Coadministration increases the risk of myopathy/rhabdomyolysis. *Avoid simvastatin/lovastatin.*
Fibric acid derivatives **Gemfibrozil** **Fenofibrate (lower incidence of myopathy)**	HMG CoA RIs	Coadministration increases the risk of myopathy/rhabdomyolysis. **Do not exceed doses of 10 mg, 10 mg, 10 mg & 20 mg for rosuvastatin, simvastatin, atorvastatin and lovastatin, respectively.**
Grapefruit juice (> 1 qt/d)	Lovastatin, simvastatin	*Do not take simvastatin if the patient consumes > 1 quart of grapefruit juice/day.*
Lovastatin, simvastatin, rosuvastatin	Warfarin	Increased prothrombin time may occur with co-administration.
Nefazodone	Lovastatin, simvastatin	Risk of myopathy increased. *Do not take simvastatin or lovastatin if the patient is on nefazodone.*
Nicotinic acid (≥ 1gram/day)	HMG CoA RIs	Coadministration increases the risk of myopathy/rhabdomyolysis. **Do not exceed simvastatin 10 mg, atorvastatin 10 mg, or lovastatin 20 mg.**
Protease Inhibitors	Lovastatin, simvastatin	*Do not take simvastatin or lovastatin if the patient is taking a protease inhibitor.*
Red yeast rice (Cholestin)	HMG CoA RIs	Red yeast rice contains HMG CoA RIs
Rifampin	Fluvastatin	Rifampin may decrease fluvastatin efficacy.
Verapamil	Lovastatin, simvastatin	Risk of myopathy increased**. Do not exceed a dose of 20 mg for simvastatin or 40 mg for lovastatin when taking verapamil.**

Bolded drugs should not be co-administered or exceed maximum dose with the drugs in the adjacent column (contraindication/warning).

ATTACHMENT B

Nicotinic Acid Formulations

Generic name	Brand name	Formulation	Strengths	Color
Nicotinic Acid (also available as generic products)	**Niacin**	Tablets	50 mg 100 mg 250 mg 500 mg	white
Niacin extended-release	Niaspan®	Tablets	500 mg 750 mg 1000 mg	Off-white Off-white Off-white

Usual Dosage and Administration

Drug (generic name)	Brand name	FDA-Approved Daily Dosage	Timing of dose
Nicotinic Acid	Niacin (various)	Initial: 100 mg daily to BID; increase by 100 mg BID-TID per week Maximum: 6 grams/d	With meals
Niacin extended-release	Niaspan® (KOS)	Initial: 500 mg HS; increase by 500 mg every 4 weeks Maximum: 2 grams/d	At bedtime along with a light snack

Recommended Doses in Patients with Impaired Renal Function and/or Taking Certain Medications

Nicotinic Acid	Impaired renal function dosage adjustment	Concomitant medication/food
Niacin		Alcohol may increase side effects of flushing and pruritus and should be avoided.
Niaspan®	No dose adjustment; caution in patients with renal disease.	Alcohol or hot drinks may increase side effects of flushing and pruritus and should be avoided around the time of ingestion.

Frequency of Liver Function Test Monitoring

Nicotinic Acid	When to perform LFT	Comments
Niacin	Perform LFTs prior to initiating therapy and every 6 to 12 weeks for the 1st year; periodically (about every 6 months) thereafter.	If the LFTs are elevated, perform a second LFT to confirm the abnormality. Notify MD or referring physician if LFTs $\geq$ 2 X ULN.
Niaspan®	Perform LFTs prior to initiating therapy and every 6 to 12 weeks for the 1st year; periodically (about every 6 months) thereafter.	Same as above.

Drug Interactions with Nicotinic Acid

Precipitant drug/food	Object drug	Comments
Nicotinic acid ($\geq$ 1gram/day)	**HMG CoA RIs**	Coadministration increases the risk of myopathy/ rhabdomyolysis. **Do not exceed simvastatin 10 mg, lovastatin 20 mg, or atorvastatin 10 mg daily**
BAS	Niaspan®	Take Niaspan 1 hour before or 4 hours after BAS.
Antihypertensive agents	Niaspan®	Niacin may potentiate the effects of ganglionic blocking agents and vasoactive drugs resulting in postural hypotension.

Bolded drugs should not be co-administered or exceed maximum dose with the drugs in the adjacent column (contraindication/warning)

ATTACHMENT C

Framingham Point Scores
Estimated 10-Year Percentage Risk of Coronary Heart Disease. (W = women, M = men)

AGE	Points (M)	Points (W)
20-34	-9	-7
35-39	-4	-3
40-44	0	0
45-49	3	3
50-54	6	6
55-59	8	8
60-64	10	10
65-69	11	12
70-74	12	14
75-79	13	16

HDL (mg/dL)	Points (M)	Points (W)
≥60	-1	-1
50-59	0	0
40-49	1	1
<40	2	2

SYSTOLIC BLOOD PRESSURE (mmHg)

T = points if untreated UT = points if untreated

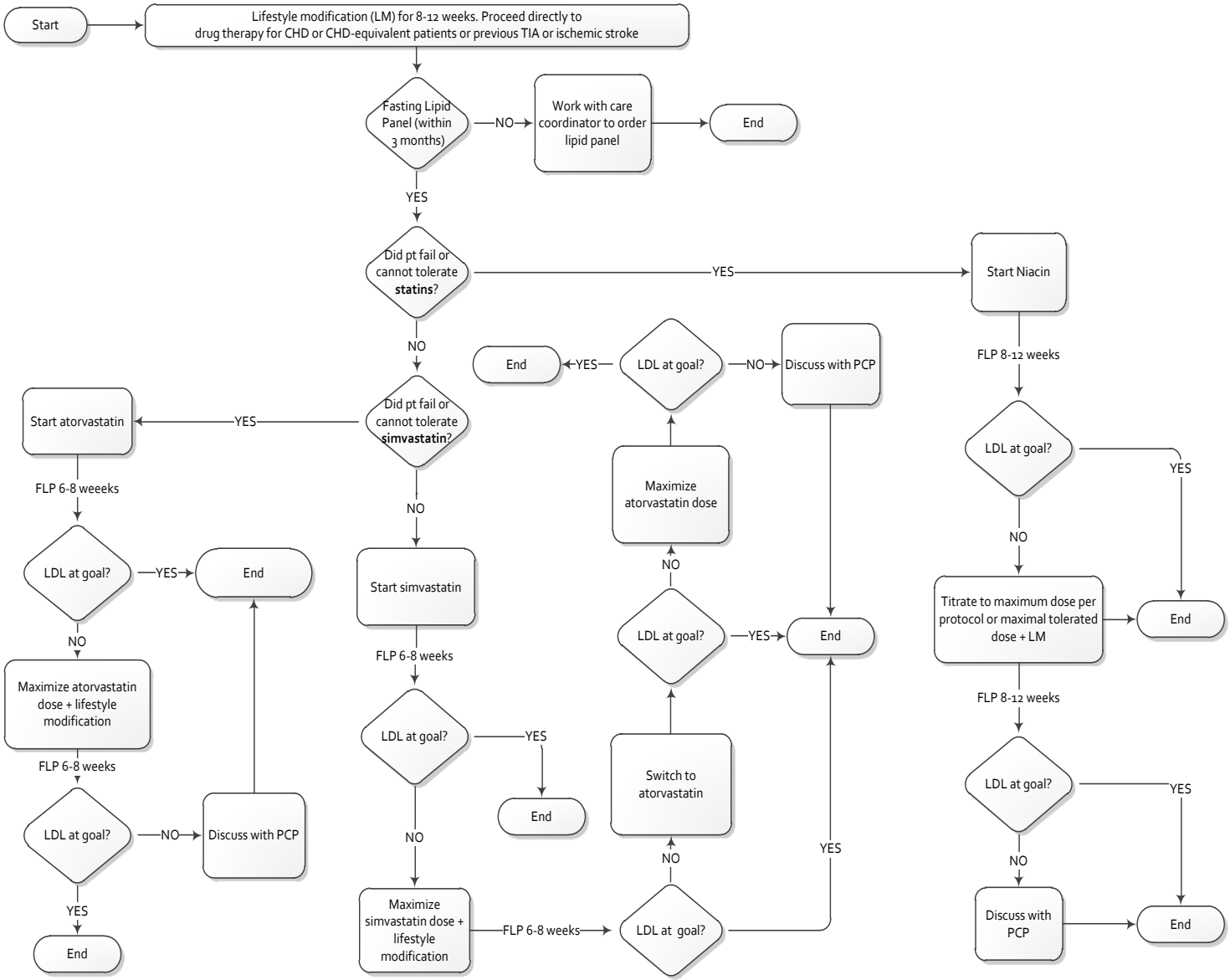
BP	UT (M)	UT (W)	T (M)	T (W)
<120	0	0	0	0
120-129	0	1	1	3
130-139	1	2	2	4
140-159	1	3	2	5
>159	2	4	3	6

POINTS FOR INDICATED AGE GROUPS

Smoking status		20-39	40-49	50-59	60-69	70-79
Nonsmoker (M)		0	0	0	0	0
Smoker (M)		8	5	3	1	1
Nonsmoker (W)		0	0	0	0	0
Smoker (W)		9	7	4	2	1
Total Cholesterol (mg/dL)						
Men	< 160	0	0	0	0	0
	160-199	4	3	2	1	0
	200-239	7	5	3	1	0
	240-279	9	6	4	2	1
	>280	11	8	5	3	1
Women	< 160	0	0	0	0	0
	160-199	4	3	2	1	1
	200-239	8	6	4	2	1
	240-279	11	8	5	3	2
	>280	13	10	7	4	2

ESTIMATED 10-YEAR PERCENTAGE RISK OF CHD

Men		Women	
Total Points	% Risk	Total Points	% Risk
< 0	< 1	< 9	< 1
0	1	9-12	1
0-4	1	13-14	2
5-6	2	15	3
7	3	16	4
8	4	17	5
9	5	18	6
10	6	19	8
11	8	20	11
12	10	21	14
13	12	22	17
14	16	23	22
15	20	24	27
16	25	≥25	≥30
≥17	>30		


Start
Lifestyle modification (LM) for 8-12 weeks. Proceed directly to drug therapy for CHD or CHD-equivalent patients or previous TIA or ischemic stroke
Fasting Lipid Panel (within 3 months)
NO
Work with care coordinator to order lipid panel
End
YES
Did pt fail or cannot tolerate statins?
YES
Start Niacin
NO
FLP 8-12 weeks
LDL at goal?
YES
End
NO
Titrate to maximum dose per protocol or maximal tolerated dose + LM
End
FLP 8-12 weeks
LDL at goal?
YES
End
NO
Discuss with PCP
End
Did pt fail or cannot tolerate simvastatin?
YES
Start atorvastatin
FLP 6-8 weeeks
LDL at goal?
YES
End
NO
Maximize atorvastatin dose + lifestyle modification
FLP 6-8 weeks
LDL at goal?
NO
Discuss with PCP
YES
End
NO
Start simvastatin
FLP 6-8 weeks
LDL at goal?
YES
End
NO
Maximize simvastatin dose + lifestyle modification
FLP 6-8 weeks
LDL at goal?
YES
NO
Switch to atorvastatin
NO
LDL at goal?
YES
End
NO
Maximize atorvastatin dose
NO
LDL at goal?
YES
End
NO
Discuss with PCP
YES