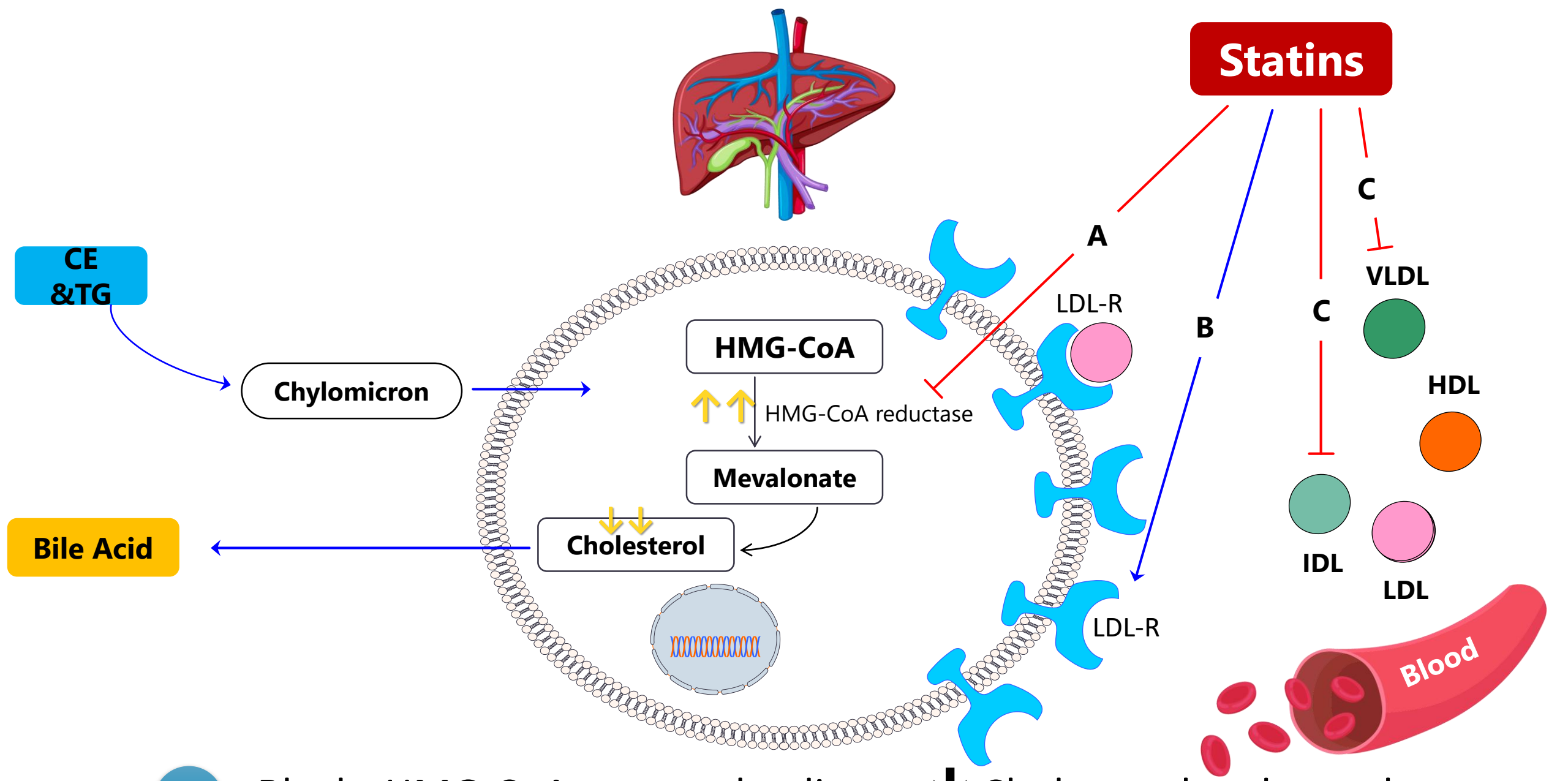
WE GUARD

Web-based Education | Guidelines Updates, Advances & Researches in Dyslipidemia

Pharmacological Management of Dyslipidemia

Z5-7297 Expiration Date: 16/08/2025

STATINS



A Blocks HMG-CoA enzyme leading to ↓ Cholesterol and mevalonate production and concentrations.

All statins possess very low systemic bioavailability due to an extensive first-pass effect.

Statins differ mainly in the degree of metabolism and the number of active and inactive metabolites.

All statins have active metabolites so that their activity depends also on the profile of both parent compound and active metabolites.

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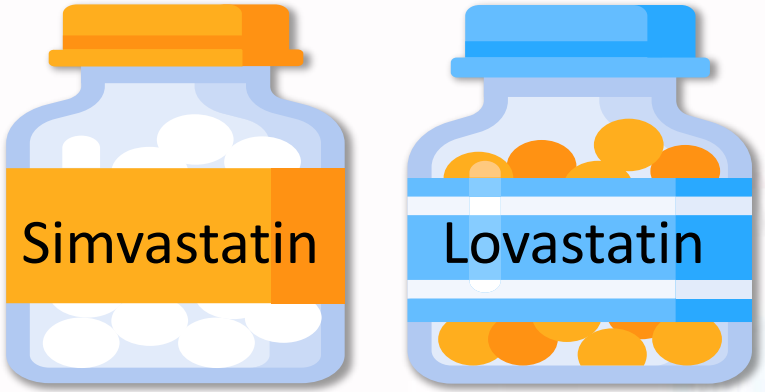
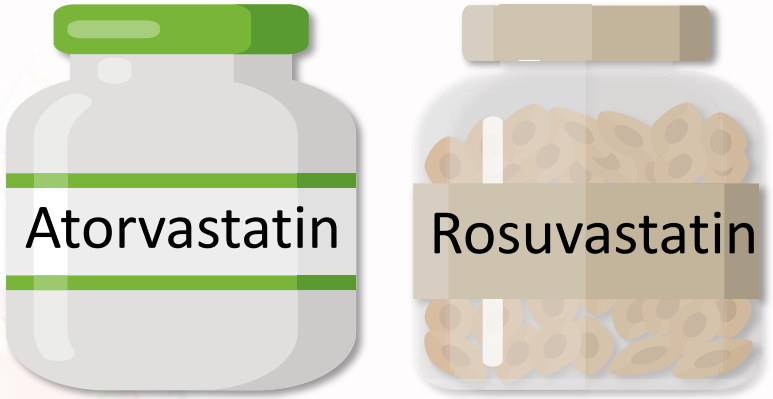


Unlike most statins, are administered as inactive lactone **prodrugs**.



Possess the longest terminal half-life (**11–20 h**).

Has the lowest protein-binding (around **50%**) when compared to other statins (**>90%**)

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In Homozygous Familial Hypercholesterolemic Patients

Do not lower LDL levels

Are effective

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Dose*

NAME : AGE :

ADDRESS: DATE :

℞

Any of the following:

Atorvastatin 10-20 mg

Atorvastatin 40-80 mg

Rosuvastatin 20-40 mg

Lovastatin 40 mg

Fluvastatin XL 80 mg

Fluvastatin 40 mg BID

Pitavastatin 2-4 mg

SIGNATURE

☐ LABEL

REFILL 1 2 3 4 5 PRN NR

3. High Intensity Statin

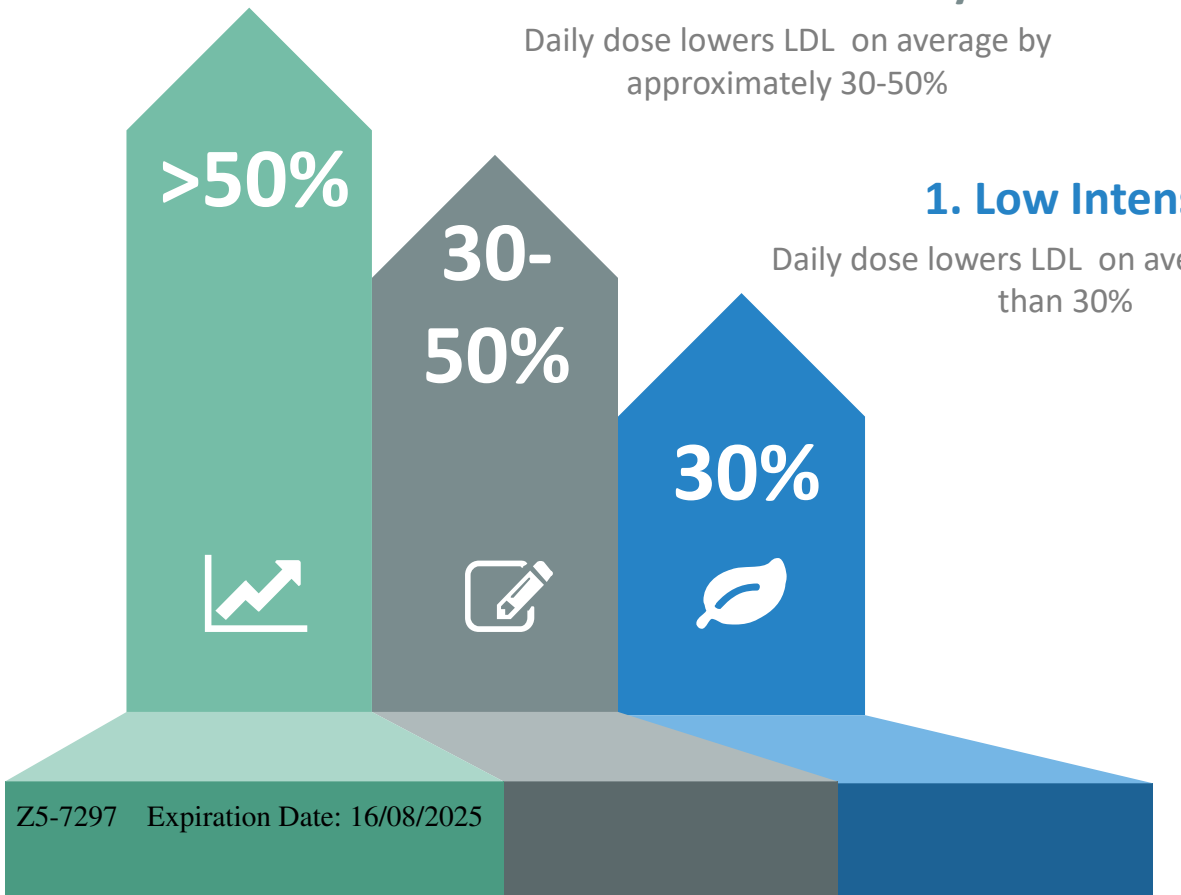
Daily dose lowers LDL on average by more than 50%

2. Moderate Intensity Statin

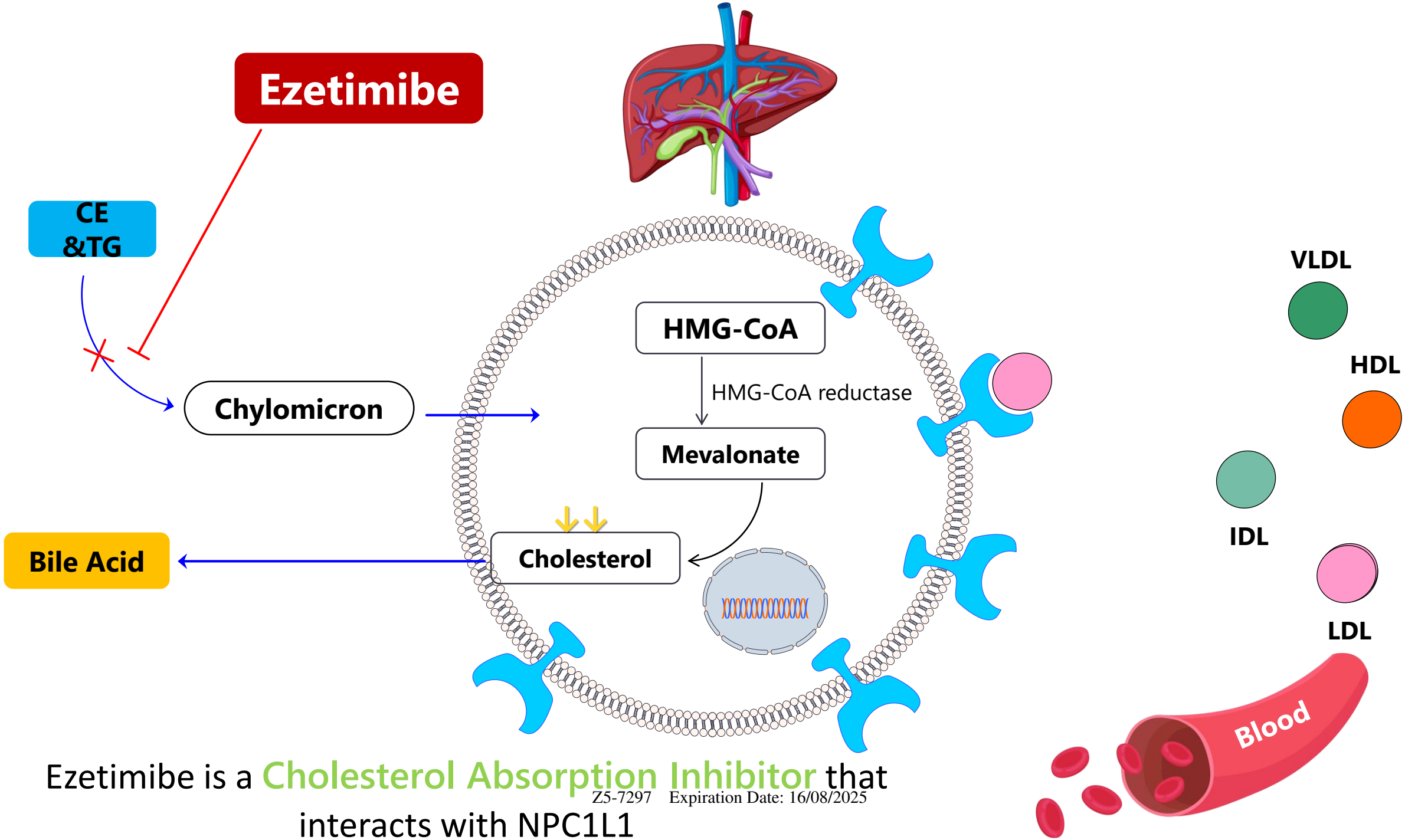
Daily dose lowers LDL on average by approximately 30-50%

1. Low Intensity Statin

Daily dose lowers LDL on average by less than 30%



Cholesterol absorption inhibitors



Ezetimibe is a Cholesterol Absorption Inhibitor that interacts with NPC1L1

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Dose and Effect on lipids

↓ 18.5%

LDL

↑3%

HDL

This do[illegible] duc[illegible]L-C in hy[illegible] l[illegible] atients b[illegible]

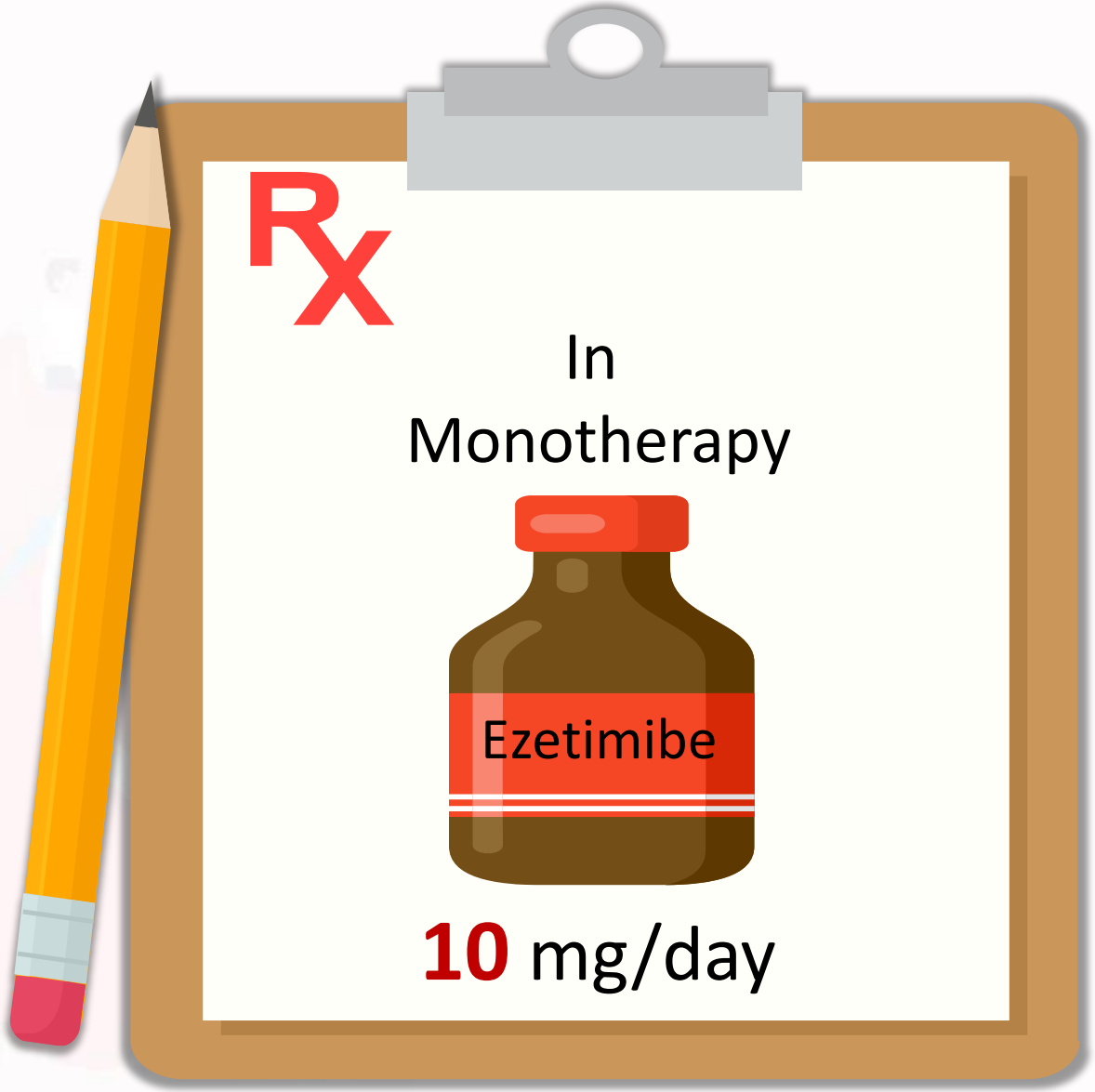
>2700

↓13%

Total Cholesterol

↓ 8%

TG



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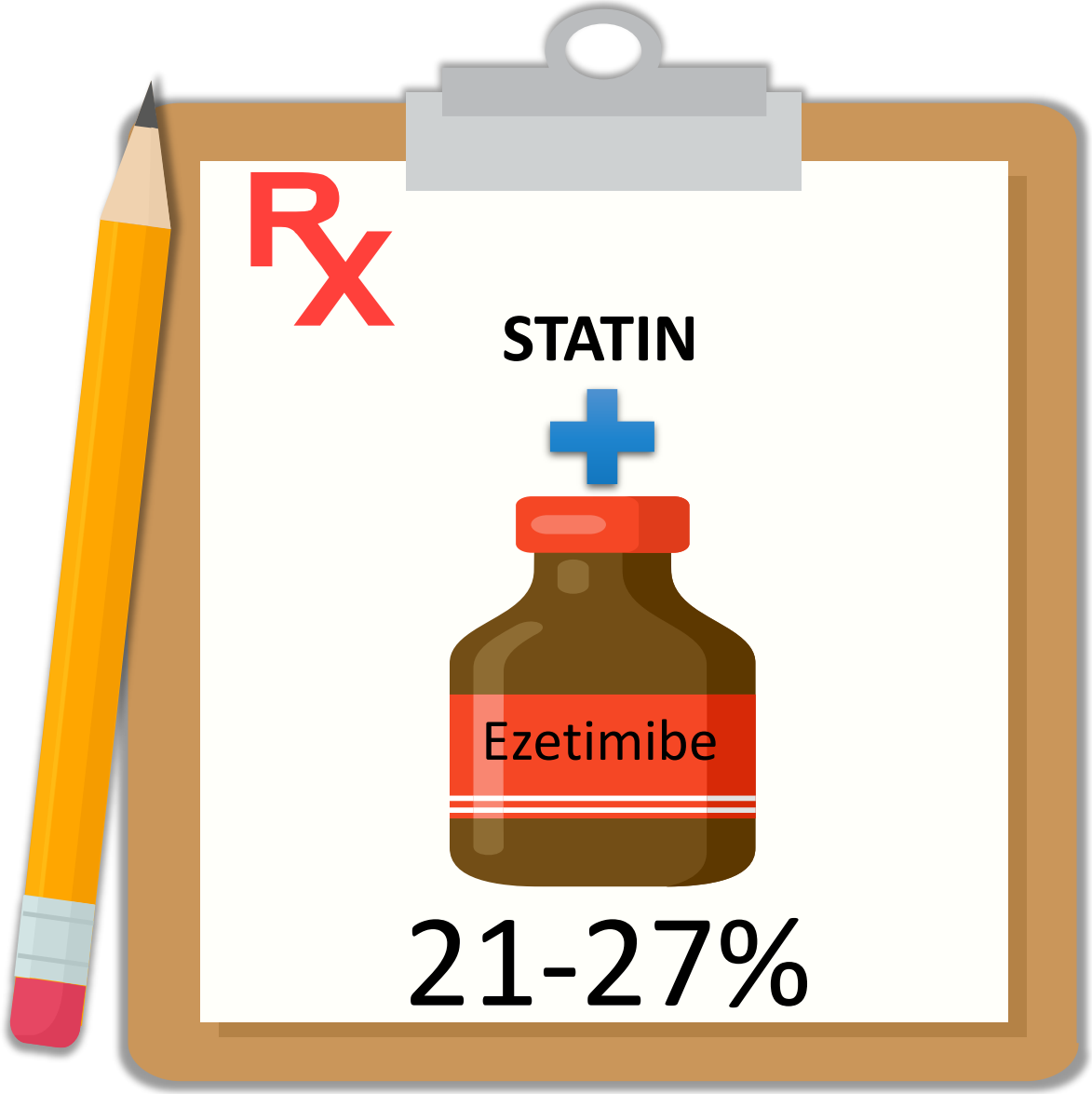
Dose and Effects on lipids

⬇⬇ in LDL-C by 15% compared with the same statins and doses in monotherapy or doubling of the statin dose



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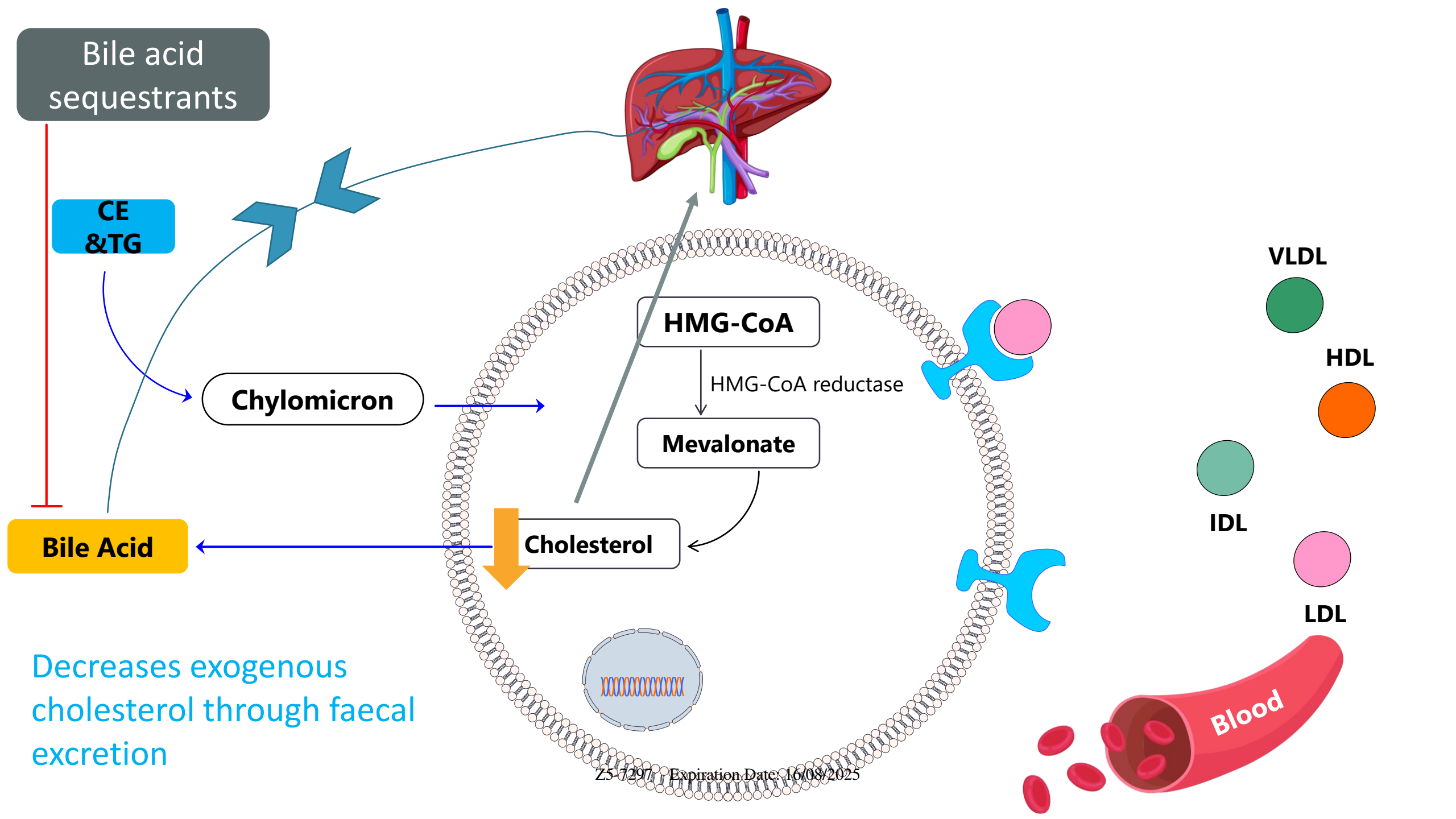
Bile acid sequestrants



Decreases exogenous cholesterol through faecal excretion

Dose and Effects on lipids

A reduction in LDL-C of 18-25% has been observed.
No major effect on HDL-C has been reported, while TGs may increase in some predisposed patients.

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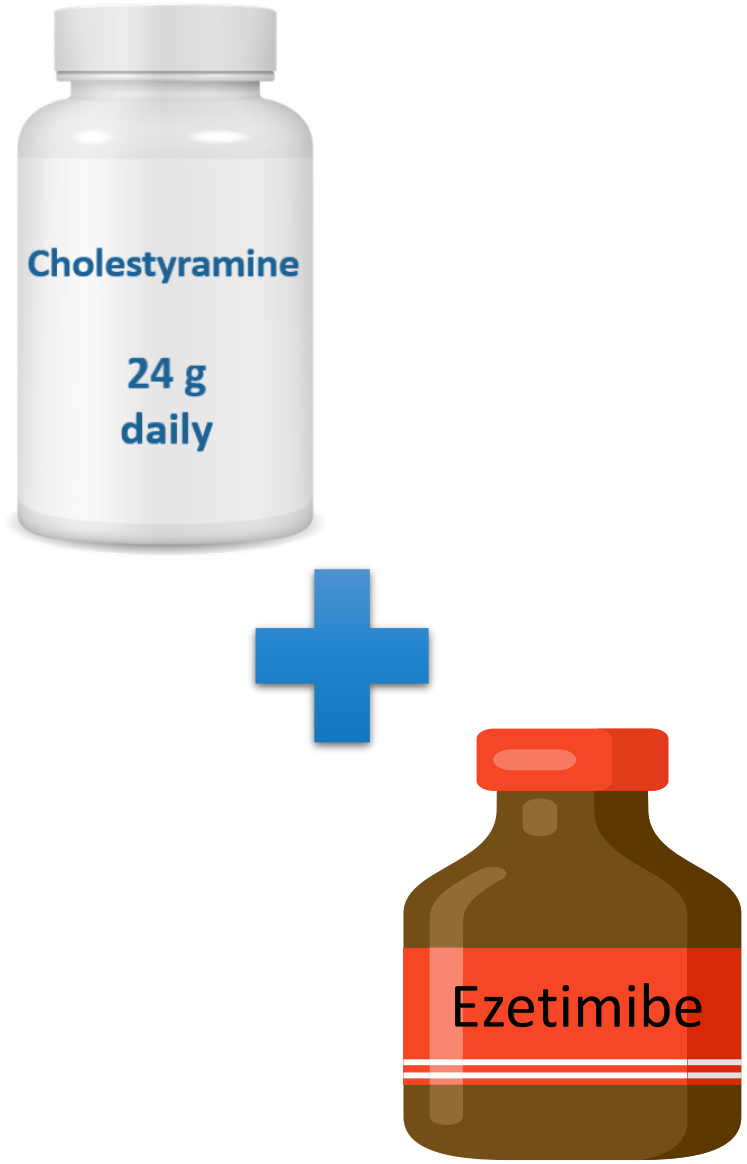

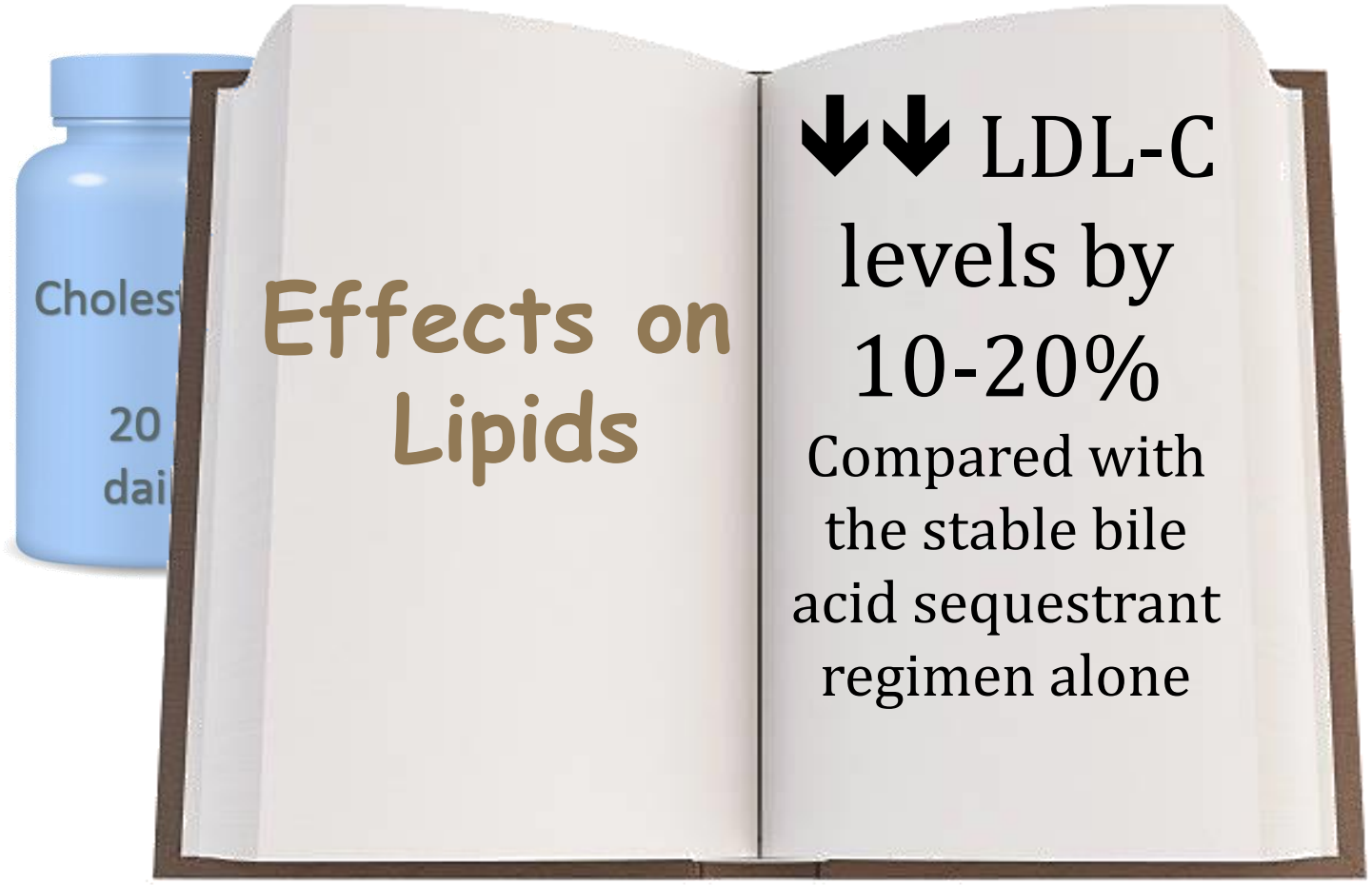

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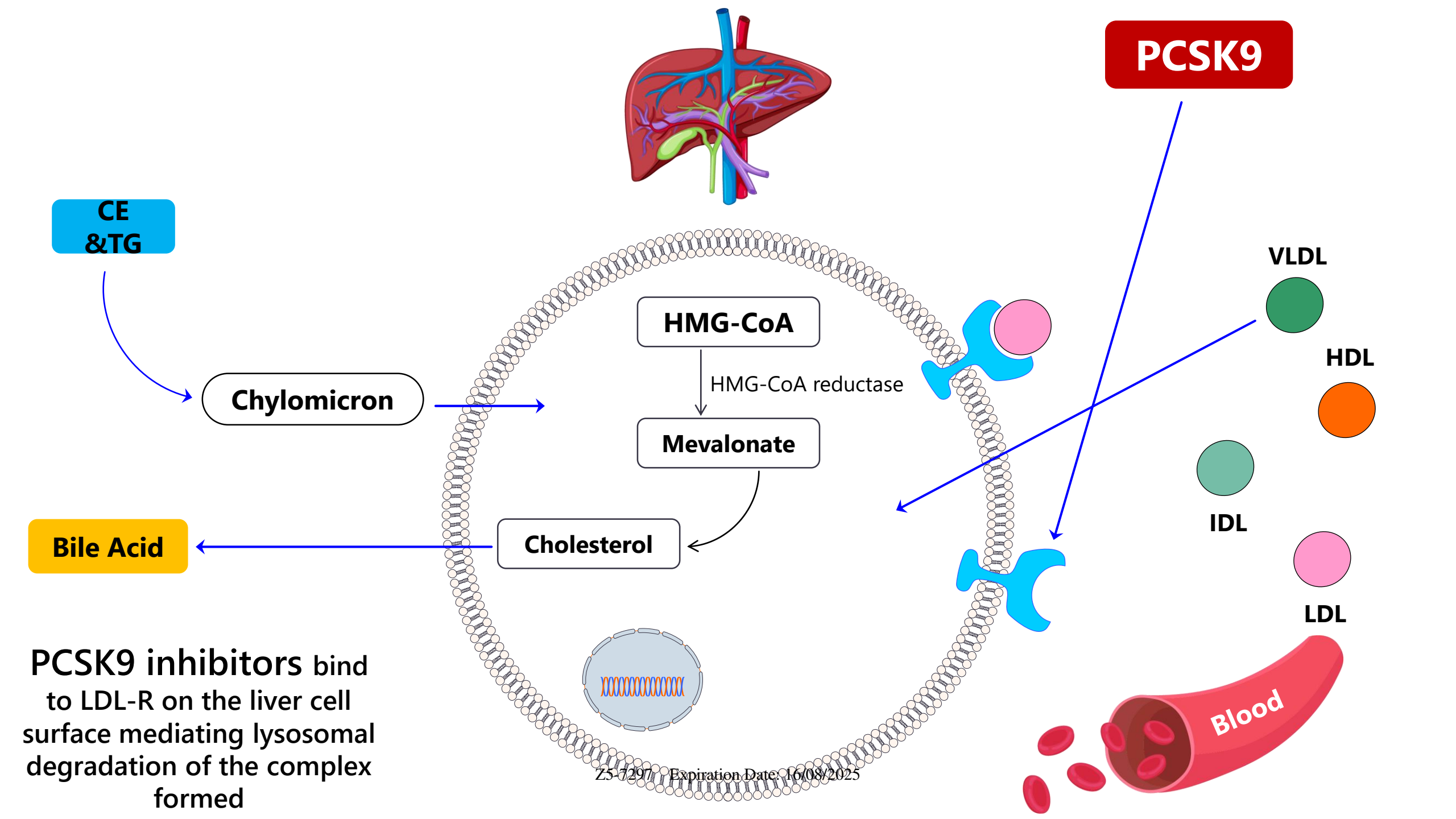
Proprotein convertase subtilisin/kexin type 9 inhibitors



PCSK9 inhibitors bind to LDL-R on the liver cell surface mediating lysosomal degradation of the complex formed

Proprotein convertase subtilisin/kexin type 9 inhibitors[1]

Effects on LDL

Evolocumab

Alirocumab

⬇⬇ LDL-C levels on average by 60%, depending on dose.

Effective in patients with HeFH and, albeit to a lower level, those with HoFH with residual LDLR expression. Receptor deficient HoFH responds poorly to the therapy.

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Proprotein convertase subtilisin/kexin type 9 inhibitors[1]

Effects on TG and HDL

Evolocumab

Alirocumab

↓↓ TG levels by 26%

↑↑ HDL levels by 9%

↑↑ ApoA-I levels by 4%

Effects on Lipoprotein(a)

Evolocumab

Alirocumab

↓↓ Lp(a) levels by 30-40%.

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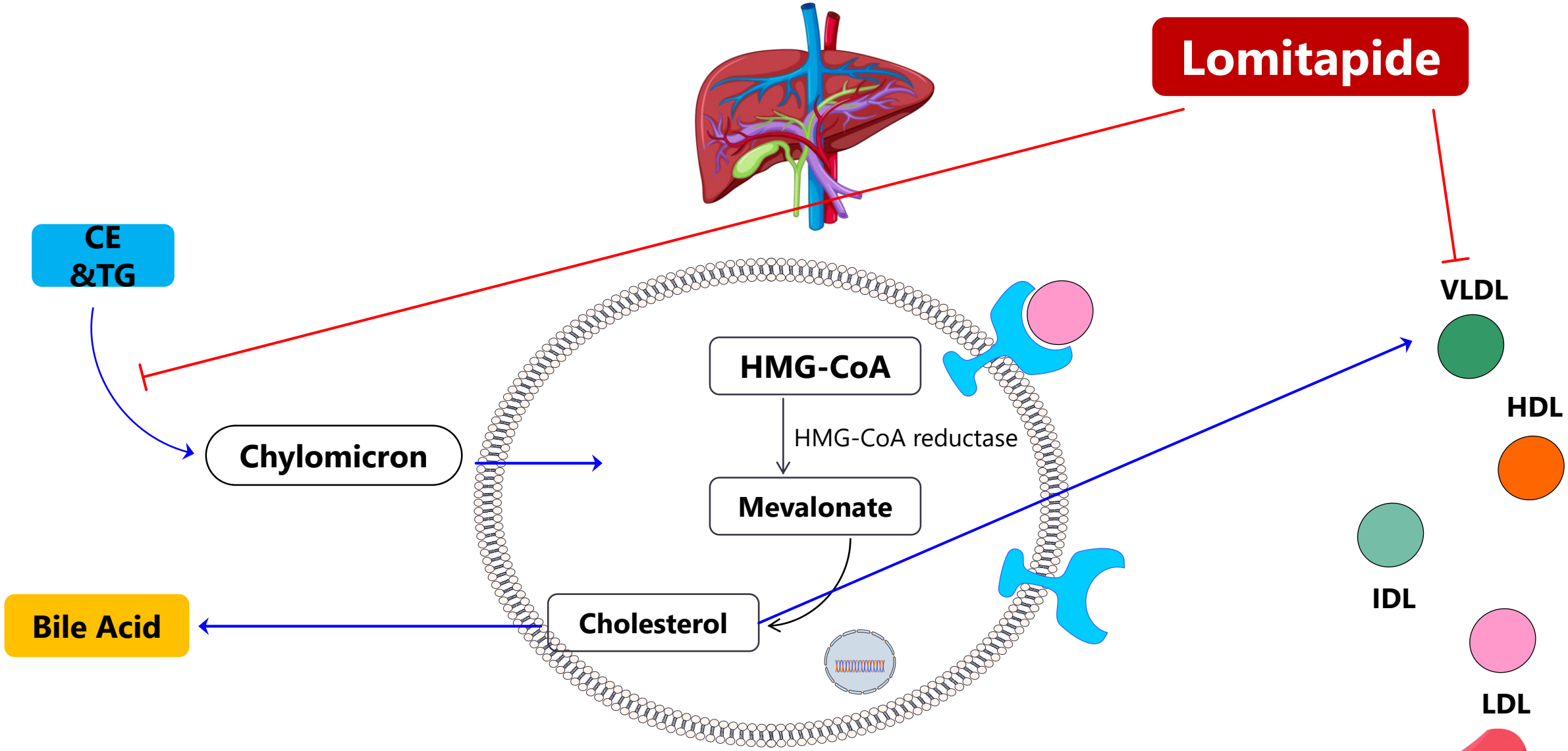
Lomitapide



Within the intestinal lumen and hepatocytes, lomitapide inhibits microsomal triglyceride transfer protein (**MTP**), which prevents the formation of apolipoprotein B, and, thus, the formation of VLDL and chylomicrons as well. Altogether, this leads to a reduction of low-density lipoprotein cholesterol.

Effects on LDL

⬇⬇ LDL-C by 50% from baseline at 26 weeks and by 44% at 56 weeks

Lomitapide ⬆⬆ ALT levels ➔⬆ fat in the liver, as well as poor GI tolerability. preventing a further increase in the dose of lomitapide in clinical trials.

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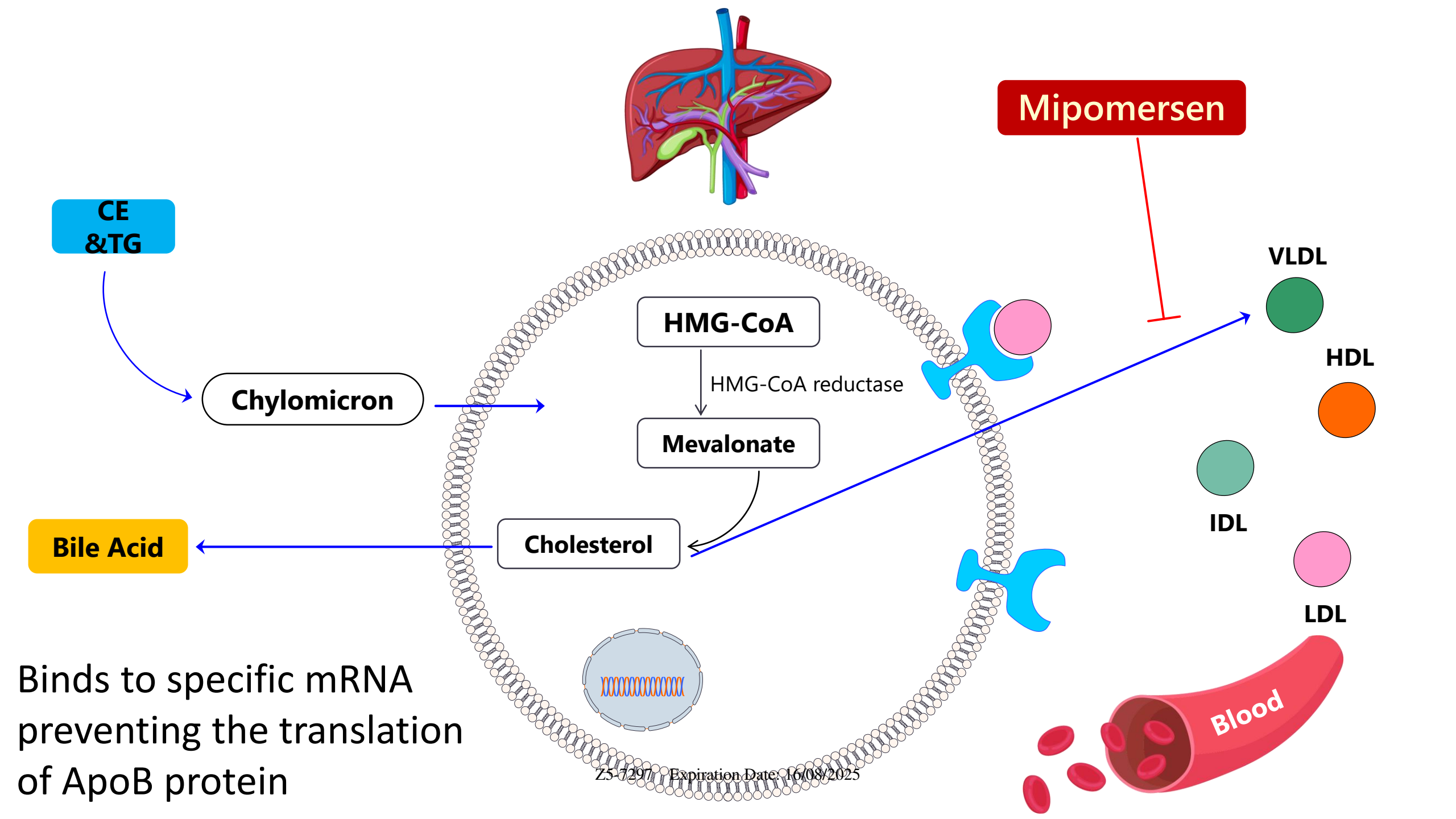
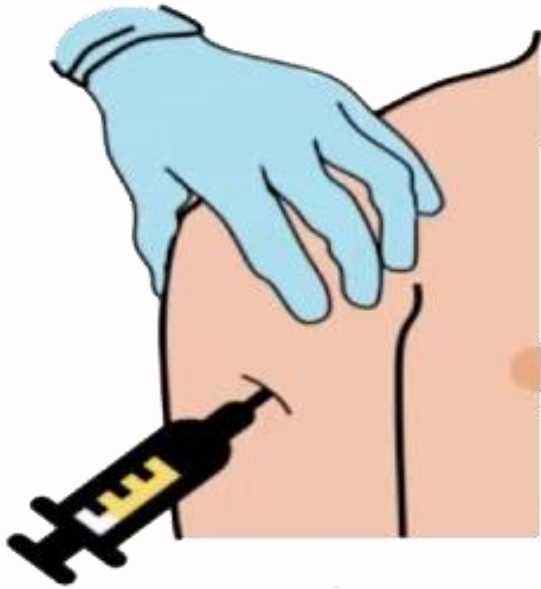
Mipomersen



Binds to specific mRNA preventing the translation of ApoB protein

Effects on LDL

⬇⬇ LDL-C in patients with Homozygous Familial Hypercholesterolemia



Mipomersen

☠ Reactions at the injection site are the most common adverse effects

☠ Mipomersen may cause liver ➔ development of steatosis.

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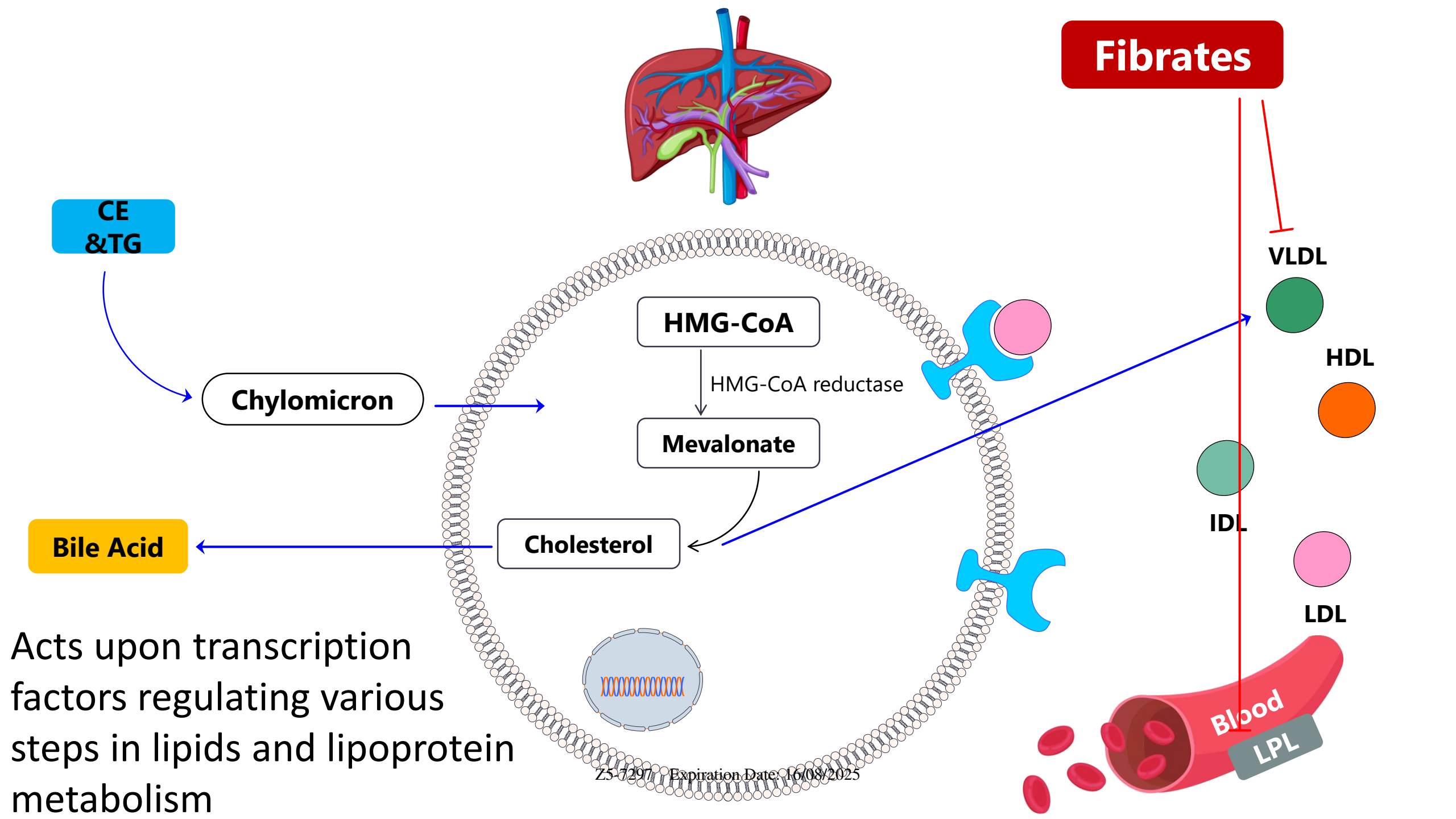
Fibrates



Acts upon transcription factors regulating various steps in lipids and lipoprotein metabolism

Effects on lipids

Fibrate class

⬇⬇ TG level by 50%

⬇⬇ LDL-C level by 20%

⬆⬆ HDL-C level by 20%

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N-3 fatty acids

N-3 fatty acids(1)

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N-3 fatty acids(1)

2

Effects on lipids

2-4 g/day decreases TG levels of up to 45%

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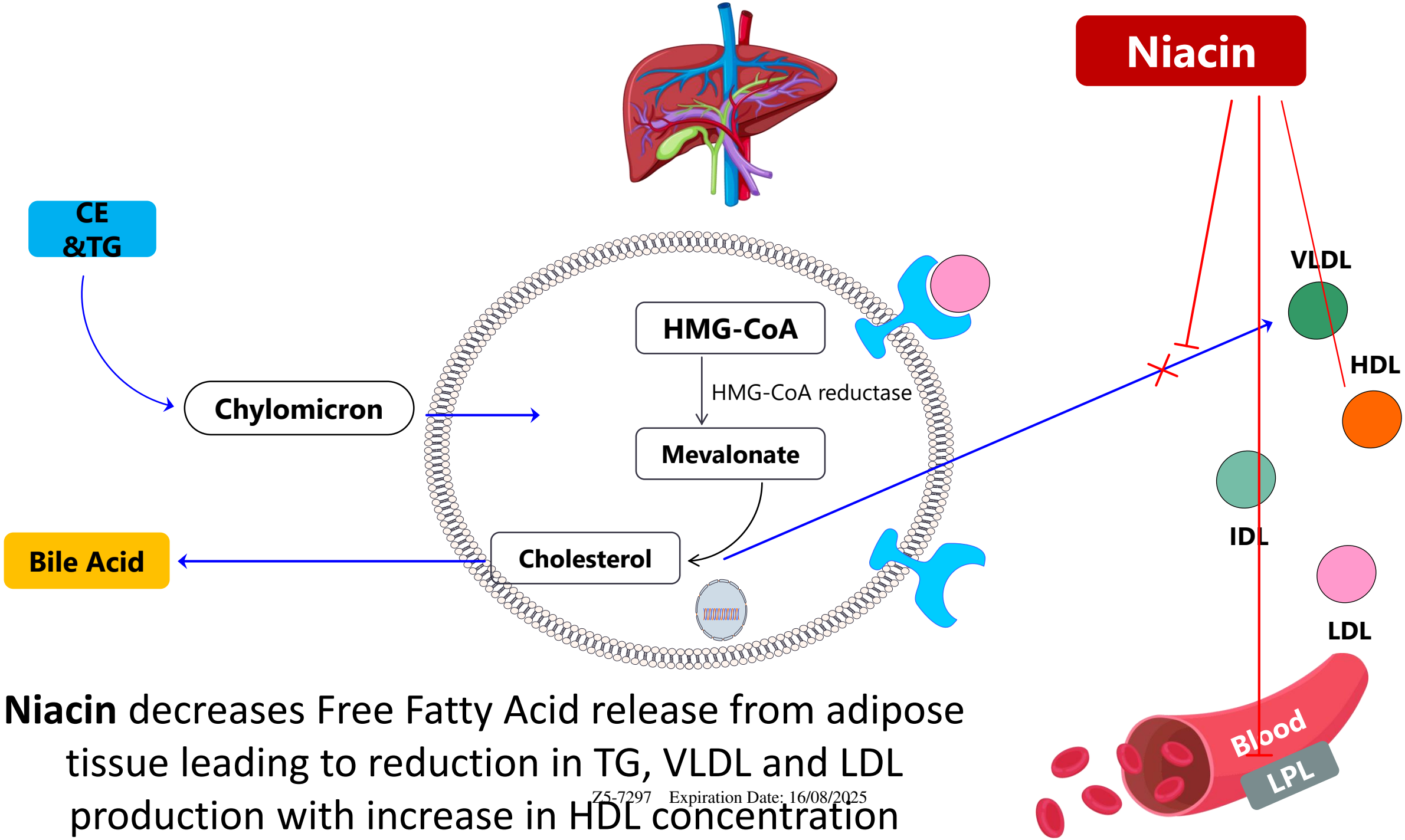
Nicotinic acid (Niacin)



Niacin decreases Free Fatty Acid release from adipose tissue leading to reduction in TG, VLDL and LDL production with increase in HDL concentration

Extended release NIACIN

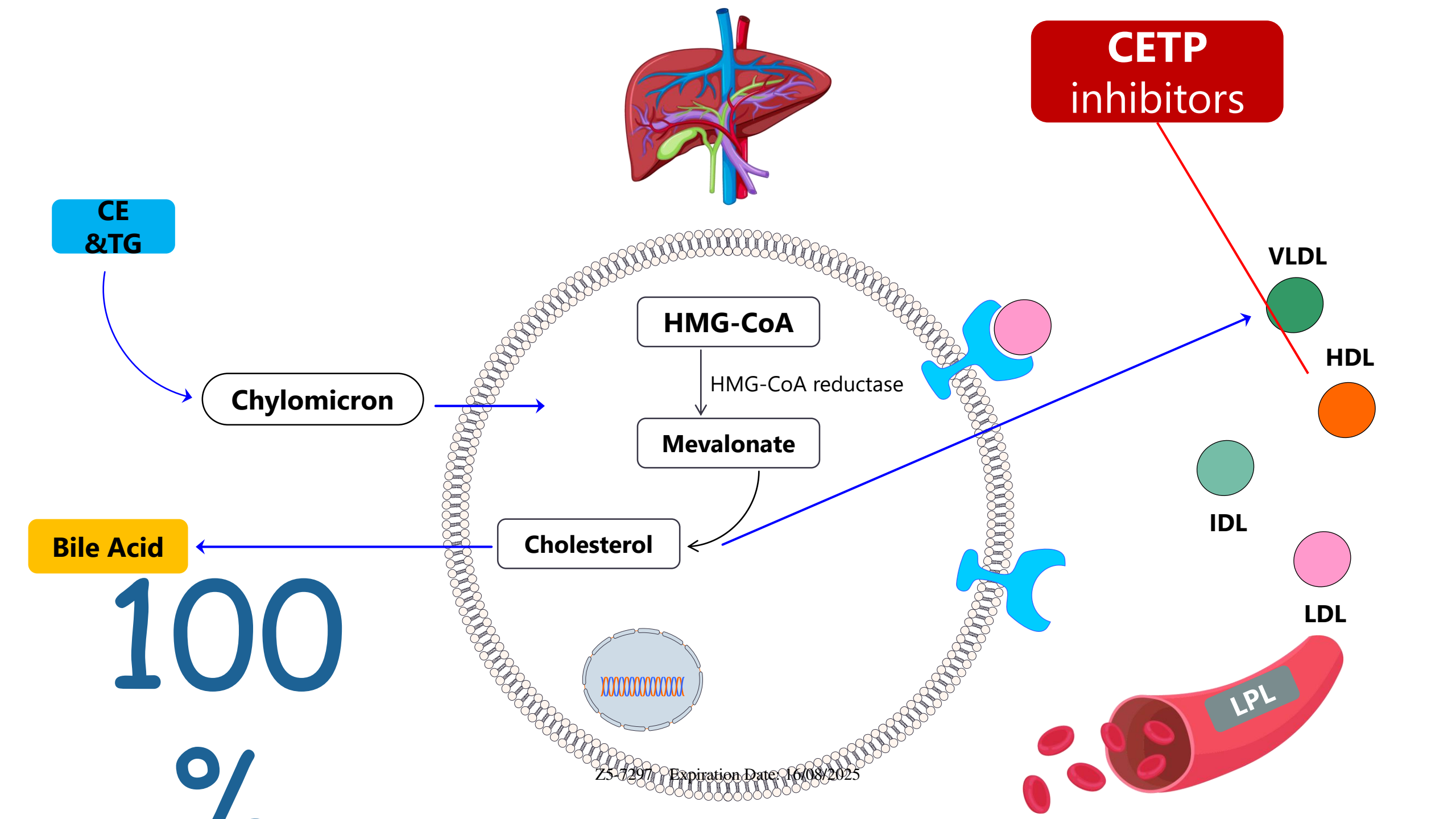
01

NIACIN + Another Drug

02

No Approval In Europe

Cholesteryl ester transfer protein inhibitors



01 **Torcetrapib** was studied to Understand its Impact in Atherosclerotic Events (ILLUMINATE) trial, which was stopped early due to increased **mortality**

02 **Dalcetrapib** ↑ HDL-C levels by 30-40% with no appreciable effect on LDL. it failed to show any benefit in ACS patients in the dal-OUTCOMES trial.

03 **Evacetrapib** ↑ HDL-C levels by 130% and ↓ LDL-C by 37%, was studied in the ACCELERATE trial, which was terminated due to **futility**.

04 **Anacetrapib** ↑ HDL(104 %) & ApoA-I (36%), ↓ LDL (17%) & ApoB (18%) was studied in the REVEAL trial. it ↓ major coronary events by 9% over a median of 4.1 years. This drug has not been submitted for regulatory approval.

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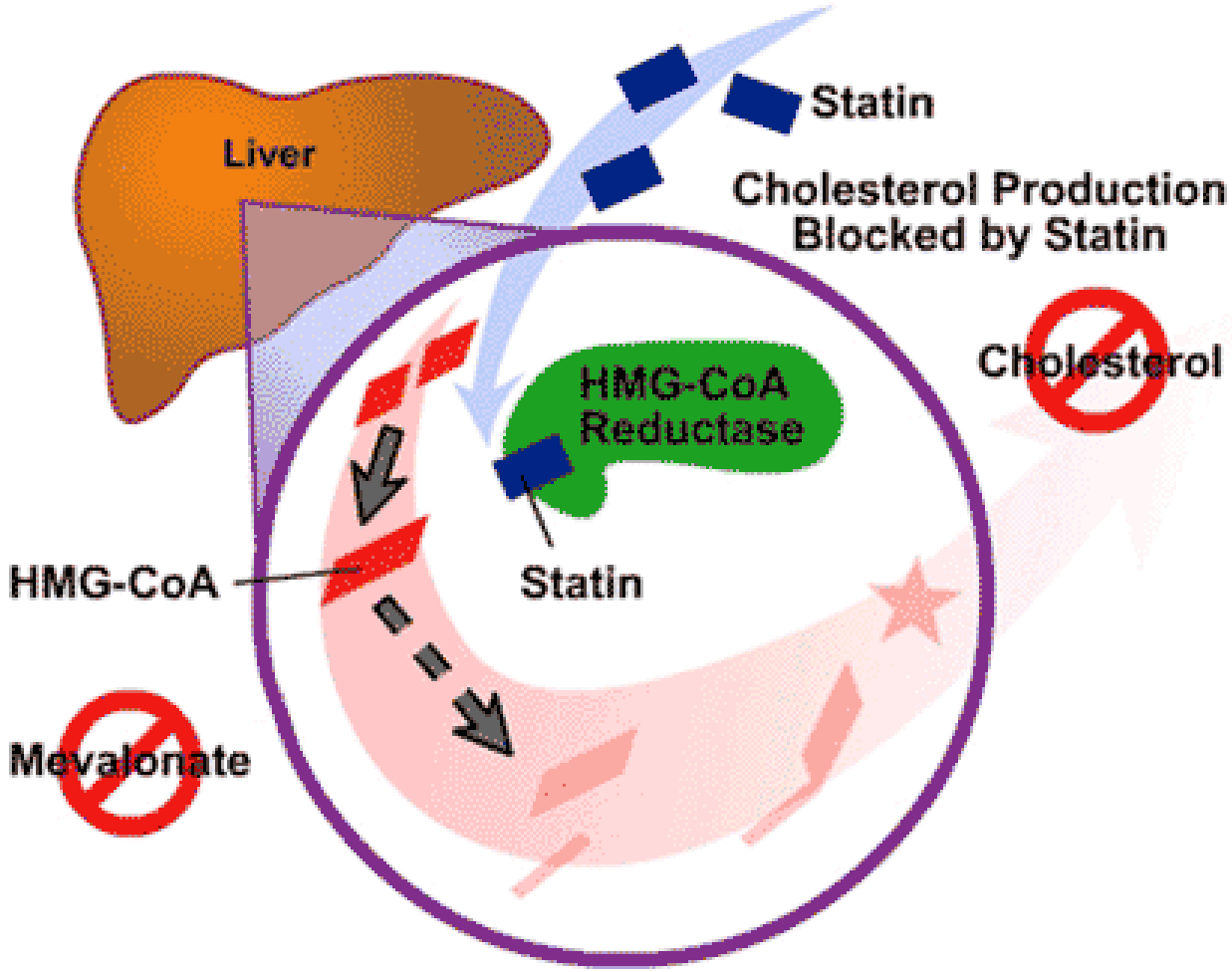
MOA Summary

Statins[1]

Mechanism of action



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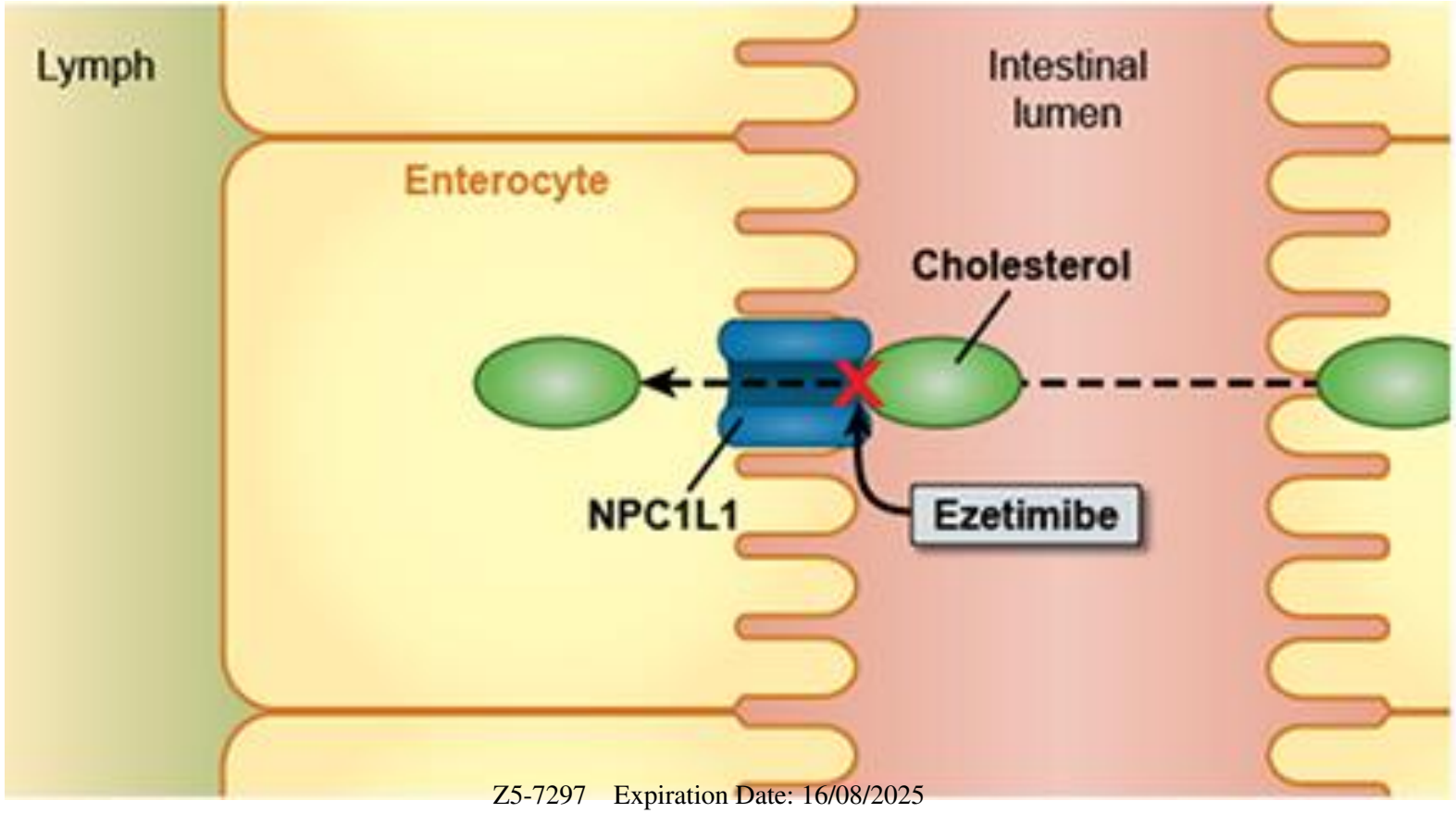
Cholesterol absorption inhibitors(1)

Mechanism of action

✓Ezetimibe interact with NPC1L1



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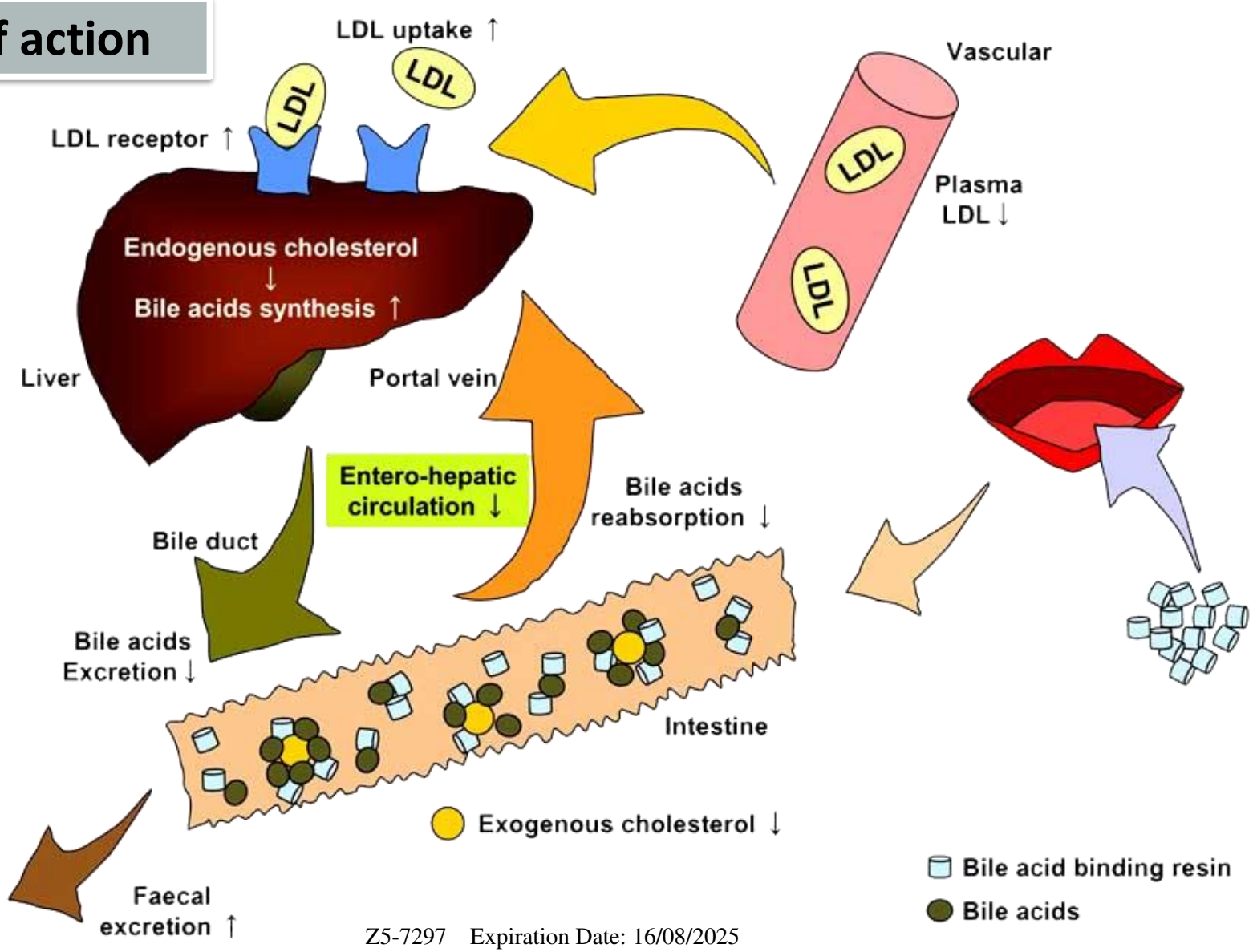
Bile acid sequestrants(1)

Mechanism of action



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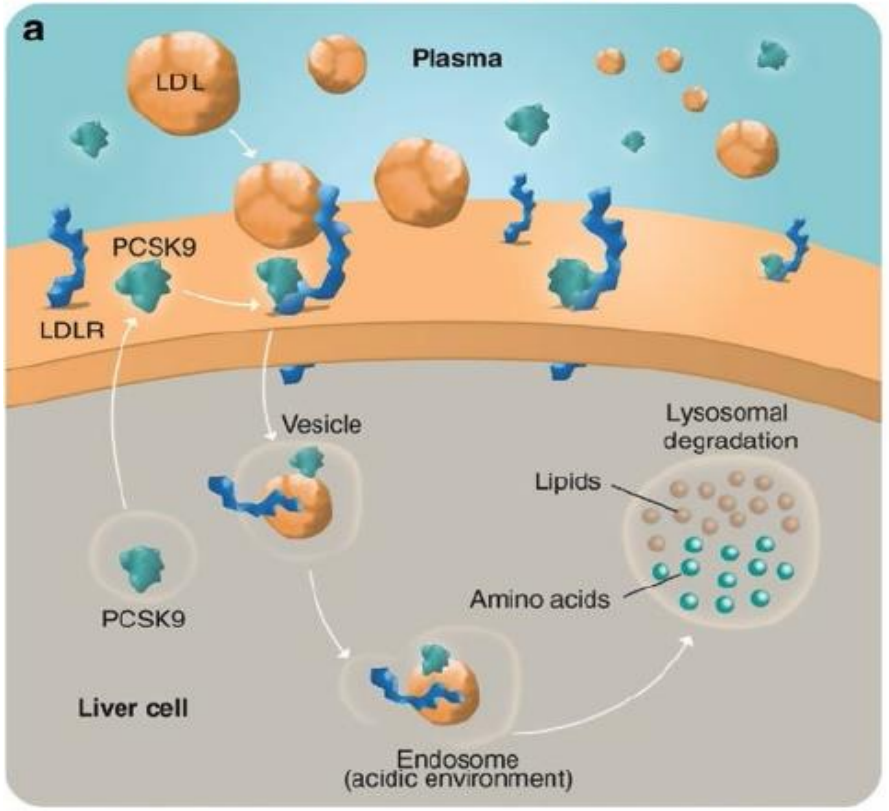
Proprotein convertase subtilisin/kexin type 9 inhibitors(1)

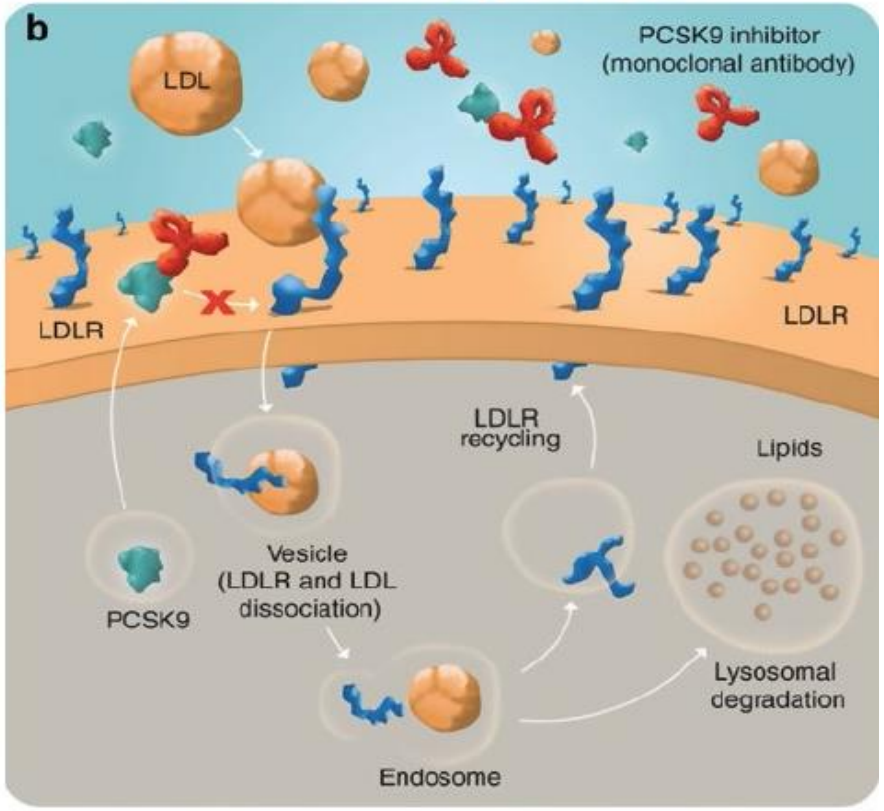
Mechanism of action

How does PCSK9 work?



a) Secreted PCSK9 binds to LDLR on the liver cell surface and mediates the lysosomal degradation of the complex formed by PCSK9 - LDLR - LDL.

How does Inhibitors work?



b) In the presence of a monoclonal antibody that binds to PCSK9, the PCSK9-mediated degradation of LDLR is inhibited, resulting in an increased uptake of LDL-cholesterol by LDLR as more LDLR are recycled at the cell surface.

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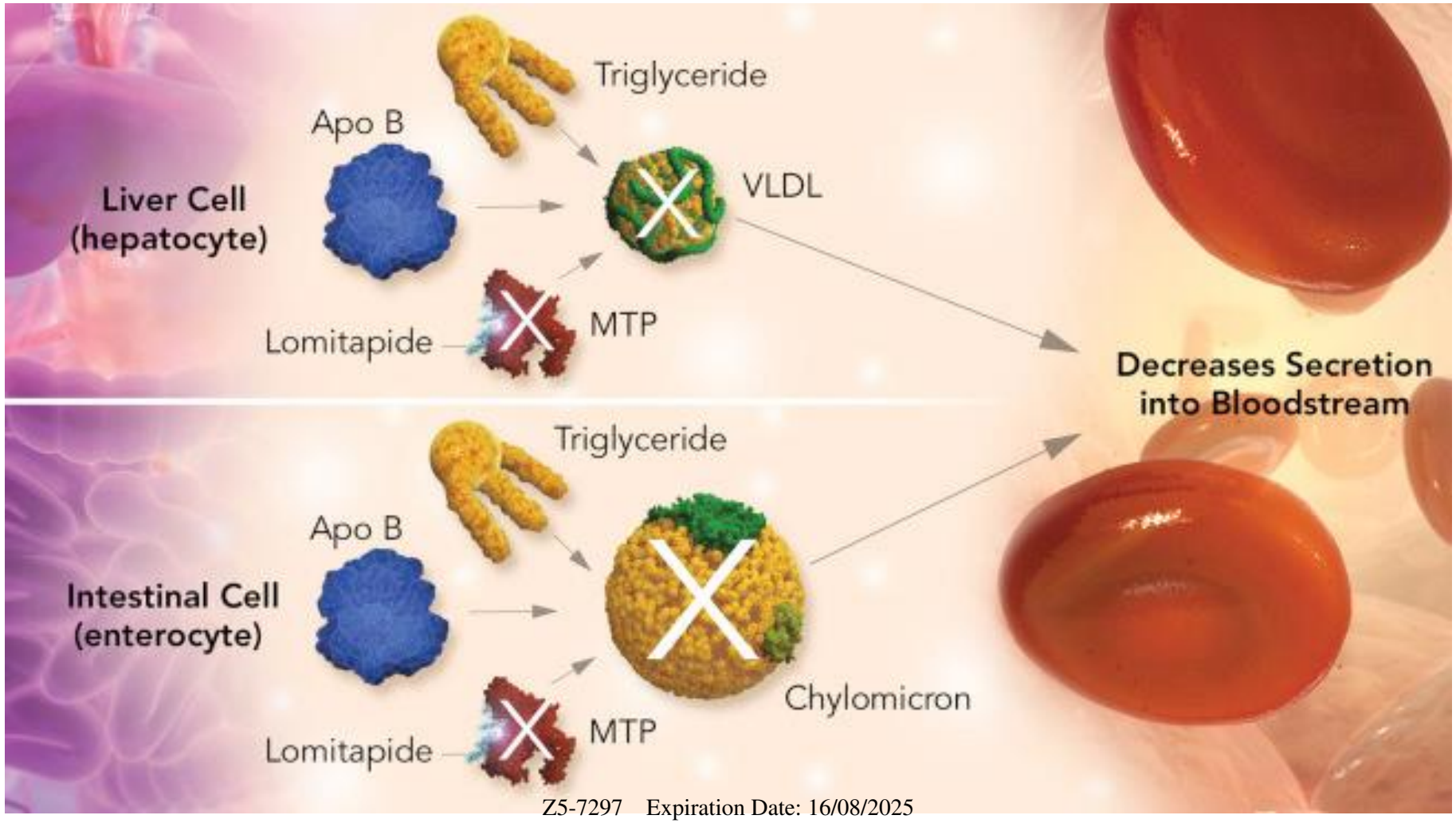
Lomitapide[1]

Mechanism of action



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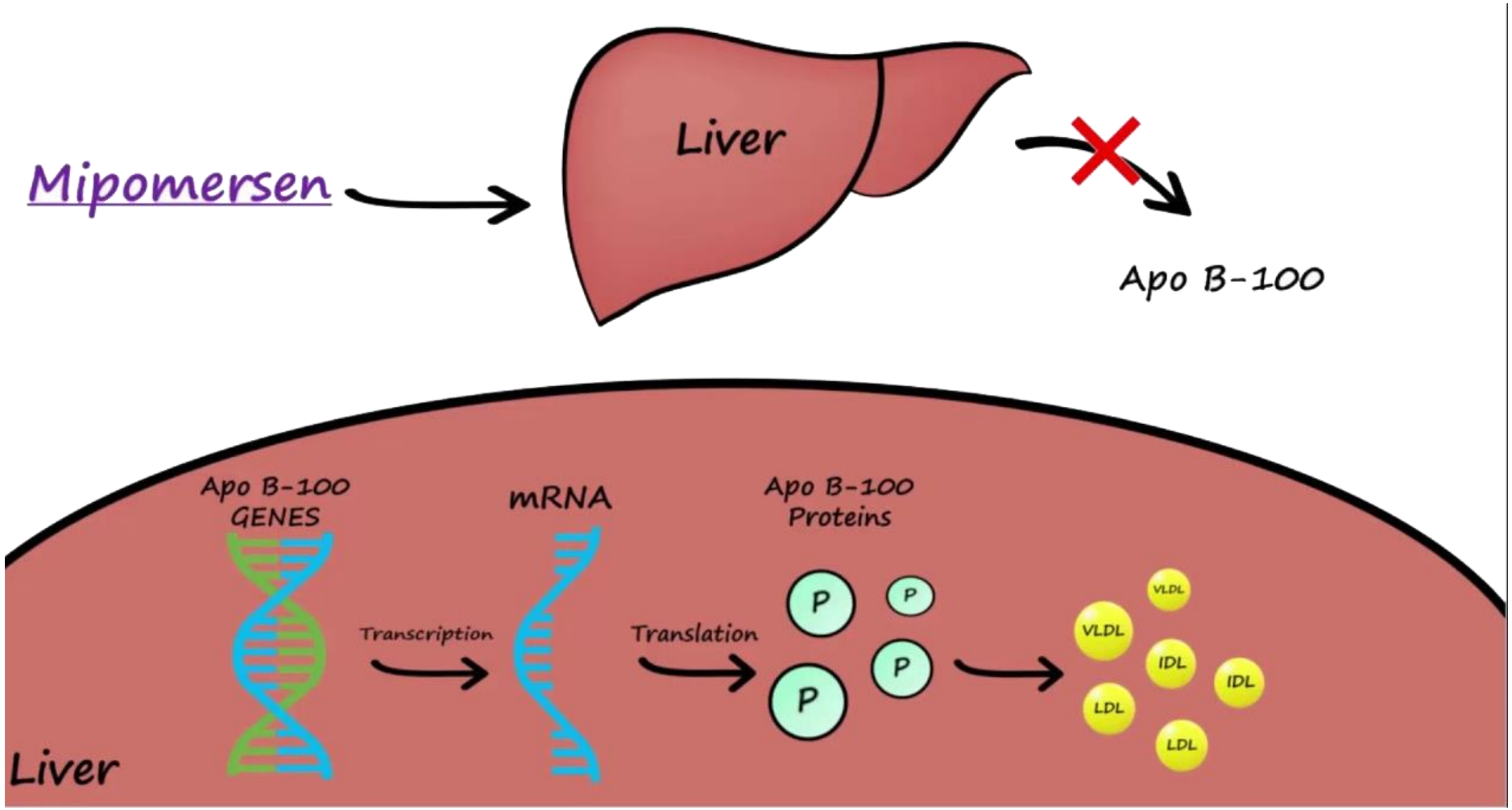
Mipomersen(1)

Mechanism of action



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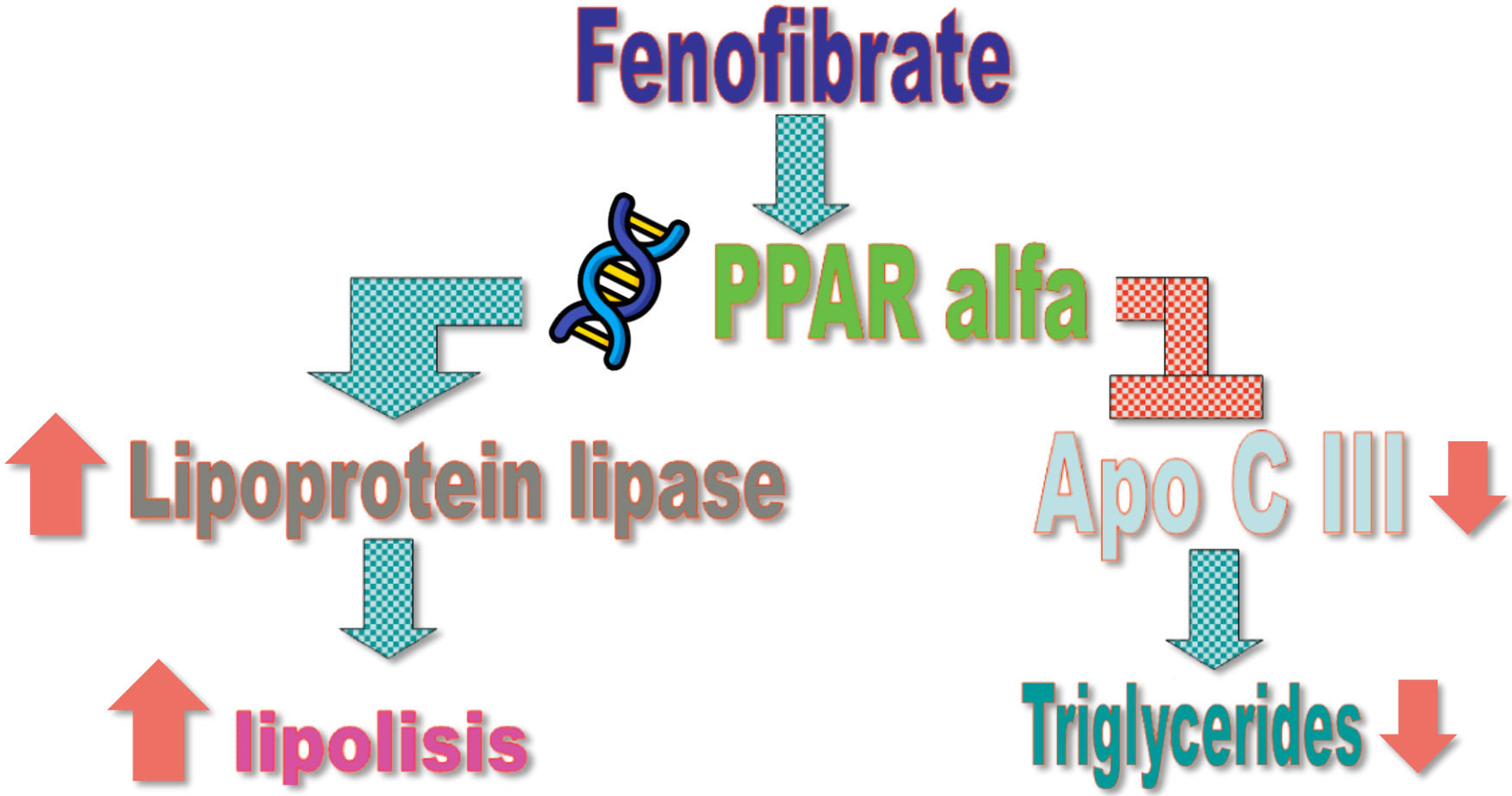
Fibrates[1]

Mechanism of action



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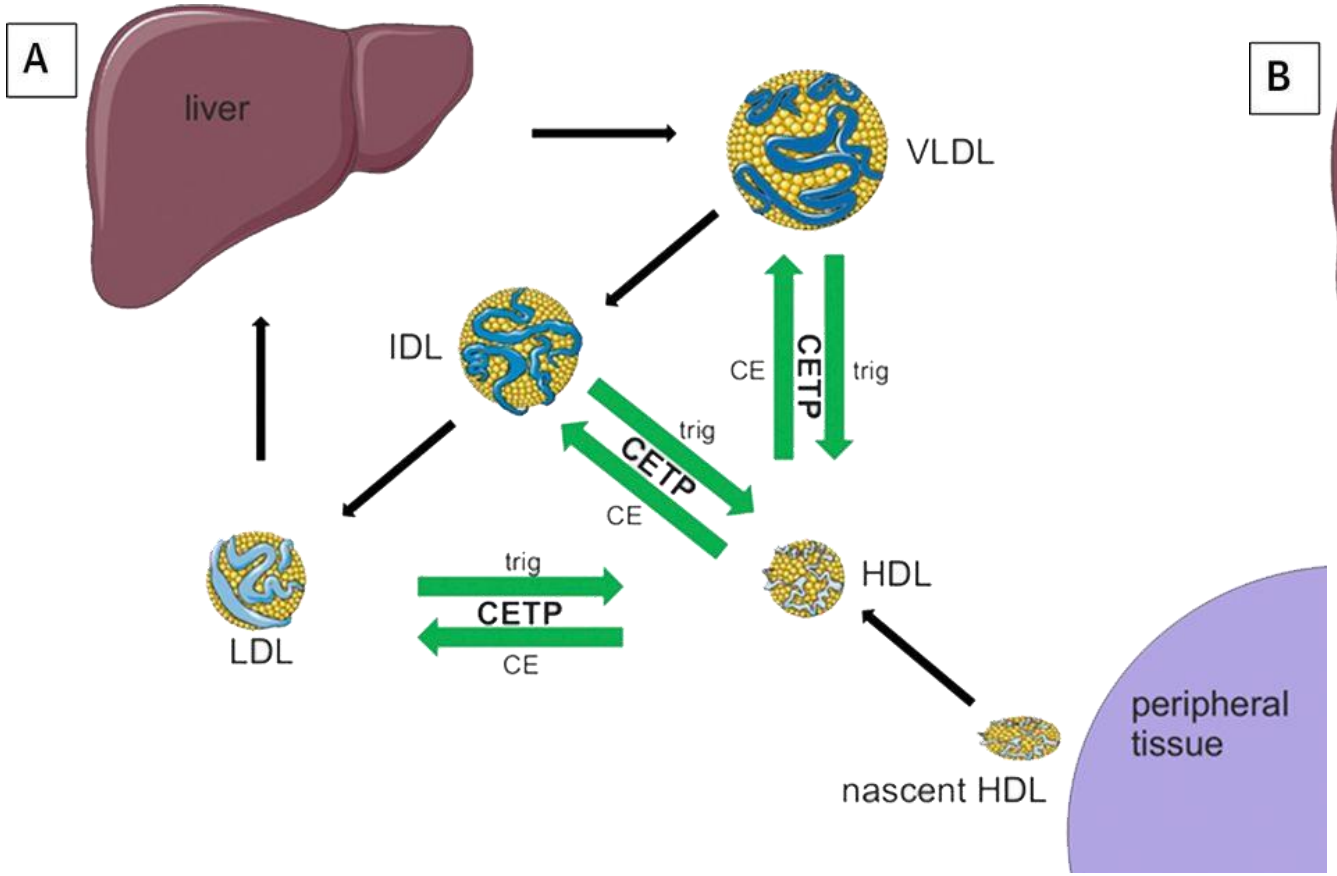
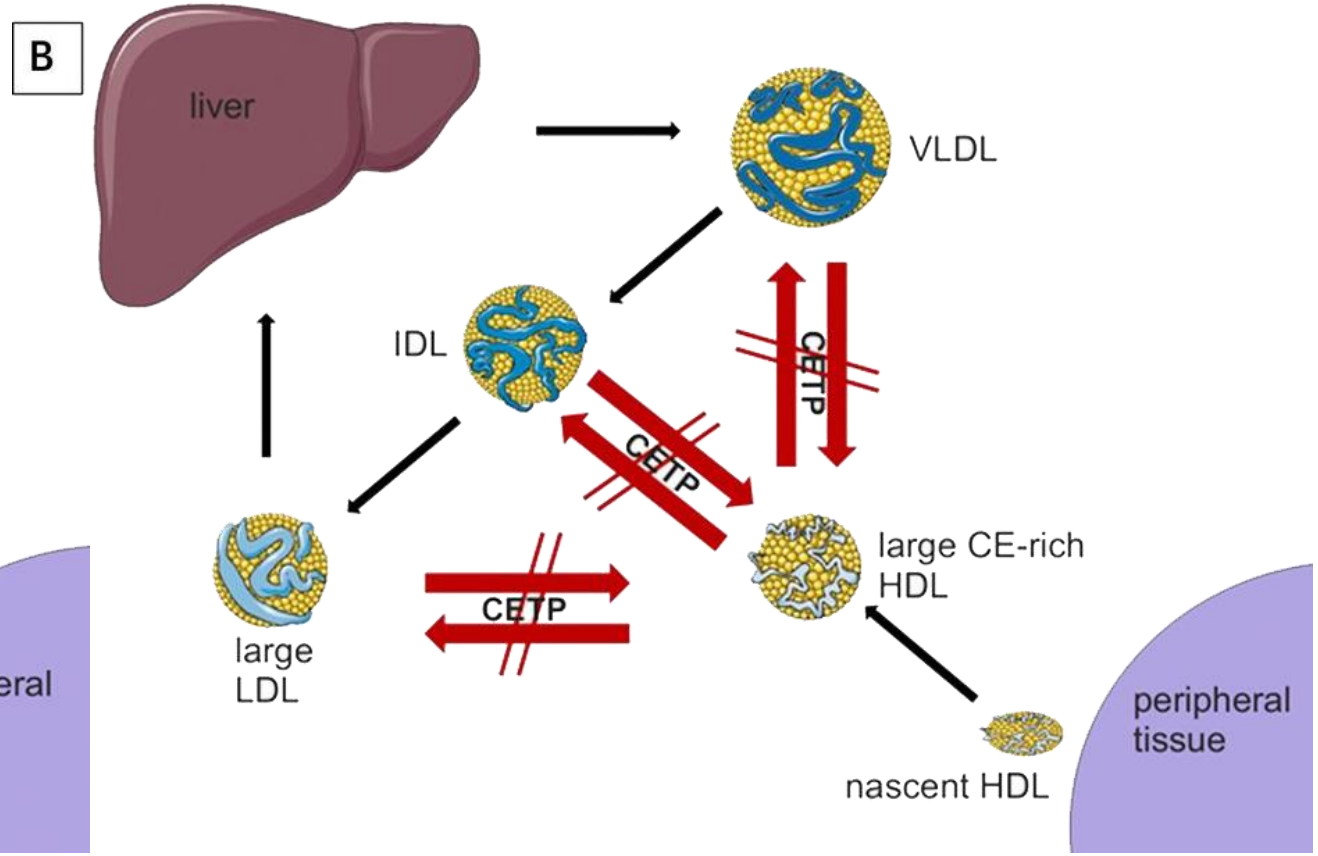
Cholesteryl ester transfer protein inhibitors[1]

Mechanism of action





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THANK
YOU

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