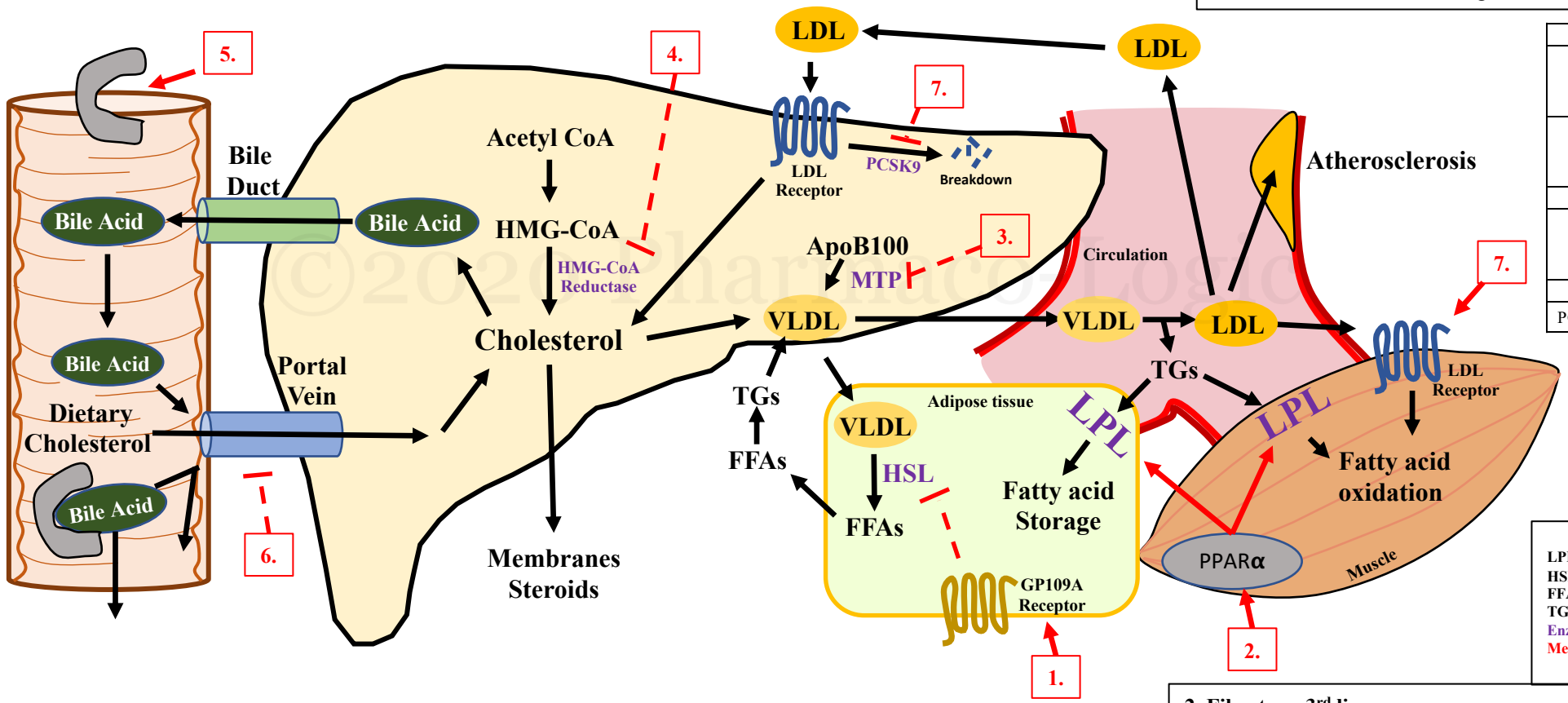
5. Bile acid binding resins - 4th line
MOA: Bind to bile acid and prevent absorption → ↓LDL
Cholestyramine
Cholestepol
Use: Hyperlipidemia
SE: GI bloating, greasy stools, changes in taste, ↑TGs, Gall stones.
DDI: Reduces absorption of lipophilic drugs: Thiazides, digoxin, warfarin, iron, propranolol, statins**
CI: intestinal inflammation, diverticulitis

4. Statins – 1st line
MOA: 1º Inhibition of HMGCoA reductase → ↑LDL Receptor → ↓LDL
2º ↑endothelial cell function (NO) → ↓platelet aggregation, anti-inflammatory/antioxidant → prevent formation of foam cells
Rosuvastatin, Atorvastatin - most potent
Simvastatin, Lovastatin – prodrugs, take in evening
Use: Hyperlipidemia, CAD, MI, ↓CV/stroke mortality
SE: Rhabdomyolysis (↑CK), myositis (isoprenoids), elevated liver enzymes, reduced insulin release (CCBs)
CI: Warfarin, pregnancy, amiodarone (simvastatin), CYP3A4 drugs (lovastatin, simvastatin, atorvastatin) CYP2C9 drugs (rosuvastatin)

3. Lomitapide
MOA: inhibit MTP → Prevent ApoB incorpation into VLDL → ↓LDL
Use: Familial hypercholesterolemia
PK: High albumin binding, extensive hepatic metabolism
SE: Abdominal discomfort, steatosis, elevated transaminases

7. PCSK9 inhibitors
MOA: Prevent breakdown of LDL receptors → LDL upregulation. → increased use
Evolocumab, Alirocumab – monoclonal antibodies
Use: Familial hypercholesterolemia
SE: Neural, delirium, neurocognitive effects



	Lipid effect
Statins	↓↓ **LDL** ↓ TG ↑ HDL
Fibrates	↓ LDL ↓↓ **TG** ↑ HDL
Bile acid resins	↓ LDL
Niacin	↓ LDL ↓ TG ↑↑ **HDL**
Ezetimibe	↓ LDL
PCSK9 inhibitors	↓ LDL

KEY
LPL – lipoprotein lipase
HSL – hormone sensitive lipase
FFAs – Free fatty acids
TGs – Triglycerides
Enzymes
Mechanism of action

6. Ezetimibe (prodrug) – 2nd line
MOA: inhibition of NPC1L1 → ↓cholesterol absorption → ↓LDL
Use: Hyperlipidemia – usually combined with statin*
SE: reversible liver damage (liver enzymes) – worse with statins, diarrhea

1. Nicotinic acid
MOA: Activate GP109A receptors → ↓HSL → ↓TGs→ ↓VLDL, ↑HDL (decreased catabolism)
Use: Hyperlipidemia
SE: Vasodilation (give NSAIDs), hyperglycemia, hyperuricemia, hypotension, hepatotoxicity
CI: Pregnancy, peptic ulcer, liver damage

2. Fibrates – 3rd line
MOA: Activate PPARα receptors → Upregulate LPL → ↓TGs
Gemfibrozil
Fenofibrate
Use: Hypertriglyceridemia
SE: ↓platelet aggregation, ↓Fibrinogen levels, ↑t-PA production, gall stone formation
CI: Warfarin (PD), Statins (myositis), kidney/liver dysfunction