

# Flagging Flagyl + Alcohol: Contraindication Or Just Bad Taste?

As of 2024, manufacturer labeling and drug information resources state that metronidazole should be avoided within 72 hours of alcohol use due to a disulfiram-like reaction (DLR).<sup>1</sup> Metronidazole remains a drug of choice for many infections including <u>intra-abdominal</u> infections and trichomoniasis. When metronidazole is the optimal antimicrobial in a patient with alcohol use, does this combination absolutely need to be avoided?

## What is a disulfiram-like reaction?

Disulfiram, an aldehyde dehydrogenase inhibitor, was historically used for treatment of alcohol use disorder. Disulfiram's mechanism of action causes acetaldehyde to elevate whenever an individual consumes alcohol. This accumulation can result in vasodilation, flushing, hypotension, vertigo, nausea, and vomiting.<sup>2</sup> Metronidazole has been thought to inhibit aldehyde dehydrogenase in a similar way to produce the same effects as disulfiram when combined with alcohol.

### How has the association between disulfiram-like reactions and metronidazole been observed?

In 1964, a case report noted a patient's reduced desire to drink alcohol, nausea, and a headache after consumption of metronidazole.<sup>3</sup> Subsequent case reports endorsed similar symptoms when the combination was taken.<sup>4</sup> However, some publications note that metronidazole with alcohol did not elicit nausea or vomiting. Instead, patients noted taste disturbances, which are widely observed reactions with metronidazole.<sup>5</sup>

Patient-reported signs and symptoms do not have a clear exposure and effect relationship. Alcohol use itself and the underlying infectious processes cannot be excluded as causative reasons for flushing, nausea, hypotension, or dizziness.

### What is the evidence refuting the drug interaction?

A 2002 double-blind study of 12 healthy male volunteers compared metronidazole to placebo in combination with alcohol. No signs or symptoms of a disulfiram-like reaction were noted and no acetaldehyde was detected.<sup>6</sup> A recent 2023 retrospective case control study among 18 patients who were administered metronidazole with ethanol found no report of DLR.<sup>7</sup> Although evidence refuting the incidence of DLR with the combination remains limited, these studies suggest that the potential interaction of alcohol and metronidazole is of low significance.

<u>Key Takeaway</u>: The use of metronidazole with alcohol is NOT a contraindication. Patients should be counseled on metronidazole side effects including dysgeusia.

### **References:**

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