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# Proton Pump Inhibitors Should Have Black-box Warnings, Group Tell FDA

Written by Christian Nordqvist

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Withdrawal from PPIs (proton pump inhibitors) can lead to severe rebound acid secretion, a complication that can force users to become dependent on them - this should be mentioned in a black-box warning, consumer group Public Citizen has told the FDA (Food and Drug Administration). Examples of PPIs include, Dexilant, Vimovo, Prilosec OTC, Prevacid 24-Hr, Zegerid, Zegerid OTC, Prevacid, [Nexium](#), , Prilosec, Protonix, and Aciphex.

**Proton Pump Inhibitors**, also known as **PPIs**, are drugs which reduce gastric acid production. They are the most powerful acid secretion inhibitors available today. PPIs are used to treat several conditions, including gastroesophageal reflux disease ([GERD](#)), Barrett's esophagus, [dyspepsia](#), gastrinomas and other conditions that cause hypersecretion of acid, laryngopharyngeal reflux, [peptic ulcer](#) disease (PUD), prevention of [stress](#) gastritis, and [Zollinger-Ellison syndrome](#). High doses of PPIs can increase the risk of [bone fractures](#), as can their long-term use.

Over the last two decades PPIs have become very popular and are now one of the most widely prescribed drugs in the world - in 2009 approximately 119 million prescriptions were dispensed in the USA alone.

Public Citizen says PPIs are frequently prescribed outside their approved uses, such as for the long term treatment of GERD (past the approved time frame) or stress ulcer prophylaxis in noncritical hospitalized patients. Up to two-thirds of all patients taking PPIs are believed not to have a verified indication for the medication. The group adds that in many cases, for those with presumed GERD on PPIs, other less acid-suppressive therapies are effective in treating symptoms, while *"in other cases, the medical problem does not even involve acid reflux."*

In a letter to the FDA, Public Citizen wrote:

"Compounding the problem of massive inappropriate use, recent evidence has documented several serious new safety problems with long-term PPI use. For some of these risks, current FDA-approved PPI labels do not mention the adverse effect at all, including the potential for developing dependence on the drugs, which results in rebound hypersecretion of stomach acid and recurrence of symptoms after stopping PPI use.

For other risks, even if mentioned, the label does not adequately explain or emphasize them. There are currently no black box warnings in the label of any PPI.

This petition outlines the current state of evidence of the risks involved with short- and long-term use of PPIs and asks that the FDA make prescribers and consumers aware of these risks through the following labeling changes."

Public Citizen is requesting that the FDA makes PPI manufacturers include black box warnings which explain the following risks for all prescription PPIs, as well as equivalent warnings on OTC PPIs:

- Rebound acid hypersecretion risk - a kind of PPI dependence that can occur even after just four weeks on the medication. Patients and health care professional should be informed about the risk of PPI dependence and warned not to take the medications beyond their time frames and indicated uses. There is no current warning about this in any PPI label.
- Fracture risk - multiple daily-dose or long-term usage of PPIs have been linked to a higher risk of osteoporosis-related fractures of the spine, wrist or hip.
- Risk of infection - both long-term and short-term PPI use have been linked to a higher risk of serious infections, such as [diarrhea](#) caused by the *C. difficile* bacterium, as well as community-acquired [pneumonia](#). None of the PPI medications have any information on pneumonia risk, while only Nexium, Vimovo and Prolosex have anything about *C. difficile* infection risk.
- [Magnesium](#) deficiency risk - patients taking PPIs may also be on other medications that prolong the QTc interval on an electrocardiogram, which could cause complications for patients with low magnesium, increasing the risk of [arrhythmias](#). Information is currently written in the HighlightsII section of all prescription PPIs, but not OTC. However, details are not inserted in a black box warning.

Public Citizen is also asking that the FDA require the following label changes for all proton pump inhibitors:

- Drug interactions

PPIs can undermine the effectiveness of clopidogrel, a heart-protecting medication, raising the risk of [heart](#)

**attack.** Omeprazole, for example, has a greater chance of interaction than other PPIs, such as pantoprazole. Even so, several PPIs have been implicated. Even though the omeprazole label has a version of this warning, the HighlightsII- section should mention that a classwide interaction cannot be ruled out.

The label also needs risk information of a potential interaction with methotrexate and mycophenolate mofetil.

- **Vitamin B12 deficiency** - information regarding a risk of B12 deficiency linked to long-term use of PPIs needs to be placed on the label, which has only been placed on one PPI label (Dexilant).
- Acute interstitial nephritis - details on the risk of drug-induced acute interstitial nephritis should be included in the appropriate section. Public Citizen says there have been 60 cases reported so far.
- GERD-treatment length consistency - all proton pump inhibitors approved for GERD treatment should have clear recommendations for treatment length.

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#### References

[Click here](#) to see the letter from Public Citizen to the FDA (PDF - 39 pages)

#### Additional information

Visit our [Acid Reflux / GERD](#) category page for the latest news on this subject, or [sign up to our newsletter](#) to receive the latest updates on Acid Reflux / GERD.

#### Citations

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**APA**

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