

## Medications and interactions

[Fluoroquinolone](#) antibiotics have been noted by Professor Heather Ashton and confirmed in a study as often causing serious complications in patients chronically taking benzodiazepines or undergoing withdrawal from benzodiazepines. This is probably the result of the [GABA](#) antagonistic effect of fluoroquinolones. Fluoroquinolones have also been found to competitively displace benzodiazepines from benzodiazepine receptors which can precipitate acute withdrawal symptoms in [benzodiazepine dependent](#) subjects. A study reported higher than usual CNS toxicity from fluoroquinolones in subjects who were dependent on or in withdrawal from benzodiazepines. Of the general public 1 – 4% of the public will experience CNS toxicity from fluoroquinolones which may be severe. The incidence of severe CNS toxicity occurs significantly more frequently in the benzodiazepine dependent population. The CNS adverse reactions from fluoroquinolones were similar to those seen in benzodiazepine withdrawal and persisted for weeks or months before subsiding. The symptoms included [depression](#), [anxiety](#), [psychosis](#), [paranoia](#), severe [insomnia](#), [parathesia](#), [tinnitus](#), hypersensitivity to light and sound, [tremors](#), [status epilepticus](#), [suicidal thoughts](#) and [suicide attempt](#). The study confirmed that fluoroquinolone CNS toxicity can be serious, occurs more frequently in benzodiazepine dependent subjects and concluded that fluoroquinolone antibiotics should be contraindicated in patients who are dependent on or in benzodiazepine withdrawal. A person with an already compromised GABA system (for example, one going through benzodiazepine withdrawal) is likely to be at an even greater risk of severe adverse reactions.<sup>[3][90][91][92][93]</sup> [NSAIDs](#) have some mild GABA antagonistic properties and some may even displace benzodiazepines from their binding site according to animal research. They do not cause as potent antagonism of GABA function as fluoroquinolones. However, NSAIDs taken in combination with fluoroquinolones cause a very significant increase in GABA antagonism which may result in very severe GABA antagonism, GABA toxicity, and seizures and other severe adverse effects (see [fluoroquinolone toxicity](#)).<sup>[94][95][96]</sup>

Benzodiazepine withdrawal related [psychosis](#) is generally unresponsive to [antipsychotic](#) agents.<sup>[39][97]</sup> [Antipsychotics](#) should be avoided during benzodiazepine withdrawal as they tend to aggravate withdrawal symptoms, including convulsions.<sup>[98][99][100][101]</sup> Some [antipsychotic agents](#) may be more risky during withdrawal than others, especially [clozapine](#), [olanzapine](#) or low potency [phenothiazines](#) (e.g., [chlorpromazine](#)), as they lower the [seizure threshold](#) and can worsen withdrawal effects; if used, extreme caution is required.<sup>[102]</sup>

[Bupropion](#), which is used primarily as an antidepressant and smoking cessation aid, is contraindicated in persons experiencing abrupt withdrawal from benzodiazepines or other sedative-hypnotics (e.g. alcohol), due to an increased risk of seizures.<sup>[103]</sup> The addition of an [SSRI](#) antidepressant has been found to have little value in the treatment of benzodiazepine withdrawal.<sup>[104]</sup> Similarly, the addition of [progesterone](#) has been found to be ineffective for managing benzodiazepine withdrawal.<sup>[105]</sup>

Avoidance of or reduction in [caffeine](#) intake is sometimes recommended due to reports of it worsening withdrawal symptoms and its stimulatory properties.<sup>[3]</sup> Interestingly, at least one animal study has shown some modulation of the benzodiazepine site by caffeine which produces a lowering of seizure threshold.<sup>[106]</sup>

Once the benzodiazepine addicted or physically dependent individual has successfully withdrawn from benzodiazepines, they should avoid taking even occasionally benzodiazepines or cross tolerant drugs such as [alcohol](#), [barbiturates](#) or the [nonbenzodiazepines Z drugs](#), which all have a similar mechanism of action, for at least four months and as long as two years, depending on personal biochemistry. This is because tolerance to benzodiazepines has been demonstrated to be still present in patients who have discontinued benzodiazepines between four months and two years post withdrawal. In these patients, even once off low dose, re-exposures to benzodiazepines typically resulted in a reactivation of the tolerance and benzodiazepine withdrawal syndrome. [\[107\]\[108\]](#) Alcohol, even mild to moderate use, has been found to be a significant predictor of withdrawal failure, probably because of its [cross tolerance](#) with benzodiazepines. [\[3\]\[108\]\[109\]](#)