- Co-administration with the maximum dose of a statin has not been evaluated in clinical studies and should be avoided unless the benefits are expected to outweigh the risks

DRUG INTERACTIONS

- Coumarin anticoagulants
- Bile-acid resins (take fenofibric acid 1 hour before or 4-6 hours after BAR)
- Cyclosporine

WARNINGS AND PRECAUTIONS

- Myopathy and rhabdomyolysis have been reported in patients taking fenofibrate. The risks for myopathy and rhabdomyolysis are increased when fibrates are co-administered with a statin (with a significantly higher rate observed for gemfibrozil), particularly in elderly patients and patients with diabetes, renal failure, or hypothyroidism
- Trilipix can increase serum transaminases. Liver tests should be monitored periodically
- Trilipix can reversibly increase serum creatinine levels. Renal function should be monitored periodically in patients with renal insufficiency
- Trilipix increases cholesterol excretion into the bile, leading to risk of cholelithiasis. If cholelithiasis is suspected, gallbladder studies are indicated
- Exercise caution in concomitant treatment with oral coumarin anticoagulants. Adjust the dosage of coumarin anticoagulant to maintain the prothrombin time/INR at the desired level to prevent bleeding complications

ADVERSE REACTIONS

The most common adverse events (≥3% of patients receiving trilipix or trilipix co-administered with statins) are headache, back pain, nasopharyngitis, nausea, myalgia, diarrhea, and upper respiratory tract infection.

USE IN SPECIFIC POPULATIONS

- **Geriatric use:** Dose selection for the elderly should be made on the basis of renal function
- **Renal impairment:** Trilipix should be avoided in patients with severe renal impairment (CrCl ≤30 mL/min based on tricor PI). Dose adjustment is required in patients with mild to moderate renal impairment (CrCl 30-80 mL/min based on tricor PI)
- The use of trilipix has not been evaluated in patients with hepatic impairment

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CLINICAL PHARMACOLOGY

Mechanism of Action

The active moiety of trilipix is fenofibric acid. The lipid-modifying effects of fenofibric acid have been explained by the activation of peroxisome proliferator activated receptor α (PPARα). Through this mechanism, fenofibric acid increases lipolysis and elimination of TG-rich particles from plasma by activating LPL and reducing production of apoCIII (an inhibitor of LPL activity). Activation of PPARα also induces an increase in the synthesis of HDL-C and apoAI and apoAII.

Pharmacodynamics

Elevated levels of Total-C, LDL-C, and apoB, and decreased levels of HDL-C and its transport complex, apoAI and apoAII, are risk factors for human atherosclerosis. The independent effect of raising HDL-C or lowering TG on the risk of cardiovascular morbidity and mortality is unknown.

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Pharmacokinetics

Absorption

Well absorbed throughout the gastrointestinal tract. The absolute bioavailability of fenofibric acid is ~81%. Peak plasma levels of fenofibric acid occur within 4 to 5 hours after a single dose under fasting conditions. C_{max} and AUC is not significantly different for a single 135 mg dose of trilipix between fasting or nonfasting.

Distribution

Upon multiple dosing of trilipix, steady state can be reached within 8 days. [Plasma] of FA at steady state are slightly more than double those following a single dose. Serum protein binding is ~99% in normal and dyslipidemic subjects.

Metabolism

Primarily conjugated with glucuronic acid and then excreted in urine. *In vivo* metabolism data indicates that fenofibric acid does not undergo oxidative metabolism (eg, cytochrome P450) to a significant extent. Fenofibric acid is a weak inhibitor of CYP2C8, CYP2C19, and CYP2A6, and a mild-moderate inhibitor of CYP2C9.

Excretion

Primarily excreted in the urine in the form of fenofibric acid and fenofibric acid glucuronide. Eliminated with a half-life of 20 hours.

EFFICACY

Pooled data from baseline to 12 weeks in patients with mixed dyslipidemia (expressed as mean % Δ).

	Trilipix	LD Statin	Trilipix + LD Statin	MD Statin	Trilipix + MD Statin
HDL-C	+16.3%	+7.4%	+18.1%	+8.7%	+17.5%
TG	-31%	-16.8%	-43.9%	-23.7%	-42%
LDL-C	-5.1%	-33.9%	-33.1%	-40.6%	-34.6
Non-HDL-C	-17.3%	-34.9%	-40.4%	-42.4%	-42%

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