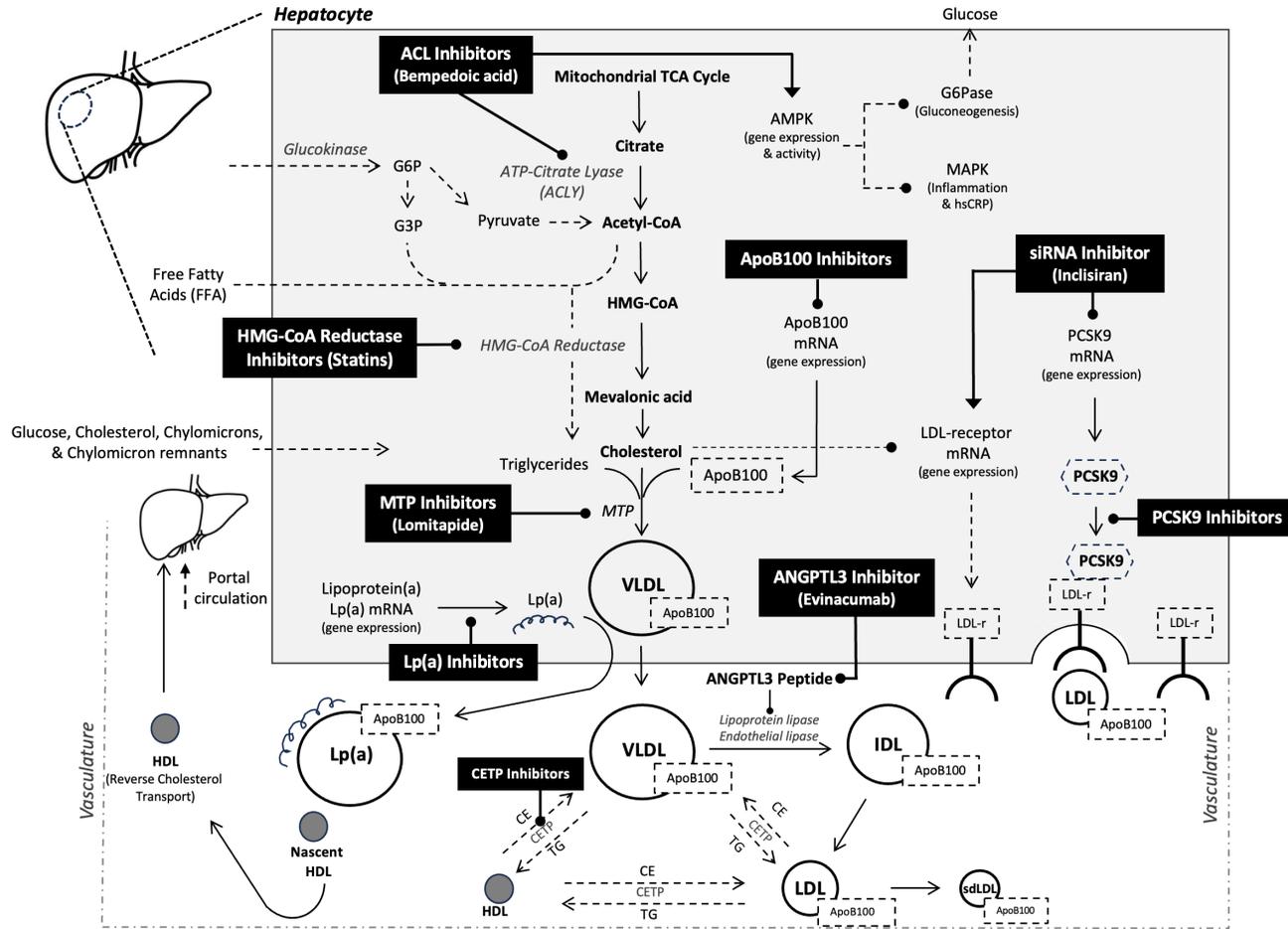


ANTILIPEMIC AGENTS BASIC SUMMARY

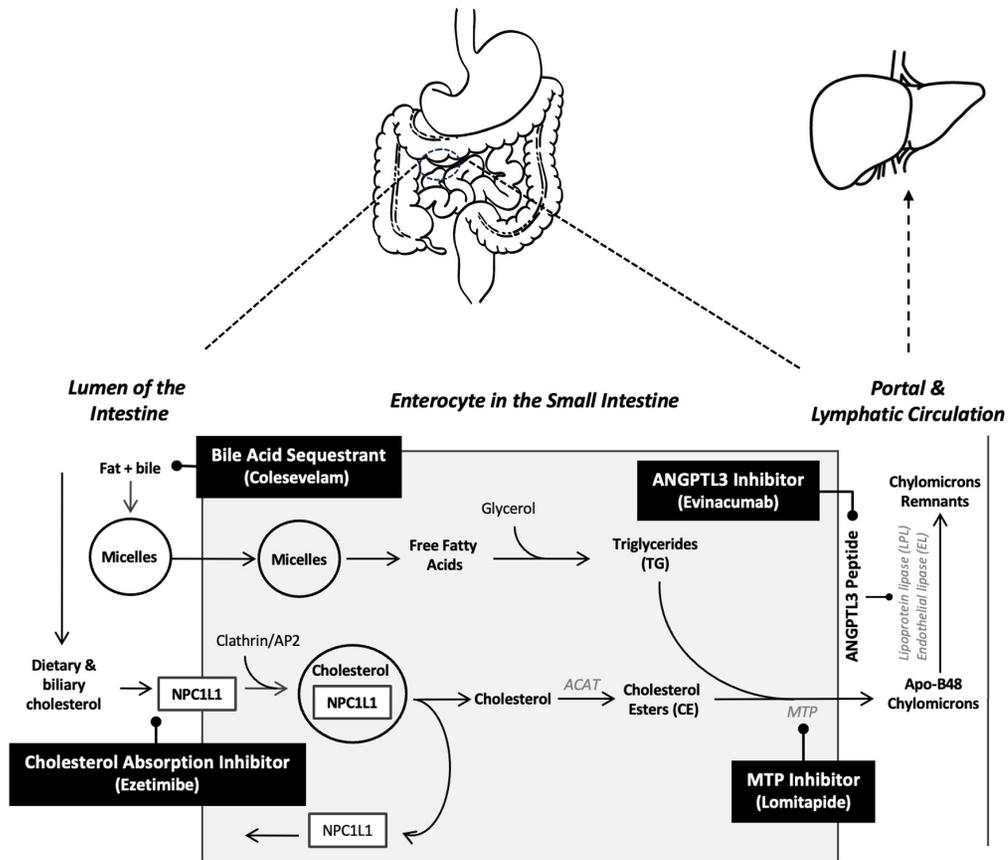
Drug Class	Example	Mechanism of Action	Target Lipid Effect	Other Lipid Effects
LDL Target – Statin				
HMG-CoA Reductase Inhibitors	<ul style="list-style-type: none"> ▪ Atorvastatin ▪ Rosuvastatin 	<ul style="list-style-type: none"> ▪ Inhibits the enzyme HMG-CoA reductase, which reduces hepatic cholesterol production ▪ Upregulates LDL receptors to extract LDL 	↓ LDL ≥ 50% (High-Intensity) ↓ LDL 30-50% (Mod-Intensity)	↓ TG ~ 20% ↑ HDL ~ 10%
LDL Target – Nonstatin				
ACL Inhibitors	<ul style="list-style-type: none"> ▪ Bempedoic acid 	<ul style="list-style-type: none"> ▪ Inhibits ATP-citrate lyase (ACL), which reduces hepatic cholesterol production ▪ Upregulates LDL receptors to extract LDL 	↓ LDL ~ 15% to 30% (> effects when used alone)	TG: Neutral ↓ HDL ~ 5%
ANGPTL3 Inhibitors	<ul style="list-style-type: none"> ▪ Evinacumab 	<ul style="list-style-type: none"> ▪ Inhibits angiotensin-like 3 peptide (ANGPTL3), which then increases lipoprotein lipase (LPL) & endothelial lipase (EL) activity, resulting in a reduction in TG, LDL, and HDL 	↓ LDL ~ 50% (added to existing max therapy)	↓ TG ~ 50% ↓ HDL ~ 30%
Bile Acid Sequestrants	<ul style="list-style-type: none"> ▪ Colesevelam 	<ul style="list-style-type: none"> ▪ Binds to bile salts to prevent their enterohepatic reabsorption/recycling 	↓ LDL ~ 15 to 30%	↑ TG ~ 10%
Cholesterol Absorption Inhibitors	<ul style="list-style-type: none"> ▪ Ezetimibe 	<ul style="list-style-type: none"> ▪ Inhibits intestinal cholesterol absorption at Niemann-Pick C1-Like 1 (NPC1L1) peptide 	↓ LDL ~ 20%	↓ TG ~ 10%, ↑ HDL ~ 5%
PCSK9 Inhibitors	<ul style="list-style-type: none"> ▪ Alirocumab ▪ Evolocumab 	<ul style="list-style-type: none"> ▪ Inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9) binding on hepatic LDL receptors, allowing for the increased hepatic clearance of circulating LDL 	↓ LDL ~ 55%	↓ ApoB100 ~ 50%
Small Interfering RNA	<ul style="list-style-type: none"> ▪ Inclisiran 	<ul style="list-style-type: none"> ▪ Decreases PCSK9-mediated degradation of LDL receptors while also increasing LDL-r gene expression to increase removal of circulating LDL 	↓ LDL ~ 50% (added to existing max therapy)	↓ TG ~ 15% ↑ HDL ~ 8%
Triglyceride (TG) Target				
Fibrates	<ul style="list-style-type: none"> ▪ Fenofibrate ▪ Gemfibrozil 	<ul style="list-style-type: none"> ▪ Stimulates PPAR-α transcription, which reduces the production of VLDL while also increasing the catabolism of VLDL in circulation (the result is a decrease in TG concentrations) 	↓ TG ~ 20% to 50%	↓ LDL ~ 5% to 20% ↑ HDL ~ 20%
MTP Inhibitors	<ul style="list-style-type: none"> ▪ Lomitapide 	<ul style="list-style-type: none"> ▪ Inhibits microsomal triglyceride transfer protein (MTP) in hepatocytes and enterocytes to reduce the formation of TG and ApoB-containing particles to reduce VLDL & LDL 	↓ LDL ~ 50% ↓ TG 35-65%	↓ ApoB100 ~ 50%
Omega-3 Fatty Acids	<ul style="list-style-type: none"> ▪ Icosapent ethyl 	<ul style="list-style-type: none"> ▪ Reduces the synthesis of TG-rich VLDL by inhibiting diacyl-glycerol acetyl-transferase (DGAT) ▪ Increases degradation of ApoB100 and fatty acid oxidation by the liver 	↓ TG ~ 40%	LDL ~ +/- ↓ ApoB100 ~ 10%
Miscellaneous Target				
Niacin	<ul style="list-style-type: none"> ▪ Niacin 	<ul style="list-style-type: none"> ▪ Reduces the peripheral mobilization of free fatty acids for the liver to use and also reduces the hepatic synthesis of TG-rich VLDL (exact mechanisms unknown) 	↓ TG ~ 40% ↑ HDL up to ~ 30%	↓ LDL ~ 5% to 20% ↓ Lp(a) ~ 25%

Note: The reported changes in lipids represent the editor's best effort to summarize the main clinical effect based on data from various reputable sources of information and reported clinical trial data. The numbers are not meant to be exact for all patients. Small variations in or use of exact numbers are not the intended goal for providing general context related to the use of these treatments in a diverse population of people with many confounders likely present.

CHOLESTEROL & LIPOPROTEIN METABOLISM PHARMACOTHERAPEUTIC INTERVENTIONS



DIETARY CHOLESTEROL ABSORPTION PHARMACOTHERAPEUTIC INTERVENTIONS



STATIN DOSE EQUIVALENCE BY LDL LOWERING INTENSITY

Statin	Low-Intensity		Moderate-Intensity		High-Intensity	
LDL-C Lowering	< 30%		30-50%		> 50%	
Rosuvastatin			5 mg	10 mg	20 mg	40 mg
Atorvastatin			10 mg	20 mg	40 mg	80 mg
Pitavastatin		1 mg	2 mg	4 mg		
Simvastatin	5 mg	10 mg	20 mg	40 mg		
Pravastatin	10 mg	20 mg	40 mg	80 mg		
Lovastatin	10 mg	20 mg	40 mg			
Fluvastatin	20 mg	40 mg	80 mg			

HMG-COA REDUCTASE INHIBITORS (STATINS)

PHARMACOKINETIC & PHARMACODYNAMIC DIFFERENCES

Characteristic	MODERATE-INTENSITY (30% to 50%)					HIGH-INTENSITY (≥ 50%)	
	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Simvastatin	Atorvastatin	Rosuvastatin
Max Dose (mg)/d	80 mg	80 mg	4 mg	80 mg	40 mg	80 mg	40 mg
Max % LDL Reduction	~ 35%	~ 40%	~ 45%	~ 35%	~ 40%	~ 60%	~ 60% +
Reduction in TG's	~ 20%	~ 20%	~ 20%	~ 20%	~ 20%	~ 35%	~ 25%
Increase in HDL	~ 10%	~ 10%	~ 10%	~ 10%	~ 10%	~ 10%	~ 10%
Plasma Half-life	3 hrs	2 hrs	12 hrs	1-2 hrs	1-2 hrs	14 hrs	19 hrs
Penetration of CNS	No	Yes	Yes	No	Yes	No	No
Renal Excretion	5%	10%	15%	20%	13%	2%	10%
Pathway of Elimination	Phase I Influx/Efflux Transporters	Phase I & II Influx/Efflux Transporters	Phase I & II Influx/Efflux Transporters	Phase II Influx/Efflux Transporters	Phase I & II Influx/Efflux Transporters	Phase I & II Influx/Efflux Transporters	Phase I & II Influx/Efflux Transporters

Note: The reported changes in lipids represent the editor's best effort to summarize the clinical effect based on data from various reputable sources of information and reported clinical trial data. The goal of this table is to provide general context related to the use of these treatments in a diverse population with likely confounders, not to document small variations or exact numbers.

HMG-COA REDUCTASE INHIBITORS (STATINS) PATHWAYS OF ELIMINATION

	MODERATE-INTENSITY STATINS (30% to 50%)					HIGH-INTENSITY STATINS (≥ 50%)	
Pathway	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Simvastatin	Atorvastatin	Rosuvastatin
Phase I Metabolism (Oxidation/Reduction)	CYP2C9 (75%) CYP3A4 (20%) CYP2C8 (5%)	CYP3A4	CYP2C8/9 (minor)	-	CYP3A4	CYP3A4	CYP2C9 (10%)
Phase II Metabolism (Conjugation)		UGT1A1 UGT1A3	UGT1A3 UGT2B7	UGT1A1 UGT1A3	UGT1A1 UGT1A3	UGT1A1 UGT1A3 UGT2B7	UGT1A1 UGT1A3
Influx Cell Membrane Transporters	OATP1B1 OATP2B1	OTAP1B1	OATP1B1 OATP1B3	OTAP1B1 OATP1B3 OATP2B1	OATP1B1	OATP1B1 OTAP1B3	OAT1B1/3 NTCP OAT2B1
Efflux Cell Membrane Transporters	BCRP P-gp	BCRP P-gp	BCRP	BCRP P-gp	BCRP P-gp	BCRP P-gp	BCRP P-gp

HMG-COA REDUCTASE INHIBITORS (STATINS) RISK OF LIVER INJURY

Common Clinical Questions	Answer
Are elevations in liver enzymes associated with statins?	Yes
Are statin-associated elevations in liver enzymes indicative of damage or dysfunction?	No
Do statins increase the incidence of liver failure, liver transplants, or death in general population?	Yes
Should liver enzymes be monitored in patients getting long-term statins?	No
Are statins “contraindicated” in chronic liver disease or compensated cirrhosis or MSALD (previously referred to as NAFLD) or liver transplantation or autoimmune hepatitis?	No
Any safety concerns since FDA changed recommendations to say no liver tests needed after starting statin?	No
Do statins need dose adjustments in HIV or HBV or HCV treatment?	Yes

Take Home Point: The risk of serious hepatotoxicity is ~0.001%. However, the risk is dose- or concentration-dependent.

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HMG-COA REDUCTASE INHIBITORS (STATINS)

DEFINITIONS FOR MUSCLE RELATED PROBLEMS

Muscle ADE	Definition
SAMS	Statin-Associated Muscle Symptoms Muscle symptoms reported during statin therapy but not necessarily caused by the statin
Myalgia	Unexplained muscle discomfort described often as “flu-like” + normal CK: soreness, aches, stiffness, cramps
Myopathy	Muscle pain or weakness with elevations in CK > 10 times the ULN
Rhabdomyolysis	Severe form of myopathy but associated with myonecrosis (CK > 40 x ULN)+ myoglobinuria or ARF/AKI

Take Home Point: The risk of serious statin-induced muscle injury (including rhabdomyolysis is < 0.1%) and appears to be dose- or concentration-dependent.

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HMG-COA REDUCTASE INHIBITORS (STATINS) RISK OF MUSCLE INJURY

Risk for Muscle Injury	Answer
Can statin-associated myalgia be reliably differentiated from placebo?	Yes
Is there a reliable index score for statin-associated myalgia?	Yes
Are statin-associated muscle complaints altered by acute or chronic activity?	Yes
Can patient's intolerant to one statin switch to another?	Yes
Is the risk of muscle injury/pain related to the dose or concentration of statins?	Yes

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HMG-COA REDUCTASE INHIBITORS (STATINS) RISK OF DIABETES

Risk for Diabetes Mellitus	Answer
What is magnitude of risk for Type 2 DM?	<ul style="list-style-type: none"> ▪ A meta-analysis suggested the risk is ~10% - 20% with OR of 1.09 (95% CI, 1.02 – 1.17) and I² = 11.2%. <ul style="list-style-type: none"> ▪ NNT over 4 years to cause 1 excess case was 255 ▪ Overall, the risk is modest and is estimated to be ~0.2% per year (depending on the risk of DM in the population assessed), but the risk does not override the CV benefit.
What is the impact of statins on glycemic control in diabetics?	<ul style="list-style-type: none"> ▪ Available data suggests a mean increase of ~0.3% or less. ▪ QOE: Low to draw a conclusion
Are there any patients who should not be started on statins due to risk of DM?	<ul style="list-style-type: none"> ▪ Due to unknown clinical importance of this risk, no changes to current recommended practice. ▪ SOR: expert opinion; QOE: Moderate
What is the mechanism for statin associated DM?	<ul style="list-style-type: none"> ▪ Unknown ▪ SOR: Expert opinion; QOE: Low
Should providers measure glycemic parameters before and during statin use?	<ul style="list-style-type: none"> ▪ The NLA endorses the ADA recommendations but advises not to delay statin therapy over it. ▪ SOR: Expert opinion; QOE: Moderate
Are there any recommendations when starting statins in patients without DM?	<ul style="list-style-type: none"> ▪ Assess for CV risk factors. ▪ Consider the measurement of A1C. ▪ Emphasize the importance of diet, weight, and physical activity. ▪ If DM develops while on a statin, emphasize weight loss, use of hypoglycemic medications (if indicated) , and provide behavioral counseling.

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HMG-COA REDUCTASE INHIBITORS (STATINS) COGNITIVE CHANGES

Cognitive Effects	Answer	SOR	QOE
Should a baseline cognitive assessment be done prior to starting?	NO	Expert opinion	Low
Are statins associated with negative effects on cognition?	NO	Strong	Low to Moderate
What should a provider do if a patient reports cognitive symptoms?	Cognitive testing & rule out other factors	Expert opinion	Low

Consider other drugs: Anticholinergic medications, 1st generation antihistamines, benzodiazepines, opioids

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LANDMARK PRIMARY PREVENTION TRIALS CORONARY HEART DISEASE

Study	Year	n	Drug	Results
LRC-CPPT	1984	1,906	Cholestyramine	CHD incidence ↓ 18.9%
HHS	1987	2,051	Gemfibrozil	CHD incidence ↓ 34%
WOSCOPS	1995	3,302	Pravastatin	Death from all CVD ↓ 32%; non-fatal MI ↓ 31%
AFCAPS/TexCAPS	1998	3,304	Lovastatin	First acute event ↓ 37%
PROSPER	2002	3,239 / 5804	Pravastatin	HR, 0.94 (0.77-1.15; p=0.19). Combined CVD no different
ASCOT-LLA	2003	10,305	Atorvastatin	Stopped early. Nonfatal MI & fatal CHD ↓ 36% and stroke ↓ 27%.
Juniper	2008	17,802	Rosuvastatin	hsCRP > 2 mg/dL; 20% risk reduction in overall mortality

LRC-CPPT = Lipid Research Clinics Coronary Primary Prevention Trial; HHS = Helsinki Heart Study; WOSCOPS = West of Scotland Coronary Prevention Study; AFCAPS/TexCAPS = Air Force/Texas Coronary Atherosclerosis Prevention Study; PROSPER = PROspective Study of Pravastatin in the Elderly at Risk; ASCOT-LLA = Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm

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LANDMARK SECONDARY PREVENTION TRIALS CORONARY HEART DISEASE

Study	Year	n	Drug	Results
4S	1994	2,221	Simvastatin	CHD mortality ↓ 42%
CARE	1996	2,081	Pravastatin	CHD death or nonfatal MI ↓ 24%
LIPID	1998	4,512	Pravastatin	CHD death ↓ 24%
MIRACL	2001	1,538	Atorvastatin	Recurrent events ↓ 16%; stroke ↓ 50%
PROSPER	2002	2,565	Pravastatin	Elderly pts* (70-82 yrs); Combined CVD ↓ by 22%
HPS	2002	20,536	Simvastatin	All cause mortality ↓ by 13%; Coronary death rate ↓ 18%
PROVE IT	2004	4,162	Atorvastatin vs Pravastatin	Composite CVD ↓ 16%

4S = Scandinavian Simvastatin Survival Study; CARE = Cholesterol and Recurrent Events Trial; LIPID = Long-term Intervention with Pravastatin in Ischemic Disease Study; MIRACL = Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering Study; PROSPER = PROspective Study of Pravastatin in Elderly at Risk; HPS = Health Protection Study; PROVE IT TIMI 22 = Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in MI 22 Study.

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STATIN & PROTEASE INHIBITOR DRUG INTERACTIONS

Characteristic	Lovastatin	Pravastatin	Simvastatin	Atorvastatin	Fluvastatin	Rosuvastatin
Protease Inhibitors						
Atazanavir/RTV	avoid	-	avoid	low dose	-	AUC ↑213% Cmax ↑600%
Fosamprenavir	avoid	-	avoid	AUC ↑150%	-	AUC ↑8%
Indinavir	avoid	-	avoid	low dose	-	-
Lopinavir / RTV	avoid	AUC ↑33%	avoid	AUC ↑ 5.8x	-	AUC ↑ 2-5 x
Nelfinavir	avoid	-	AUC ↑505%	AUC ↑ 74%	-	-
Saquinavir /RTV	avoid	level ↓50%	AUC↑ 3059%	Level ↑450%	-	-
Tipranavir / RTV	avoid	-	avoid	AUC ↑ 9x	-	-
Darunavir / RTV	avoid	AUC ↑ 5-fold	avoid	Low dose	-	-

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**MONOCLONAL ANTIBODY (mAb)
SUBSTEM B NAMING & TYPE - WORLD HEALTH ORGANIZATION**

Name Ending	Type of Antibody
-umab	100% human antibody
-zumab	Humanized (only 5-10% mouse make up the complementarity-determining-regions (CDR))
-ximab	Chimeric (67% human Fc or constant regions + 33% mouse make up the variable regions)
-omab	Murine (100% mouse)
-xizumab	Combined humanized & chimeric chains
-axomab	Rat/Mouse Chimer
-emab	Hamster
-amab	Rat
-imab	Primate



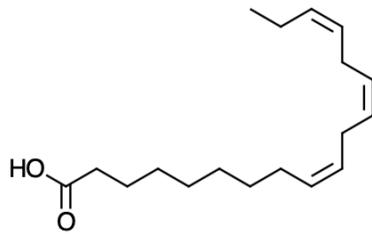
MONOCLONAL ANTIBODY (mAb) SUBSTEM A NAMING & TARGET - WORLD HEALTH ORGANIZATION

Name Ending	Target Class	Example
-b(a)--mab	Bacterial	-bixumab; -bumab
-c(i)--mab	Cardiovascular	-cixumab; -cumab
-f(u)--mab	Fungal	-fuzumab; -fumab
-k(i)--mab	Interleukin	-kiximab; -kumab
-l(i)--mab	Immunomodulating	-liximab; -lumab; -lixizumab
-n(e)--mab	Neural	-nezumab; -numab
-s(o)--mab	Bone	-somab; -sumab
-tox(a)--mab	Toxin	-toxazumab; -toxumab
-t(u)--mab	Tumor	-tuzumab; -tumab; -tomab
-v(i)--mab	Viral	-vizumab; -vumab

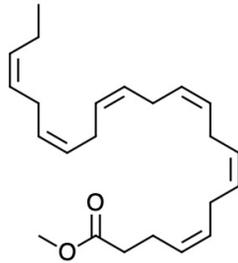
Note: If Substem B starts with an "x" or "z", a 2nd vowel (noted in parenthesis) is added to avoid problems with pronunciation.

OMEGA FATTY ACIDS

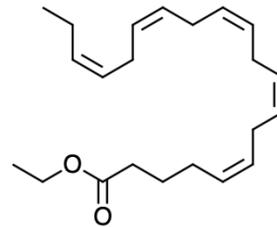
OMEGA-3 FATTY ACIDS



ALA
(alpha-linolenic acid)
20:3(ω -3)

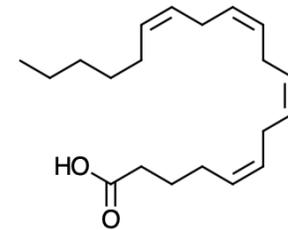


DHA
(docosahexaenoic acid)
20:6(ω -3)



EPA
(eicosapentaenoic acid)
20:5(ω -3)

OMEGA-6 FATTY ACID



AA
(arachidonic acid)
20:4(ω -6)

COMPARISON OF OMEGA-3 FATTY ACIDS

PUFA	Brand Name	Indications	Fatty Acid Content	Notes
Omega-3 Ethyl Esters	Lovaza	Hypertriglyceridemia	<ul style="list-style-type: none"> ▪ EPA = 465 mg ▪ DHA = 375 mg 	<ul style="list-style-type: none"> ▪ Take without regard to meals. ▪ Causes more GI effects (dysgeusia, dyspepsia, “fishy burps”) ▪ Refrigerate the capsules to reduce “fishy” burps.
Icosapent Ethyl	Vascepa	Hypertriglyceridemia CVD risk reduction with elevated TG	<ul style="list-style-type: none"> ▪ EPA 960 mg 	<ul style="list-style-type: none"> ▪ Take with food (given this way during clinical trials). ▪ LDL elevations may be reduced since DHA is absent.

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