Icosapent Ethyl (IPE): When and Why?

Key Takeaways

The **2021 CCS Dyslipidemia Guidelines** recommend icosapent ethyl (IPE) for the reduction of CV risk in patients with:

- o ASCVD or diabetes with CV risk factors
- o Fasting triglyceride between 1.5-5.6 mmol/L despite maximally-tolerated statin therapy

IPE is dosed at 2 g orally bid and this recommendation does not extend to other omega-3 fatty acid formulations

What is IPE?

IPE is a non-statin therapy that consists of a highly purified, pharmaceutical-grade form of the omega-3 fatty acid, eicosapentaenoic acid (EPA).

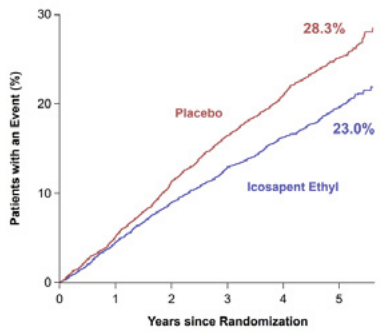
Dosing

IPE is dosed at 2 g orally twice daily. This guidelines recommendation is specifically for IPE, and it should not be extended to other omega-3 fatty acid formulations that have not demonstrated high-quality evidence for cardioprotection.

What are the benefits?

IPE has been shown to **reduce triglycerides** and it has pleiotropic cardioprotective actions beyond triglyceride-lowering that include **enhanced lipid metabolism, anti-inflammatory and antithrombotic effects, antioxidant effects, cell membrane and plaque stabilization, and improved endothelial function.**

REDUCE IT
Primary endpoint: CV death, MI, stroke, coronary revascularization, unstable angina



CV, cardiovascular; RRR, relative risk reduction; HR, hazard ratio; MACE, major adverse cardiovascular event; MI, myocardial infarction; NNT, number needed to treat.Bhatt DL, et al. N Engl J Med. 2019; 380:11-22.

What does the data show?

REDUCE-IT was a randomized, double-blind, placebo-controlled trial involving patients with established ASCVD or diabetes with CV risk factors, who had been receiving statin therapy and who had elevated triglycerides. The median duration of follow-up was 4.9 yrs.

Baseline characteristics:

- 70.7% were enrolled on the basis of secondary prevention
- 72.2% male
- Media age: 64 yrs
- Median LDL-C: 1.94 mmol/L
- Median HDL: 1.03 mmol/L
- Median triglyceride: 2.44 mmol/L

Efficacy:

- The primary CV outcome of CV death, nonfatal myocardial infarction (MI), stroke, coronary revascularization, or unstable angina, for IPE vs. placebo, was 17.2% vs. 22.0% (hazard ratio [HR] 0.75, 95% confidence interval [CI] 0.68-0.83; p < 0.0001)
- Secondary outcomes, for IPE vs. placebo:
  - Change in TG levels at 1 year: -39.0 mg/dL vs. 4.5 mg/dL
  - Change in LDL at 1 year: 2 mg/dL vs. 7 mg/dL
  - CV death or MI: 9.6% vs.12.4%, p < 0.001
  - All MI: 6.1% vs. 8.7%, p < 0.001
  - Revascularization: 5.3% vs. 7.8%, p < 0.001
  - All-cause mortality: 6.7% vs. 7.6%, p = 0.09
  - Atrial fibrillation/flutter: 5.3% vs. 3.9%
  - Serious adverse bleeding events: 2.7% vs. 2.1%, p = 0.06

What are the guidelines' recommendations around IPE?

In the 2021 CCS Dyslipidemia Guidelines, IPE is recommended to decrease the risk of CV events in persons with established ASCVD or diabetes with 1 or more CVD risk factors, whose fasting triglyceride level is between 1.5 and 5.6 mmol/L despite maximally-tolerated statin therapy.

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References: Pearson GJ, et al. 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults. Can J Cardiol. 2021;37(8):1129-1150. doi:10.1016/j.cjca.2021.03.016; Nelson JR, et al. EPA's pleiotropic mechanisms of action: a narrative review. Postgrad Med. 2021;133(6):651-664. doi:10.1080/00325481.2021.1921491; Bhatt DL, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med. 2019;380(1):11-22. doi:10.1056/NEJMoa1812792.