



February 2021

Subject: Serious risks of abuse, misuse, addiction; physical dependence and withdrawal reactions with benzodiazepines, including KLONOPIN® (clonazepam) Tablets or VALIUM® (diazepam) Tablets

Dear Healthcare Provider:

The purpose of this letter is to inform you of important safety information for benzodiazepines, including KLONOPIN® (clonazepam) Tablets and VALIUM® (diazepam) Tablets and the risks of abuse, misuse, and addiction; and physical dependence and withdrawal reactions.

KLONOPIN® is indicated for the treatment of patients who have:

- Seizure Disorders: Lennox-Gastaut syndrome (petit mal variant), akinetic and myoclonic seizures. In patients with absence seizures (petit mal) who have failed to respond to succinimides Klonopin may be useful.
- Panic Disorder: with or without agoraphobia, as defined in DSM-V.

VALIUM® is indicated for the management of:

- Anxiety disorders or for the short-term relief of the symptoms of anxiety, symptoms of acute alcohol withdrawal (relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis), adjunctively for the relief of certain types of skeletal muscle spasms, or adjunctively in convulsive disorders.

Serious Risks With Use of KLONOPIN® and/or VALIUM®

Abuse, Misuse, and Addiction

The use of benzodiazepines, including KLONOPIN® or VALIUM®, exposes users to the risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines often (but not always) involve the use of doses greater than the maximum recommended dosage and commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes, including respiratory depression, overdose, or death.

Acute Withdrawal Reactions

The continued use of benzodiazepines, including KLONOPIN® or VALIUM® may lead to clinically significant physical dependence. Abrupt discontinuation or rapid dosage reduction of KLONOPIN® or VALIUM® after continued use, or administration of flumazenil (a benzodiazepine antagonist) may precipitate acute withdrawal reactions, which can be life-threatening (e.g., seizures). Patients at an increased risk of withdrawal adverse reactions after benzodiazepine discontinuation or rapid dosage reduction include those who take higher dosages (i.e., higher and/or more frequent doses), and those who have had longer durations of use.

Protracted Withdrawal Syndrome

In some cases, benzodiazepine users have developed a protracted withdrawal syndrome with withdrawal symptoms lasting weeks to more than 12 months. As a result, there may be difficulty in differentiating withdrawal symptoms from potential re-emergence or continuation of symptoms for which the benzodiazepine was being used.

Prescriber Action

- Before prescribing KLONOPIN® or VALIUM® and throughout treatment, consider the patient's condition and the other medications being taken, and assess the risk of abuse, misuse, and addiction e.g., using a standardized screening tool, visit: <https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools>
- If a substance use disorder is suspected, evaluate the patient and institute (or refer them for) early treatment, as appropriate.
- Counsel patients, particularly those at elevated risk, about the risks and proper use of KLONOPIN® or VALIUM® and monitor for signs and symptoms of abuse, misuse, and addiction throughout treatment.
- Prescribe the lowest effective dosage for the shortest duration; avoid or minimize concomitant use of CNS depressants and other substances associated with abuse, misuse, and addiction (e.g., opioid analgesics, stimulants) and advise patients on the proper disposal of unused drug.
- Advise patients to seek immediate medical attention if they experience serious symptoms, such as difficulty breathing or seizures and encourage patients to read the Medication Guide they receive with their prescription.
- To reduce the risk of withdrawal reactions, use a gradual taper to discontinue KLONOPIN® or VALIUM® or reduce the dosage (a patient-specific plan should be used to taper the dose) and ensure ongoing monitoring and support as needed to avoid serious withdrawal symptoms or worsening of the patient's medical condition.

Reporting Adverse Events

Health care providers and patients are encouraged to report adverse events or side effects related to the use of KLONOPIN® and VALIUM® to Genentech at 1-888-835-2555.

Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088) or online (www.fda.gov/medwatch).

Company Contact Point

You may also contact the Genentech Medical Communications department at 1-800-821-8590 if you have any questions about the information contained in this letter or the safe and effective use of KLONOPIN® and/or VALIUM®.

This letter is not intended as a complete description of the benefits and risks related to the use of KLONOPIN® and/or VALIUM®. Please refer to the enclosed [full prescribing information](#) and medication guides for these products.

Sincerely,



Jamie Freedman MD, PhD
Head of U.S. Medical Affairs