

State of Vermont  
Department of Vermont Health Access  
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<http://dvha.vermont.gov>

**NOTE: Important Pharmacy Program Change**  
**Select Benzodiazepines to have Daily Quantity Limits**  
**Alprazolam/Alprazolam ER Move to PA Required**  
**Effective October 16<sup>th</sup>, 2014**

October 9<sup>th</sup>, 2014

Dear Prescriber:

The Drug Utilization Review (DUR) Board last year examined benzodiazepine utilization in pharmacy claims for beneficiaries of the public programs of the Department of Vermont Health Access (DVHA) and considered the literature and clinical guidelines that addressed the use of benzodiazepines. This review focused on the anxiolytic benzodiazepines and did not include the sedative/hypnotic benzodiazepines. Particular consideration was given to the role of these medications in anxiety and panic disorder related conditions. The National Institute of Drug Abuse (NIDA) and the DEA has identified benzodiazepines as one of the classes of prescription drugs with a high potential for diversion and abuse. The risk for dependence on and abuse of benzodiazepines is particularly high in individuals with a history of multi-substance abuse. The DUR Board is especially concerned about benzodiazepines prescribed in combination with opiates and buprenorphine products. After careful deliberation, the Board voted to implement daily quantity limits on select benzodiazepines and to move alprazolam and alprazolam ER to a non-preferred position requiring prior authorization (PA).

Benzodiazepines produce CNS depression by enhancing the effects of the major inhibitory neurotransmitter, gamma-aminobutyric acid (GABA), thereby decreasing brain activity. Benzodiazepines, particularly those having a rapid onset, are abused to produce a euphoric effect. Tolerance often develops after long term use requiring larger doses to achieve the desired effect. Physical and psychological dependence may develop. Withdrawal symptoms, the severity of which is dependent on the dose, duration of use, and drug used, include anxiety, insomnia, dysphoria, tremors, and seizures. The doses of benzodiazepines taken by abusers are usually in excess of the recommended therapeutic dose. Evidence regarding significant long term risks of benzodiazepines has continued to grow. One study has shown that those prescribed benzodiazepines have significantly increased risks of developing a benzodiazepine use disorder (*Am J Psychiatry* 2010; 167:1247-1253.) Another recent study concluded that benzodiazepine use is associated with an increased risk of Alzheimer's disease (*BMJ* 2014;349:g5205).

Treatment options for anxiety and related disorders include psychological and pharmacological treatments. Cognitive behavioral therapy (CBT) can be effectively delivered as individual or group therapy for most anxiety and related disorders. In addition, a variety of self-directed or minimal intervention formats (e.g., self-help books or internet/computer-based programs with or without minimal therapist contact) have demonstrated significant improvements in anxiety symptoms. Various antidepressants including selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and others have demonstrated efficacy in the treatment of anxiety and related disorders. Almost all current treatment guidelines include SSRIs and SNRIs as preferred initial treatments, since they are generally safer and better tolerated than other antidepressants. Benzodiazepines may be useful as adjunctive therapy early in treatment, particularly for acute anxiety or agitation, to help patients in times of acute crises, or while waiting for onset of adequate efficacy of SSRIs or other antidepressants. Due to concerns about possible dependency, sedation, cognitive impairment, and other side effects, benzodiazepines should almost always be restricted to short-term use, and generally dosed regularly rather than as-needed.

Alprazolam continues to be the most frequently abused benzodiazepine, based on focus group interviews with drug users, numbers of poison control center calls and proportions of NFLIS (National Forensic Laboratory Information System) drug reports. Its quick onset of action leads to euphoria. Most concerning is that it may be very difficult to taper and discontinue patients off alprazolam therapy when it is no longer needed. In one report, up to one-third of patients were unable to discontinue therapy (*J Clin Psychopharmacol* 1998;18:12S-18S). In contrast,

patients appear to be able to successfully discontinue clonazepam therapy more easily using a slow tapering strategy. Therefore, it is the opinion of the DUR board that alprazolam should be avoided in clinical practice.

Beginning 10/16/2014, select anxiolytic benzodiazepines will have daily quantity limits as indicated in the table below. Additionally, alprazolam and alprazolam ER will move to PA required. According to the SPMI (severe and persistent mental illness) guidelines implemented in 2006, current users of alprazolam and alprazolam ER will be able to continue therapy without PA as long as there are no gaps in therapy of greater than 4 months. The daily quantity limit parameter will be effective immediately on 10/16/2014. Patients who we were able to identify as refilling prescriptions on a monthly basis that exceeded the new daily quantity limits were given 6 week prior authorizations to override the quantity limit edits. These PAs will expire on 12/01/2014. An additional sheet is included in this letter if any of your patients were identified as requiring such a PA.

Per our current pharmacy claims activity, you have issued a benzodiazepine prescription for at least one DVHA patient in the last 45 days. Please evaluate your patients for ongoing need of benzodiazepine therapy. If you would like to receive a list of all your patients currently filling claims for benzodiazepines, please contact our on-site Catamaran Client Services Manager, Michelle Sirois at 1-802-879-5940.

If you believe your patient is not able to be titrated down to the maximum daily quantity limit, a second reconsideration will need to be requested of the DVHA Medical Director. Exceptions will be granted by the Clinical Call Center for patients previously maintained on these quantities for seizure disorders or if the medication is being prescribed for 10 days or less for alcohol withdrawal. Approval for prescriptions exceeding daily quantity limits will be assessed on a patient by patient basis after relevant clinical information supporting the request is provided by the prescriber.

If you have questions related to this change in benefit coverage, please feel free to contact our on-site Catamaran Clinical Consultant, Diane Neal, R.Ph, at 1-802-879-5605.

Thank you for your continued support of the State of Vermont's clinical pharmacy programs.

Sincerely,

J. Scott Strenio, M.D.  
Medical Director

### Anxiolytic Benzodiazepines DVHA Preferred Drug Status and Daily Quantity limits

PREFERRED PRODUCT – NO PA REQUIRED	QUANTITY LIMIT PER DAY	PA REQUIRED
Chlordiazepoxide (generic) 5, 10 & 25 mg caps	---	---
Clonazepam (generic) 0.5, 1 & 2 mg tabs	4 or 3 (2 mg)	Klonopin® 0.5, 1 & 2 mg tabs
Clonazepam ODT (generic) 0.125, 0.25, 0.5, 1 & 2 mg orally disintegrating tabs	4 or 3 (2 mg)	---
Clorazepate (generic) 3.75, 7.5 & 15 mg tabs	---	Tranxene T® 3.75, 7.5 & 15 mg tabs
Diazepam (generic) 2, 5 & 10 mg tabs	---	Valium® 2, 5 & 10 mg tabs
Lorazepam (generic) 0.5, 1 & 2 mg tabs	4	Ativan® 0.5, 1 & 2 mg tabs
Oxazepam (generic) 10, 15 & 30 mg caps	---	
	4	Alprazolam, Xanax® 0.25, 0.5, 1 & 2 mg tabs
	2	alprazolam ER, alprazolam XR, Xanax XR® 0.5, 1, 2 & 3 mg extended release tabs
	3	alprazolam ODT 0.25, 0.5, 1 & 2 mg orally disintegrating tabs, Niravam® 0.25 mg
	---	Alprazolam IntensoI® (alprazolam concentrate) 1 mg/ml
	---	Diazepam IntensoI® (diazepam concentrate) 5 mg/ml
	---	Lorazepam IntensoI® (lorazepam concentrate) 2 mg/ml