



CITIZEN PETITION REQUESTING AMENDMENTS TO BENZODIAZEPINE LABELING

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THE PETITIONERS

We, the petitioners, are individuals who experienced a serious adverse reaction to benzodiazepines and found no answers to our perplexing symptoms from our medical care providers. Ultimately, answers were found after joining one of the many Internet groups established to support those going through benzodiazepine dependency and withdrawal (Benzosupport.com, established in 2007, current membership of 8,404). Our review of benzodiazepine drug labeling demonstrated this class of drug does not disclose sufficient information to medical providers and patients to prevent the development of physical dependency and withdrawal. This deficient labeling has led many physicians to not recognize and properly treat patients suffering this devastating adverse reaction. Thousands in the US and worldwide have experienced these same symptoms of physical dependency and withdrawal, all from the same root cause—a lack of adequate information in all benzodiazepine labeling.

In the United States, the most commonly prescribed benzodiazepines are Ativan (lorazepam), Xanax (alprazolam), Klonopin (clonazepam) and Valium (diazepam). There are at least 20 different benzodiazepines. We have observed recurring issues in relation to this class of drug and feel it is necessary to point out inconsistent and deficient areas in all FDA approved benzodiazepine package inserts/labels and accompanying drug literature. These deficient areas are a major factor leading to both doctor and patient misinformation and the unnecessary development of physical dependency and withdrawal. We request corrections are made in all benzodiazepine labeling to enhance drug safety for the millions prescribed these drugs.

Benzodiazepines became available in the 1960's and were soon the most frequently prescribed drugs in the United States. According to 'Drug Topics', a professional pharmaceutical journal, five benzodiazepine drugs appeared in the top 200 generic drugs by unit in 2007. Together they represent over 100 million benzodiazepine prescriptions written in the US in 2007. The US population for 2007 was approximately 304 million people. 'WebMD' states nearly eleven percent (11%) of a large population surveyed as far back as 1990 reported some benzodiazepine use in the previous year; about two percent (2%) of the adult population of the US (around 4 million people) appear to have used prescribed benzodiazepines regularly for five to ten years or more. Thus, this petition is addressing drug safety for a staggering number of people.

Included as attachments are full drug labels for Ativan, Klonopin, Valium and Xanax.

INTRODUCTION

When one goes to their doctor and is prescribed one of the benzodiazepines, the last thing on their mind is they will get “hooked” on this drug if taken as prescribed. Benzodiazepines are only meant to be taken for short periods of time; they are temporary solutions to problems such as anxiety and sleeplessness. In fact, safe and appropriate use of benzodiazepines is for no longer than two to four weeks if taken daily. They were never meant to be the long-term solution to these problems. Unfortunately, doctors prescribe and allow multitudes of people to stay on these drugs for months and, in many cases, years. Taking benzodiazepines for more than two to four weeks frequently leads to the development of tolerance and physical dependency. All benzodiazepine package inserts and literature accompanying the drug mention the possibility of developing physical dependency and subsequent withdrawal symptoms. However, unbeknownst to most providers, pharmacists, and patients, only the makers of Ativan clearly mention in their package inserts and accompanying drug literature that benzodiazepines should be prescribed for no longer than two to four weeks of use, and they warn stopping abruptly after only one week of use can cause withdrawal symptoms. All benzodiazepines have the same mode of action affecting the gamma-aminobutyric acid-benzodiazepine receptor complex (GABA receptors), which ultimately leads to nervous system depression and the risk for developing physical dependency with short-term use.

If tolerance and physical dependency occur and patients and their medical providers do not recognize this has happened, patients frequently find themselves inaccurately diagnosed, and the fact they are actually experiencing withdrawal is overlooked. This misdiagnosis often results in physicians prescribing increased doses of benzodiazepines or other classes of drugs in an effort to alleviate symptoms or treat nonexistent disease entities, which are actually manifestations of withdrawal. Consequently, proper treatment is not rendered, with resultant devastating physical, psychological, and social outcomes.

If tolerance and physical dependency is recognized, the patient will need to be correctly withdrawn from their benzodiazepine. Once tolerance and physical dependency have occurred, patients often have a very difficult and long road ahead of them going through the withdrawal process. There is also the serious risk of developing benzodiazepine withdrawal syndrome/protracted withdrawal syndrome. There is evidence that in some cases the often debilitating symptoms of withdrawal can last for months or years after the drug is out of the system, due to the changes the drug caused within the brain which led to physical dependency. Time away from the drug is required to heal and help the brain/CNS-central nervous system go back to a pre-drug state. The issue of protracted withdrawal is never mentioned in any package inserts/labels and accompanying drug literature for any benzodiazepine drug or by most doctors who prescribe the drug.

(Note: Petitioners are aware benzodiazepines have an appropriate role to play in such applications as procedural sedation, short-term crisis sedation, as anti-epileptics when other drugs are not effective, etc. This petition is not intended to address such legitimate applications of their use).

ACTION REQUESTED

Petitioners hereby request the FDA take action to amend all benzodiazepine labels/drug inserts and supporting information by requiring that:

1. All FDA - approved benzodiazepine package inserts/labels and accompanying drug literature are made to match the same warnings as Ativan's package inserts which state that "benzodiazepines should be prescribed for short periods only (e.g., 2-4 weeks)."
2. All FDA - approved benzodiazepine package inserts/labels and accompanying drug literature are made to match the same warnings as Ativan's, that states withdrawal has been noted to "appear following cessation of the recommended dose after as little as one week of therapy." (*Labels need to clearly define the symptoms of physical dependency, drug tolerance and withdrawal, as well as the risks of developing physical dependency and withdrawal with short-term use*).
3. All FDA - approved benzodiazepine package inserts/labels and accompanying drug literature need to address the issue of protracted withdrawal, which can possibly be avoided if benzodiazepines are only prescribed for 2-4 weeks' use.
4. All FDA - approved benzodiazepine package inserts/labels and accompanying drug literature are changed to define and clear up confusion that exists in the medical community around the terms 'physical dependency' and 'addiction/abuse', which are two different things.
5. Dose equivalencies and half-life tables of all FDA - approved benzodiazepines are given to doctors and pharmacists. (*This is key for understanding how to taper the various benzodiazepines, since there is variation in the half-lives and equivalencies*).
6. All FDA - approved benzodiazepine package inserts/labels and accompanying drug literature are amended to give clear instructions on tapering after short and long term use.
7. The FDA gets the above information to doctors, pharmacists and patients:
 - Physicians and pharmacists are promptly notified of the changes in 'Action Requested' for all FDA - approved benzodiazepine products.
 - All FDA - approved benzodiazepine manufacturers disclose on their websites the same information as requested above in "Action Requested."
 - Patient leaflets are supplied by pharmacists to go along with all FDA-approved benzodiazepine prescriptions. These leaflets are to contain the same information as requested above in "Action Requested." These leaflets should also give toll-free numbers and websites for all benzodiazepine manufacturers.
8. A 'Black Box Warning' is applied to all FDA - approved benzodiazepine products.

STATEMENT OF GROUNDS

SECTIONS 1 THROUGH 8

1. BENZODIAZEPINES SHOULD ONLY BE USED FOR TWO TO FOUR WEEKS

A. ATIVAN'S DRUG LITERATURE COMPARED TO OTHER FDA APPROVED BENZODIAZEPINE DRUG LITERATURE

We have requested all FDA-approved benzodiazepine package inserts/labels and accompanying drug literature be amended to contain standardized, comprehensive information. The grounds for this request are as follows:

- a) All benzodiazepines affect the GABA neurotransmitters. The potential risks for developing tolerance or physical dependency with one benzodiazepine, apply to all benzodiazepines. Consequently, all benzodiazepine labels and literature should contain consistent information and warnings.
- b) Ativan's package inserts and accompanying drug literature (Biovail Pharmaceuticals) were modified on July 7, 2007, and state that benzodiazepines should be prescribed for short periods only, i.e. two to four weeks. They also state that withdrawal symptoms can occur in as little as one week on the drug with cessation of recommended doses (see below, taken from Ativan's insert).

"In general, benzodiazepines should be prescribed for short periods only (e.g., 2-4 weeks). Extension of the treatment period should not take place without reevaluation of the need for continued therapy. Continued long-term use is not recommended. Withdrawal symptoms (e.g., rebound insomnia) can appear following cessation of the recommended dose after as little as one week of therapy. Abrupt discontinuation of product should be avoided and a gradual dosage-tapering schedule followed after extended therapy."

None of the other FDA-approved benzodiazepine labels are as clear as Ativan's; they mention that benzodiazepines are recommended for short-term use, but the phrase "short-term" is vague and undefined. Warnings on all package inserts and accompanying drug literature need to be made much clearer for both doctors and patients. This will help prevent the needless suffering that occurs when patients develop physical dependency and withdrawal. The following information highlights some of the problems associated with the other benzodiazepine labels:

c) Roche Valium:

*"INDICATIONS: Valium is indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic." **What is short term? Short term needs to be defined as two to four weeks.***

*"Once physical dependence to benzodiazepines has developed, termination of treatment will be accompanied by withdrawal symptoms. The risk is more pronounced in patients on long-term therapy." **Unfortunately this statement does not define long term. Only Ativan's label mentions that anything over two to four weeks is too long.***

"Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol have occurred following abrupt discontinuance of diazepam. These withdrawal symptoms may consist of tremor, abdominal and muscle cramps, vomiting, sweating, headache, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases, the following symptoms may occur: derealization, depersonalization, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. The more severe withdrawal symptoms have usually been limited to those patients who had received excessive doses over an extended period of time. Generally milder withdrawal symptoms (e.g., dysphoria and insomnia) have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months. Consequently, after extended therapy, abrupt discontinuation should generally be avoided and a gradual dosage tapering schedule followed."

The Valium label states that if one takes the drug for several months, there may be an issue with physical dependency and mild withdrawal symptoms. Unfortunately, some people take the drug for only one or two months and develop debilitating withdrawal symptoms. Consequently, it is critical that all FDA-approved benzodiazepines state clearly that this class of drug is not recommended for over two to four weeks of use.

The Roche 'Klonopin' label is also less clear than Ativan's label when it comes to describing drug usage. There is no clearly stated limit on the time the drug should be used.

d) Klonopin states:

*"There is no body of evidence available to answer the question of how long the patient treated with clonazepam should remain on it. Therefore, the physician who elects to use Klonopin for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient." **The "body of evidence" is made more clear in Ativan's label as well as in medical literature by doctors worldwide; this will be addressed later in the petition.***

"Physical and psychological dependence withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (e.g., convulsions, psychosis, hallucinations, behavioral disorder, tremor, abdominal and muscle cramps) have occurred following abrupt discontinuance of clonazepam. The more severe withdrawal symptoms have usually been limited to those patients who received excessive doses over an extended period of time. Generally milder withdrawal symptoms (e.g., dysphoria and insomnia) have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months."

Klonopin's statement above, just like with Valium's, can make doctors or consumers wrongly assume that if they have not taken high doses of Klonopin for an extended period of time they will not be in danger of physical dependency and withdrawal. Most doctors are not aware that anything over two to four weeks is an extended period of time. Many wrongly assume that there is no risk of severe withdrawal symptoms if the drug is taken for several months or a few years at a low dose. This above information can cause doctors to minimize their patients' issues with withdrawal symptoms. Often, doctors are not aware of the speed in which physical dependency and withdrawal can develop. Patients who have been prescribed a therapeutic dose benzodiazepine for only a few months have developed problems with drug tolerance and subsequent withdrawal symptoms. This is evidence that a strong warning recommending a time limit of only two to four weeks' use needs to be on all labels.

The Pfizer 'Xanax' label is also not clear when it comes to their drug, in that there is no stated limit to the time the drug should be used

e) Xanax states:

*"The necessary duration of treatment for panic disorder patients responding to XANAX is unknown. After a period of extended freedom from attacks, a carefully supervised tapered discontinuation may be attempted, but there is evidence that this may often be difficult to accomplish without recurrence of symptoms and/or the manifestation of withdrawal phenomena." **Xanax, like all benzodiazepines, is a schedule IV drug; therefore, the duration a patient stays on the drug needs to be clearly defined, as stated on Ativan's label of two to four weeks' use and is not recommended for longer use.***

"Dependence and withdrawal reactions, including seizures and certain adverse clinical events, some life threatening, are a direct consequence of physical dependence to XANAX. These include a spectrum of withdrawal symptoms; the most important is seizure (see DRUG ABUSE AND DEPENDENCE). Even after relatively short-term use at the doses recommended for the treatment of transient anxiety and anxiety disorder (i.e., 0.75 to 4.0 mg per day), there is some risk of dependence. Spontaneous reporting systems data suggest that the risk of dependence and its severity appear to be greater in patients treated with doses greater than 4 mg/day and for long periods (more than 12 weeks). However, in a controlled post marketing discontinuation study of panic disorder patients, the duration of treatment (3 months compared to 6 months) had no effect on the ability of patients to taper to zero doses. In contrast, patients treated with doses of XANAX greater than 4 mg/day had more difficulty tapering to zero dose than those treated with less than 4 mg/day."

Due to the acknowledgment in the Xanax label that there is a risk of dependence and withdrawal from short-term use, the need to address appropriate usage becomes very important. The Xanax label needs to clearly state, as Ativan's does, that "In general, benzodiazepines should be prescribed for short periods only (e.g., 2-4 weeks)."

B. DRUG TRIALS ONLY LAST A FEW MONTHS

It should be noted that the drug trials for benzodiazepines lasted a few months at most. Therefore, in applying what is gleaned from the trials where withdrawal effects were noted with short term use, one can conclude this class of drug is not meant for longer term use. Since it is not clearly stated in all labels that the drug is not meant for over two to four weeks' use, there is confusion as to the actual duration of time a consumer can safely use this drug without risking physical dependency and withdrawal.

Physical dependency and issues with withdrawal when getting off the drug were noted in these short-term drug trials:

Klonopin states:

"The efficacy of Klonopin was established in two 6- to 9-week trials in panic disorder"

"The effectiveness of Klonopin in long-term use, that is, for more than 9 weeks, has not been systematically studied in controlled clinical trials."

"However, there are not sufficient data from adequate and well-controlled long-term clonazepam studies in patients with panic disorder to accurately estimate the risks of withdrawal symptoms and dependence that may be associated with such use."

Valium states:

"The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient."

Xanax states:

"Demonstrations of the effectiveness of XANAX by systematic clinical study are limited to 4 months duration for anxiety disorder and 4 to 10 weeks duration for panic disorder; however, patients with panic disorder have been treated on an open basis for up to 8 months"

"Seizures attributable to XANAX were seen after drug discontinuance or dose reduction in 8 of 1980 patients with panic disorder or in patients participating in clinical trials where doses of XANAX greater than 4 mg/day for over 3 months were permitted. Five of these cases clearly occurred during abrupt dose reduction, or discontinuation from daily doses of 2 to 10 mg. Three cases occurred in situations where there was not a clear relationship to abrupt dose reduction or discontinuation. In one instance, seizure occurred after

discontinuation from a single dose of 1 mg after tapering at a rate of 1 mg every 3 days from 6 mg daily. In two other instances, the relationship to taper is indeterminate; in both of these cases the patients had been receiving doses of 3 mg daily prior to seizure." **In people who used the drug for 3 months and did not have a pre-existing seizure disorder, seizures were noted in some cases.**

Ativan states:

"The effectiveness of Ativan (lorazepam) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies."

Still benzodiazepines are often prescribed for timeframes much longer than the duration limits of the drug trials.

C. IT IS WELL ESTABLISHED THAT BENZODIAZEPINES SHOULD BE PRESCRIBED FOR ONLY TWO TO FOUR WEEKS

- a) Professor Heather Ashton, DM, Clinical Psychopharmacology Unit, Department of Psychiatry, Royal Victoria Infirmary, Newcastle upon Tyne, England.

"Guidelines for the Rational Use of benzodiazepines: When and What to Use."

Review Article from: *Drugs* 48 (1):25-40, 1994:

"Long term use of benzodiazepines carries an undisputed risk of inducing dependence. Approximately 35% of patients taking benzodiazepines for more than four weeks develop dependence as evidenced by the appearance of withdrawal symptoms if dosage is reduced or the drugs are stopped."

"Benzodiazepines are initially very efficacious in inducing and prolonging sleep. However, tolerance to the hypnotic effects develops rapidly, sometimes after only a few days of regular use. Sleep latency, Stage 2 sleep, SWS, REMS, and intrasleep awakenings all tend to return to pre-treatment levels after a few weeks."

- b) Lader, M., "Withdrawal Reactions After Stopping Hypnotics In Patients With Insomnia," *CNS Drugs*, 1988, 10, 425-40:

"Together with the risks of rebound and withdrawal, the risk-benefit ratio for the benzodiazepines becomes adverse beyond about two weeks of continuous administration."

- c) M.A. Cormack, R.G. Owens, M.E. Dewey, "The Effect of Minimal Interventions by General Practitioners on Long-Term Benzodiazepines Use." *Royal College of General Practitioners*, October 1989, 39, 408-411:

"It has been estimated that one in three patients prescribed benzodiazepines in normal therapeutic doses for six weeks would experience withdrawal symptoms if treatment were withdrawn abruptly. Even with gradual withdrawal, patients would request further prescriptions. Thus, there is a considerable risk of dependence even in comparatively short-term use."

- d) **Richard Friedman, psychiatrist and director of the Psychopharmacology Clinic at New York Weill Cornell Medical Center in Manhattan, Time Magazine, October 21, 2001:**

"Episodic anxiety is best treated with an entirely different class of drugs known as benzodiazepines, including Valium, Xanax, Ativan and Klonopin. These work within minutes, not weeks - but they're potentially addictive, so they shouldn't be used for more than two weeks or so."

- e) **Drug-addiction expert Dr. Garth McIver, 'The Vancouver Province,' December 31, 2001:**

"Doctors who prescribe benzodiazepines continuously are courting disaster. What we need to realize is that benzodiazepines are addictive... The drugs should not generally be prescribed for longer than a few weeks. You use them clinically when it is indicated for short periods of time. Short-term use is certainly less than three months. In general practice I wouldn't be using them for more than two to three weeks... It is a drug that takes a much longer detox procedure than almost anything else"

- f) **The Royal College of Psychiatrists, July 2001:**

"The most common tranquillisers are the Valium-like drugs, the benzodiazepines (most sleeping tablets also belong to this class of drugs). They are very effective at relieving anxiety, but we now know that they can be addictive after only four weeks regular use. When people try to stop taking them they may experience unpleasant withdrawal symptoms which can go on for some time. These drugs should be only used for short periods, perhaps to help during a crisis. They should not be used for longer-term treatment of anxiety."

- g) **Dr. Ide Delargy, Irish College of General Practitioners, Irish Examiner, May 21, 2001:**

"There is inappropriate prescribing going on, not always consciously, but there are some doctors who know what they are doing and they are doing it for financial reasons. Most of the people being given benzodiazepines should not be on it and definitely shouldn't be on it longer than four weeks, but many are taking it for years."

- h) **Dr. Miriam Stoppard, Fellow of the Royal College of Physicians, Life Time Ltd. UK:**

"Physical and psychological dependence on tranquillisers can happen in an alarmingly short space of time. You reach a stage where you can't cope without tranquillisers and are terrified of trying to stop taking them... Suffering withdrawal from tranquillisers is no joke, but it can be done. Those who have gone through it say that it must be harder than coming off heroin."

D. OTHER INTERNATIONAL GUIDELINES FOR BENZODIAZEPINE USE

- a) "Committee on Safety of Medicines" U.K. Government Bulletin to Prescribing Doctors, January 1988, Current Problems 1988; Number 21: 1-2 'Benzodiazepine, Dependence and Withdrawal Symptoms'

"There has been concern for many years regarding benzodiazepine dependence (Br. Med.J, 1980: 280, 910-912). Such dependence is becoming increasingly worrying. Withdrawal symptoms include anxiety, tremor, confusion, insomnia, perceptual disorders, fits, depression, gastrointestinal, and other somatic symptoms. These may sometimes be difficult to distinguish from the symptoms of the original illness. It is important to note that withdrawal symptoms can occur with benzodiazepines following therapeutic doses given for short periods of time. Withdrawal effects usually appear shortly after stopping a benzodiazepine with a short half-life, or up to several days after stopping one with a long half-life. Symptoms may continue for weeks or months. No epidemiological evidence is available to suggest that one benzodiazepine is more responsible for the development of dependency or withdrawal symptoms than another."

The Committee on Safety of Medicines recommends that the use of benzodiazepines should be limited in the following ways:

AS ANXIOLYTICS:

- *Benzodiazepines are indicated for the short-term relief (four weeks only) of anxiety that is severe, disabling, or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness.*
- *The use of benzodiazepines to treat short-term 'mild' anxiety is inappropriate and unsuitable.*

AS HYPNOTICS:

- *Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or subjecting the individual to extreme distress.*

DOSAGES:

- *The lowest dose, which can control the symptoms, should be used. It should not be continued beyond four weeks.*
- *Long-term chronic use is not recommended.*
- *Treatment should always be tapered off gradually.*
- *Patients who have taken benzodiazepines for a long time may require a longer period for the withdrawal process, during which time doses are reduced.*
- *When a benzodiazepine is used as a hypnotic, treatment should, if possible, be intermittent.*

PRECAUTIONS:

- Benzodiazepines should not be used alone to treat depression or anxiety associated with depression. Suicide may be precipitated in such patients.
 - They should not be used for phobic or obsessional states.
 - They should not be used for the treatment of chronic psychosis.
 - In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.
 - Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed, and aggressive behavior towards self and others may be precipitated. Extreme caution should therefore be used in prescribing benzodiazepines in patients with personality disorders.
- b) Many nations around the world have addressed the issue of benzodiazepine use and all are recommending a safe period of four weeks or less.

CANADA

'The Effects of Tranquillization: Benzodiazepine Use in Canada', Health Canada, 1982. Ruth Cooperstock, Scientist, Addiction Research Foundation, and Jessica Hill, Regional Director, Ontario Health Promotion Director. Published by the authority of The Minister of National Health and Welfare, 1982:

"It is generally agreed that, lacking evidence that the anti-anxiety properties of these drugs exceed two to four weeks, and since anxiety is typically episodic, courses of one to two weeks are recommended."

"Efficacy as an anti-anxiety agent has not been demonstrated for longer than a few weeks and, because of the risk of dependency as well as with individual variation in dose response, continuous use should not exceed two weeks."

NEW ZEALAND

'Benzodiazepines - Use & Abuse: A Guide for Prescribers' Department of Health, Wellington, New Zealand, 15 March 1989:

"Benzodiazepines have been prescribed freely for many years but only recently have the dangers of dependence been understood. Short term treatment may be beneficial but longer term use, more than four weeks, could well be harmful to the patient."

NORWAY

'Guidelines for the Prescription of benzodiazepines in Norway' National Board of Health Statens Helsetilsyn Vanedannende legemidler Forskrivning og forsvarlighet, September 14, 2001:

GUIDELINES:

- Benzodiazepines should only be used under acceptable clinical conditions.
- The doctor should be critical of repeat prescriptions because of the risk of dependence.
- Patients suffering from chronic illness should be monitored carefully.

- Before benzodiazepine treatment begins, both doctor and patient should devise a treatment plan and agree on the purpose, duration, and end of treatment.
- Regular daily use of benzodiazepines should not exceed 4 weeks.
- Dosage should be proportional to the duration of treatment.
- Careful verbal and written information should be given on the occasion of the first prescription.
- If treatment is necessary for longer than the agreed time, the patient should attend for an appointment with the doctor. The doctor shall then emphasize the risks of reduced effectiveness and the development of withdrawal problems.

CHECKLIST:

- Is treatment indicated based on the patient's own history or diagnosis?
- Has non-medical treatment first been evaluated?
- Was both verbal and written information given on the occasion of the first prescription?
- Has the smallest quantity been prescribed?
- Have elderly people been prescribed half the normal adult dose?
- Has it been emphasized that daily use will not exceed 2 weeks?
- Has there been a re-evaluation and consultation on the occasion of a subsequent prescription?

DENMARK

Role of the Pharmaceutical Industry

"The National Board of Health (Sundhedsstyrelsen) advises that the prescription of benzodiazepines be restricted to a maximum of 2 weeks (sleeping pills) or 4 weeks (anxiolytics)" March 1, 2003.

IRELAND

Report of the Benzodiazepine Committee, Department of Health and Children, Ireland, August 2002 (PDF File):

"Anxiety: benzodiazepines should not usually be prescribed for longer than one month. Sleep: Prescription should be: limited to between 2 and 4 weeks; at the lowest effective dose; and prescribed intermittently."

"Benzodiazepine Guidelines: Prescription should be limited only to people assessed as needing it. Doses must be within the therapeutic ranges. They should not be prescribed for longer than four weeks. Patients should be reviewed regularly. Doctors should not issue repeat prescriptions. Doctors should reduce prescriptions to get patients off entirely."

c) THE UNITED NATIONS HAS ISSUED STATEMENTS AND HAS TAKEN ACTION REGARDING BENZODIAZEPINES.

"The United Nations Economic and Social Council, Commission on Narcotic Drugs", Forty fourth session, Vienna, 20-29 March 2001: (excerpts)

UNITED NATIONS

"Benzodiazepines"

2001 Agenda Item 7(e) Implementation of the international drug control treaties: Other matters arising from the international drug control treaties.

• **TRAINING FROM HEALTH PROFESSIONALS:**

Emphasizes the importance of initial and in-service training for relevant health professionals concerning the appropriate use of benzodiazepines. Such training should include diagnostic tools, methods for stopping treatment and information about alternative therapies or medicines;

• **ROLE OF THE PHARMACEUTICAL INDUSTRY:**

Make available to the public smaller package sizes (for one to-two week treatment) and appropriate pharmaceutical formulations with suitable doses for individual therapeutic use;

Provide health professionals with proper information on the dependence liability of benzodiazepines, including how to implement and follow up therapeutic procedures, in particular with regard to therapeutic discontinuation protocols;

• **WITHDRAWAL:**

Any prescription should be part of a pre-established therapeutic programme, with a beginning and an end, for the prescription of the medication.

The following countries were signers to this document:

Austria, Belgium, Czech Republic, Finland, France, Germany, Greece, Hungary, Italy, Netherlands, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland, The former Yugoslav Republic of Macedonia, Turkey and United Kingdom of Great Britain and Northern Ireland: Revised draft resolution.

E. SURVEY FROM BENZOSUPPORT.ORG

Benzodiazepines are supposed to be prescribed for two to four weeks only, but a survey of 346 people showed that fifty percent (50%) had been prescribed this drug for more than five years. Twelve percent (12%) had been prescribed the drug for more than 20 years. Only five percent (5%) had been prescribed the drug for three months or less. We see many posts from people who have not taken this survey but state they were placed on benzodiazepines for extended time periods. <http://www.benzosupport.org/Survey%20Results.htm>

2. RISKS OF DEVELOPING PHYSICAL DEPENDENCY, TOLERANCE WITHDRAWAL AND WITHDRAWAL SYMPTOMS WITH SHORT TERM BENZODIAZEPINE USE

We request that the symptoms of tolerance, physical dependency and withdrawal be better defined in package inserts/labels and accompanying drug literature. We request that warnings are made to match **Ativan's warning, that physical dependency and withdrawal have been noted to "appear following cessation of the recommended dose after as little as one week of therapy."** As it stands today, most doctors prescribe benzodiazepines for well over two to four weeks and often for years. Frequently doctors are unaware of the fact that this drug is not meant for use for more than two to four weeks and they do not understand the symptoms of physical dependency, drug tolerance and withdrawal.

The grounds for this request are as follows:

Tolerance, physical dependency, and withdrawal are well-documented problems associated with the prescribing of benzodiazepines for more than two to four weeks.

A. PHYSICAL DEPENDENCY

- a) American Psychiatric Association Task Force on Benzodiazepine Dependency. 'Benzodiazepine Dependence, Toxicity, and Abuse.' Washington DC: APA, 1990:

"The presence of a predictable abstinence syndrome following abrupt discontinuance of benzodiazepines is evidence of the development of physiological dependence. Historically, long-term, high-dose, physiological dependence has been called addiction, a term that implies recreational use. In recent years, however, it has become apparent that physiological adaptation develops, and discontinuance symptoms can appear after regular daily therapeutic dose administration... in some cases after a few days or weeks of administration. Since therapeutic prescribing is clearly not recreational abuse, the term dependence is preferred to addiction, and the abstinence syndrome is called a discontinuance syndrome."

- b) K. Jean Lennane, FRACP, DPM, Director, Drug and Alcohol Services, Rozelle and Gladesville Hospitals, The Rozelle Hospital, Church Street, Leichhardt, NSW 2040. 'TREATMENT OF BENZODIAZEPINE DEPENDENCE' The Medical Journal of Australia, Vol. 144, May 26, 1986:

"The first benzodiazepine agent was introduced in 1960. The first report of probable dependence appeared in 1961 and the introduction of newer and "better" benzodiazepine drugs over the next 24 years has been followed equally promptly by reports of dependence problems. Because of the weight of evidence that now implicates all known benzodiazepine drugs, the UN Commission on Narcotic Drugs last year imposed the same international regulations on them as apply to narcotic and other known dependence-producing drugs."

- c) **N. Hockings, B.R. Ballinger, 'Hypnotics and Anxiolytics', in New Drugs, London: British Medical Association, 1983, 149-155:**

"Dependence on the benzodiazepines does occur. Patients taking these drugs, even at therapeutic doses, for two or more months, may develop a physical withdrawal syndrome. The cardinal feature of the syndrome is anxiety, which may be mistakenly interpreted as a recrudescence of the original anxiety for which the drug was prescribed."

- d) **Roderigo, E. K., et. al., "Health of Long Term Benzodiazepine Users", British Medical Journal, 1988, 296, 603-66:**

"New prescriptions of benzodiazepines occur in response to a physical rather than psychological disorder. Long term users report extensive physical ill health and high levels of emotional distress."

- e) **Simpson, R.J., "Benzodiazepines in General Practice." Ian Hallstrom (Ed) Benzodiazepine Dependence. Oxford University Press, 1993:**

"The long term benzodiazepine group experienced significantly more episodes of major and minor somatic illness than controls."

- f) **Ashton, H., "Protracted Withdrawal Syndromes From benzodiazepines," Journal of Substance Abuse Treatment, 1991, 8, 19-28:**

"There is a history in long term users of steadily increasing anxiety, with the development of new symptoms such as agoraphobia, perceptual distortions, and depersonalization."

- g) **Mellinger, G. D., et. al., "Prevalence and Correlation of Long Term Regular Use of Anxiolytics," Journal of American Medical Association, 1984, 251, 375-9:**

"Poor physical health distinguished between long term users and others more sharply than any other factors at a rate seven times that of non users."

- h) **Lennane, K. J., "Treatment of Benzodiazepine Dependence," Medical Journal of Australia, 1986, 144, 594-97:**

"Patients who are dependent --- may face a very unpleasant illness, in many cases very much worse than the condition for which they were prescribed drugs in the first place".

- i) **Williams, P., "Long Term Benzodiazepine Use in General Practice." In Freman H., et. al., (eds) "The benzodiazepines in Current Clinical Practice." Royal Society Medical Services, 1987, 19-31:**

"19/22 patients (long term benzodiazepine users) were allotted a diagnosis relating to depression - The longer the duration of treatment, the less chance of stopping (benzodiazepine use)."

j) **Diazepam, Drug Research, 1970, 20, 876-77:**

"Continued use (of diazepam) can provoke depressive manifestations which may give rise to diagnostic errors."

k) **Professor Malcolm H Lader, Professor of Clinical Psychopharmacology, Institute of Psychiatry, University of London. Royal Maudesley Hospital BBC Radio. The Facts 1991:**

"We knew from the start that patients taking markedly increased doses could get dependent, but thought only addictive personalities could become dependent and that true addiction was unusual. We got that wrong. What we didn't know, but know now, is that even people taking therapeutic doses can become dependent."

B. TOLERANCE/TOLERANCE WITHDRAWAL

The term 'tolerance withdrawal' is used when the body gets used to a given dose of a benzodiazepine and needs more to feel normal. The body starts to react with withdrawal symptoms until it gets more of the drug, which causes it to stabilize and then feel normal. In some cases the body gets so tolerant that no amount of drug is effective and the person is unable to stabilize. Once someone is tolerant to the drug, it is a sign that they are physically dependent. Time away from the drug is what calms symptoms; it can take approximately six to eighteen months off, and sometimes longer, for symptoms to calm down.

Professor Heather Ashton, DM, Clinical Professor, Psychopharmacology Unit, Department of Psychiatry, Royal Victoria Infirmary, Newcastle upon Tyne, England. The following is taken from The Ashton Manual:

"Tolerance to many of the effects of benzodiazepines develops with regular use: the original dose of the drug has progressively less effect and a higher dose is required to obtain the original effect. This has often led doctors to increase the dosage in their prescriptions or to add another benzodiazepine so that some patients have ended up taking two benzodiazepines at once."

"Tolerance to the anxiolytic effects develops more slowly but there is little evidence that benzodiazepines retain their effectiveness after a few months. In fact long-term benzodiazepine use may even aggravate anxiety disorders. Many patients find that anxiety symptoms gradually increase over the years despite continuous benzodiazepine use, and panic attacks and agoraphobia may appear for the first time after years of chronic use. Such worsening of symptoms during long-term benzodiazepine use is probably due to the development of tolerance to the anxiolytic effects, so that "withdrawal" symptoms emerge even in the continued presence of the drugs."

Valium and Xanax labels touch only slightly on issues of tolerance:

Valium states:

"Some loss of response to the effects of benzodiazepines may develop after repeated use of Valium for a prolonged time."

Xanax states:

"Do not increase the dose even if you think the medication "does not work anymore" without consulting your physician."

C. WITHDRAWAL

- a) **Professor Heather Ashton, Clinical Psychopharmacology Unit, Department of Psychiatry, Royal Victoria Infirmary, Newcastle upon Tyne, England. From "The Ashton Manual"**

"The benzodiazepine withdrawal syndrome has been described by many authors. The syndrome can be of considerable severity and has similarities to abstinence syndromes associated with alcohol, opiates, and barbiturates. The symptoms may develop insidiously while the patient continues to take therapeutic doses or may occur on dosage reduction or drug withdrawal. In the latter case, the onset of the syndrome is related to the pharmacokinetic properties of the benzodiazepine involved, appearing sooner with rapidly eliminated drugs. The time course is often characterized by the early appearance of acute anxiety and psychotic symptoms (1-2 weeks after withdrawal), followed by a prolonged period (many months) of gradually diminishing mixed psychological and somatic symptoms."

- b) **Professor C. Heather Ashton DM, FRCP 'Protracted Withdrawal Syndromes from Benzodiazepines' first published: Journal of Substance Abuse Treatment Vol. 8 pp. 19-28 · 1991**

"Drug withdrawal syndromes, in general, tend to consist of mirror images of the drugs' initial effects. Thus, abrupt withdrawal from chronic usage of beta adrenoceptor antagonists such as propranolol may give rise to tachycardia and palpitations; abrupt withdrawal from antihypertensive doses of clonidine may be followed by hypertension, anxiety, and other signs of increased sympathetic activity. Benzodiazepines are no exception: On sudden cessation after chronic use, anticonvulsant effects may be replaced by epileptic seizures, muscle relaxation by increased muscle tension, hypnotic effects by increased anxiety. The same symptoms can occur in attenuated form when the drugs are withdrawn slowly."

- c) **Professor Malcolm Lader, member of the Committee on the Review of Medicines, 'Brass Tacks', BBC2, October 20, 1987.**

"When somebody comes into my office and says that they've been trying to stop their lorazepam, my heart sinks because I know I shall have twice as much of a problem as getting them off, say, Valium: the symptoms are more severe, they're more persistent, more bizarre, and people are much more distressed by them. I feel that this compound should not now be prescribed because of the problems which may arise in some patients."

- d) **Ed Walker, staff doctor in accident and emergency, Dewsbury, West Yorkshire, writing in the British Medical Journal, 1997:**

"Benzodiazepines are, of course, addictive. And coming off any addictive substance is difficult and unpleasant. For some it is particularly unpleasant."

- e) **S.Trickett, 'Withdrawal from Benzodiazepines'. Journal of the Royal College of General Practitioners 1983; 33: 608:**

"Thousands of people could not possibly invent the bizarre symptoms caused by therapeutic use of benzodiazepines and reactions to their withdrawal. Many users have to cope, not only with a frightening range of symptoms, but also with the disbelief and hostility of their doctors and families. It is not uncommon for patients to be "struck off" if they continue to complain about withdrawal symptoms. Even when doctors are concerned and understanding about the problem, they often have little knowledge of withdrawal procedure, even less about treatment."

- f) **Peter Breggin, 'Analysis of Adverse Behavioral Effects of Benzodiazepines With a Discussion on Drawing Scientific Conclusions from the FDA's Spontaneous Reporting system', The Journal of Mind and Behavior Winter 1998, Volume 19, Number 1, Pages 21-50**

"When patients try to reduce or stop their medication they do not realize that their increased insomnia and or anxiety are a result of rebound. The patient's personal and work relationships may deteriorate due to physical, cognitive and emotional problems induced by the drug. Withdrawal can be experienced as torture, and the effects of withdrawal can disrupt social and occupational life. Rage, mania and other drug-induced reactions that reach psychotic proportions can ruin lives and wreak havoc among loved ones and innocent bystanders."

- g) Liz Wood, from the United Kingdom, Midlands co-coordinator for 'Victims of Tranquillisers' (VOT), writes:

"There are some symptoms that researchers believe are seen mainly in benzodiazepine withdrawal and rarely seen in anxiety. Examples are perceptual symptoms like undulating floors. However, as a general rule, symptoms that develop during benzodiazepine ingestion and withdrawal are different from the original anxiety problem and are symptoms of a withdrawal syndrome. Usually, there are clusters of symptoms that appear together."

LIST OF BENZODIAZEPINE WITHDRAWAL SYMPTOMS

It should be noted that most people do not get all the symptoms on the list; on the other hand, there may be symptoms experienced not listed.

- Double Vision
- Sore and tired eyes
- Blurred vision
- Screwing up of the eyes
- Panic attacks
- Fear of being alone
- Tiredness
- Tension between the eyes
- Dizziness
- Agitated sight
- loss of control of the movement of the eyes
- Brain moving within the skull
- Buildings appear to be leaning
- Speech appears to be two feet in front of you when speaking
- Thoughts and feeling that you are dying
- Legs arms and head very heavy
- Difficulty in writing slowly
- Rapid blinking of the eyes
- Tight band around the head
- Sharp throbbing pain in the wrists
- Fear of water
- Loss of concentration
- Hair loss
- Tinnitus
- Speech difficulties
- Inability to write
- Inability to read
- Seizures
- Loss of interest in people and things
- Pupils of eyes become minute
- Iris in eyes changes colour
- Agoraphobia
- Feeling of vulnerability
- Feeling of extreme cold
- Extremely nervous and jumpy
- Muscle wastage
- Impotence
- Unable to walk
- Nightmares
- A fear of insanity
- Loss of memory
- Pains in the temple
- Depersonalisation
- Derealisation
- Repetitive thoughts
- Heartburn
- A feeling of impending doom
- Loss of self respect

- Earache
- Sinus problems
- Feelings of worms under the scalp
- Feelings of the spirit being out of synchronisation with the body
- Depression
- Problems of decaying teeth and gums
- Insomnia
- Vertigo
- Anxiety
- Allergies to food
- Extremely disturbed
- Twitching of the head
- Numbness, pain, pins and needles
- Saliva running from the mouth while sleeping
- Neuralgia
- Cracked and sore lips
- Pains in the neck to the shoulder blades
- Tickling and itching feeling over the whole body
- Heavy pounding heart when climbing stairs
- Breathlessness
- Intense fuzzy feeling in the head
- Cuts and abrasions take weeks to heal
- Severe muscular rigidity all over
- Demented and murderous thoughts
- Irrational rage
- Extreme thirst
- Toe and finger nails change colour from pink to grey
- Feeling bloated
- Diarrhoea
- Constipation
- Rashes and blotches on the skin
- Pains in the lungs
- Pains in the chest
- Flashbacks
- Severe cramping in the stomach
- Electric shock and muscular spasms
- Swallowing difficulties
- Dry mouth
- Hallucinations
- Hypersensitivity to light and sound
- Inability to cope with a lot of information
- Feelings of shaking inside and out
- Hyperactivity
- Aching joints and muscles
- Restlessness
- Restless legs in bed at night
- Paranoia
- Overbreathing
- Arms and legs feel detached from the body
- Grinding teeth
- Intense jaw pain
- Jaws clamped together
- Total loss of confidence
- Hysterical and inappropriate laughter
- Waves, sparks and flashes of light
- Body feels like jelly
- Sweating
- Inability to comprehend the simplest of things
- Obsessive behaviour
- Suicidal feelings
- Nausea
- Flu like symptoms
- Disorientation
- Lack of co-ordination
- Metallic taste in mouth
- Phobias
- Fear of losing control
- Clumsiness

D. MISINFORMATION: TOLERANCE, PHYSICAL DEPENDENCY, AND WITHDRAWAL

Patients in tolerance, physical dependency, and withdrawal are frequently misdiagnosed by their providers as having an increase in the underlying symptoms which initially led to their being prescribed benzodiazepines (panic attacks, insomnia, anxiety, etc.). These symptoms can be very intense and unlike anything experienced before. Symptom onset can occur while taking the drug as prescribed; this is an example of tolerance withdrawal.

Pfizer's XANAX insert adds to confusion regarding withdrawal and panic disorder:

"Relapse or return of illness was defined as a return of symptoms characteristic of panic disorder (primarily panic attacks) to levels approximately equal to those seen at baseline 6 before active treatment was initiated. Rebound refers to a return of symptoms of panic disorder to a level substantially greater in frequency, or more severe in intensity, than seen at baseline. Withdrawal symptoms were identified as those which were generally not characteristic of panic disorder and which occurred for the first time more frequently during discontinuation than at baseline."

"Panic disorder (DSM-IV) is characterized by recurrent unexpected panic attacks, i.e., a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart, or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded, or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from oneself); (10) fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes."

The above statement by Pfizer in regard to XANAX is misleading, since the symptoms of tolerance and withdrawal can look like panic symptoms; as a result, doctors often misdiagnose actual withdrawal as panic disorder.

The common practice of adding in additional "psych meds" to treat withdrawal symptoms can cause a "chemical stew" making a patient completely nonfunctional. In our support group we frequently read posts of patients who are on drug cocktails of multiple benzodiazepines, sleeping aids, anti-depressants, and mood stabilizers given by doctors who are either trying to treat benzodiazepine withdrawal or are misreading the symptoms of withdrawal as something else.

During withdrawal simple tasks, such as shopping, which were once enjoyable can become

overwhelming to an individual as the CNS is highly sensitized, making any kind of stimulation intolerable. Benzodiazepine withdrawal can have an exceedingly pervasive psychological, social, and occupational impact. Rendered nonfunctional due to their withdrawal symptoms, countless people have lost their jobs and livelihood. It is often necessary for family and friends to carry out day-to-day obligations for these patients.

Providers need a clear understanding of the concept of tolerance and physical dependency as related to benzodiazepines and of the associated withdrawal symptoms. Awareness of this issue will help differentiate an underlying psychiatric or physical condition from drug induced tolerance, physical dependency, and withdrawal.

a) Professor C. Heather Ashton, FRCP, Emeritus Professor of Clinical Psychopharmacology at the University of Newcastle upon Tyne, England, and author B.M. Maletsky state:

"Only 2 of 12 patients had previous psychiatric problems. The appearance of symptoms after regular benzodiazepine use that all patients developed, similar symptoms irrespective of any psychiatric history and the improvement after drug withdrawal, all suggest the symptoms resulted from benzodiazepine use and not from any underlying anxiety neuroses." Ashton, H. "Benzodiazepine Withdrawal: An Unfinished Story." British Medical Journal, 1984, 288, 1135-40."

b) B. Maletsky, "Addiction to Diazepam." International Journal of Addiction, 1976, 11, 95-115:

"Age, sex, and the presence or absence of a history of psychiatric, alcoholic, or drug related problems had no bearing on development of tolerance or withdrawal, thus raising the question about the validity of the 'addiction prone' concept."

There has been failure by the medical community to recognize that therapeutic dosing can lead to tolerance, physical dependency, and withdrawal. This in turn often leads doctors to increase benzodiazepine doses or add in other psychoactive drugs in an effort to combat the problems caused by the benzodiazepine. Our board has had members misdiagnosed with PTSD, bipolar disorder, multiple sclerosis, restless leg syndrome, Parkinson's, and a myriad of other conditions. This practice leaves patients in an even worse state and compounds the difficulties they will face getting off the drug or stabilizing.

When patients do not understand their perplexing symptoms, they frequently seek medical care, where they are not accurately diagnosed and become subject to unnecessary rounds of costly diagnostic testing which rarely identify the true cause of their symptoms; this is both very expensive and an unnecessary use of healthcare resources, and is potentially dangerous to patients due to repeated exposure to the known hazards of testing such as CT scanning, etc.

- c) **The B.C. Women's Addiction Foundation in Vancouver, Canada has stated the following:**

"If manifestations of withdrawal are not clearly explained or understood, patients can become chronic users of the health system as they attempt to deal with a range of health problems (including gastric, neurological, neuro-muscular, and cardiac problems.)"

"There is no question that there are significant numbers of Canadians, particularly women, who are seriously affected by benzodiazepine use. Withdrawal from benzodiazepines, even from short-term use, can be a harrowing experience involving severe physical and psychiatric manifestations. Because most patients lack support and information, they may never be able to withdraw and therefore suffer chronic ill health and mental health problems for the rest of their lives."

- d) **Professor Heather Ashton, 'DRUG NEWSLETTER', Northern Regional Health Authority, No. 31, C. DM, April 1985:**

"It is estimated that a withdrawal syndrome is experienced by 30-50% of people stopping chronic treatment with benzodiazepines but dependence has also been reported after only 6 weeks of treatment with diazepam. A very wide range of symptoms has been reported, some of which may resemble anxiety states and imply a recurrence of the original problem. However, these symptoms are reported by people irrespective of a history of psychiatric disorders, and by those who were originally prescribed benzodiazepines for conditions unrelated to anxiety, such as backache."

- e) **'The Treatment of Benzodiazepine Dependence', first published in *Addiction*, 89: 1535-1541 · 1994, Prof. C. Heather Ashton DM, FRCP:**

"Studies in general practice suggest that only 30-40% of long-term prescribed users have difficulty withdrawing (Murphy & Tyrer, 1988). This figure may be an underestimate since a high proportion of eligible patients (up to 50%) decline to enter withdrawal programs (Tyrer, 1983). Indeed, many patients have resisted previous exhortations to withdraw and are now only emerging, often reluctantly (Edwards, Cantopher & Olivieri, 1990), as GPs review their prescription practices. In patients referred to withdrawal clinics, the incidence of withdrawal symptoms may be 100% (Petursson & Lader, 1981)."

- f) **'Prescribing Benzodiazepines in Clinical Practice', Resident & Staff Physician, Jan. 2008, Vol.54, No.1, Raymond Pary, M.D & Susan Lewis, ARNP:**

"Any person who takes benzodiazepines for a long time will develop physical dependency or tolerance to the medication effects and withdrawal symptoms upon discontinuing the drug."

- g) C. Hallström, M. Lader, 'Benzodiazepine Withdrawal Phenomena', Int. Pharmacopsychiat, 1981, 16, 235-244:**

"Benzodiazepine dependence would be of minor clinical significance if it occurred only in those few individuals taking high doses of drugs; but it would be very important indeed if it supervened even to a minor degree in patients on usual clinical doses. Our clinical impression is that many patients experience symptoms on reduction or withdrawal of their benzodiazepine medication, and that whilst these symptoms somewhat resemble those of anxiety they differ qualitatively and are often more severe than those for which the medication was originally given."

- h) Professor Malcolm H. Lader, Royal Maudesley Hospital, BBC Radio 4, 'The Facts', 1991."The Medical profession:**

"I think, the medical profession is fairly ashamed of what has happened. It's allowed this very untrammelled prescribing to go on. My estimate is that there's something between a quarter and half a million people in this country, at this moment, who would have problems trying to stop their tranquillisers. They would need help to do so and there's been a sense that they're difficult to treat, difficult to deal with and a lot of these patients are just kept on their medication indefinitely. No real attempt is made to help them come off. The Government should tackle this problem face on. There are thousands of people out there who are not receiving treatment, hundreds of GPs who don't know really how to treat these patients. There are self-help groups who are crying out for funding just to keep going at a very low level. I think the Government should now acknowledge the problem and set funds aside, because if the Government doesn't do that, these people will go to their graves with their tranquilliser bottles beside them."

- i) Dr. Doug Coleman, addiction specialist, British Columbia, Canada:**

"These (pills) relax people and put them to sleep, but they also cause physical dependence. It's not as dramatic a story as heroin or cocaine, but if you totalled all the damage, benzos would be comparable. Tranquillizers, the group of drugs formally called benzodiazepines, are too easily prescribed by well-meaning physicians who don't know enough about the drugs' addictive qualities."

- j) Professor Louis Appleby, National Director for Mental Health, The Tranquilliser Trap, BBC Panorama, May 13, 2001:**

"It is difficult to defend that we have such a huge problem of benzodiazepine prescription and long-term use and therefore dependence."

3. PROTRACTED WITHDRAWAL SYNDROME

We have requested a statement be added to all benzodiazepine package inserts and accompanying drug literature indicating the possibility of developing a protracted withdrawal syndrome. The grounds for this request are as follows:

A. BENZODIAZEPINES ARE KNOWN TO HAVE A POST WITHDRAWAL SYNDROME

Many people we encounter that have experienced benzodiazepine withdrawal still have symptoms months and even years after the drug is stopped. Most doctors seem to think that after the drug is out of the body for a maximum of 30 days, the patient will no longer have withdrawal symptoms. If only it were that simple. What most doctors miss is that the brain and CNS literally have to heal after the changes/physical dependency caused by the drug, and this can take time. An average of six to eighteen months after stopping the drug is when most people typically start to see healing and symptoms diminish, but even after 18 months some people still have lingering symptoms indicative of the changes caused by benzodiazepines.

- a) Ashton, H., 'Benzodiazepine Withdrawal: An Unfinished Story.' *British Medical Journal*, 1984, 288, 1135-40:

"The benzodiazepine withdrawal syndrome is much longer than that of any other drug of dependence."

- b) Professor C. Heather Ashton, DM, FRCP, first published in: *Psychiatric Annals*, 25:3/March 1995, pp174-179:

"For some chronic benzodiazepine users, withdrawal can be a long, drawn-out process. A sizable minority, perhaps 10% to 15% develop a "post-withdrawal syndrome," which may linger for months or even years. This syndrome is clearly not a disease entity; it probably represents an amalgam of pharmacological and psychological factors directly and indirectly related to benzodiazepine use. Nevertheless, an awareness that symptoms may be protracted is important for clinicians supervising benzodiazepine withdrawal; proper management of the post-withdrawal phase can decrease its severity and duration and improve the prospects for eventual recovery."

- c) Schöpf J. 'Withdrawal Phenomena After Long-Term Administration Of Benzodiazepines. A Review Of Recent Investigations.' *Pharmacopsychiatria*, 16(1):1-8 1983 Jan:

"Recent studies report the occurrence of withdrawal reactions in a significant number of patients after long-term use of benzodiazepines, i.e. daily use for one year or more. The abstinence syndrome is partially characterized by anxiety, dysphoria, sleep disturbances and other unspecific symptoms. In addition, some patients experience symptoms, which, so far, have not been described as a typical part of a withdrawal

syndrome, especially disturbances of sensory perception. The withdrawal syndrome is less acutely distressing than a classical withdrawal syndrome of the barbiturate type, but occasionally it can show a protracted course."

- d) **Rapport D.J, Covington E.C, 'Motor Phenomena in Benzodiazepine Withdrawal.'** Cleveland Clinic Foundation, Ohio. **Hospital Community Psychiatry, 40(12):1277-9 1989 Dec:**

"Chronic use of benzodiazepines, the most widely prescribed of all psychotropic medicines, may lead to severe symptoms of withdrawal when the drugs are discontinued. The authors describe two cases of benzodiazepine withdrawal accompanied by unusual muscle activity. The neurologic mechanism for the motor abnormalities appears to be marked disinhibition of subcortical motor areas normally inhibited by gamma-aminobutyric acid. The motor phenomena may persist long after the more common signs of withdrawal have resolved and, if unrecognized, can lead to such misdiagnoses as drug seeking, conversion, hysteria, or malingering."

- e) **A. Higgitt, P. Fonagy, B. Toone, P. Shine, 'The Prolonged Benzodiazepine Withdrawal Syndrome: Anxiety or Hysteria' St Charles Hospital, London, United Kingdom, Source: Acta Psychiatria Scandinavia, 82(2):165-8 1990 Aug:**

"In an attempt to establish whether prolonged withdrawal symptoms after stopping intake of benzodiazepines is caused by return of anxiety, hysteria, abnormal illness behaviour or the dependence process itself producing perhaps a prolonged neurotransmitter imbalance, a group of such patients suffering prolonged withdrawal symptoms (PWS) was compared on a range of psychophysiological measures with matched groups of anxious and conversion hysteria patients and normal controls. It was found that the psychophysiological markers of anxiety were not marked in the PWS group; nor were the averaged evoked response abnormalities found to be associated with cases of hysterical conversion in evidence. The PWS group were hard to distinguish from normal controls on the basis of psychophysiological measures and thus it was felt to be unlikely to be an affective disturbance. It was concluded that PWS is likely to be a genuine iatrogenic condition, a complication of long-term benzodiazepine treatment."

- f) **Professor C. Heather Ashton, DM, FRCP 'Protracted Withdrawal Symptoms From Benzodiazepines' Published in Comprehensive Handbook of Drug & Alcohol Addiction 2004:**

"The acute withdrawal phase may merge imperceptibly into a more protracted phase in which symptoms gradually decline but may be punctuated by wave-like recurrences

interspersed with windows of normality that gradually extend in frequency and duration toward eventual, but occasionally incomplete, recovery. From current evidence, symptoms that are most likely to be long lasting are anxiety and insomnia, depression, various sensory and motor phenomena, and gastrointestinal disturbances."

"Observations of patients followed up for longer periods suggest that, at least in some individuals, typical benzodiazepine withdrawal symptoms, including paraesthesiae, sensory hypersensitivity, muscle spasms, and tinnitus as well as less specific symptoms such as anxiety, insomnia, and depression, can take 6 to 12 months to subside completely(8,16-23). A further problem is the interpretation of "baseline" symptoms. Patients presenting for withdrawal often have many "typical" benzodiazepine withdrawal symptoms, as well as high levels of anxiety, even while still taking the drugs(1,21). Although these symptoms may return to prewithdrawal levels in a matter of weeks following an acute withdrawal peak, follow-up observations show that such symptoms may continue to improve over subsequent months. Even without specific treatment, they may decline to levels well below "baseline", sometimes enabling patients to resume their normal lives after years of incapacity (1,19,21)."

"In a minority of patients, benzodiazepine withdrawal is followed by a protracted post-withdrawal syndrome lasting many months. Both pharmacological and psychological factors may be involved and the symptoms include anxiety, insomnia, depression, cognitive impairment and a variety of perceptual, motor, and gastrointestinal disturbances. Treatment for benzodiazepine dependence should take into account prolonged symptoms, which may be minimised by gradual dosage reduction and long-term therapeutic contact with appropriate psychological support."

- g) Professor C. Heather Ashton 'Protracted Withdrawal Syndromes From Benzodiazepines' DM, FRCP, Dept. of Pharmacological Sciences, University of Newcastle upon Tyne, England. 1: Substance Abuse Treatment. 1991; 8(1-2):19-28:**

"The benzodiazepine withdrawal syndrome is a complex phenomenon which presents serious difficulties in definition and measurement. It is particularly difficult to set out precise limits on its duration. Many withdrawal symptoms are a result of pharmacodynamic tolerance to benzodiazepines, some mechanisms for which are discussed. Such tolerance develops unevenly in different brain systems and may be slow to reverse. Withdrawal symptoms occurring in the first week after cessation of drug use tend to merge with more persistent symptoms that may last for many months. These prolonged symptoms do not necessarily constitute "true" pharmacological withdrawal symptoms, but are nevertheless related to long-term benzodiazepine use. Such symptoms can include anxiety, which may partly result from a learning deficit imposed by the drugs, and a variety of sensory and motor neurological symptoms. The protracted nature of some of these symptoms raises the possibility that benzodiazepines can give rise not only to slowly reversible functional changes in the central nervous system, but may also occasionally cause structural neuronal damage".

B. SURVEY FROM BENZOSUPPORT.ORG

In 2007, an ongoing survey of 346 people showed that on average it took people 12 months to recover after they completely stopped taking benzodiazepines. Sixty-seven percent (67%) felt they had reached this stage after 12 months off, ninety-one percent (91%) indicated they felt recovered after two years off, and ninety-eight percent (98%) after three years off. This was for the recovered group. Four percent (4%) of those who answered the survey were still unwell (protracted withdrawal) when off for 36 months plus, but we do not have that broken down any further as in four years off, five years off, etc.

Withdrawal symptoms are the result of changes to the GABA neurotransmitters that have occurred as the body adapted to being on a benzodiazepine. While healing, the CNS may be hypersensitive for some time. Stress, stimuli, excitement (good or bad), certain foods (like sugar, caffeine, alcohol), as well as supplements or other drugs can set off more intense withdrawal symptoms. With time away from benzodiazepines and all substances that affect the CNS, one typically sees withdrawal symptoms start to slowly diminish as the body heals the changes that caused the drug induced physical dependency.

4. CONFUSION REGARDING THE TERMS PHYSICAL DEPENDENCY AND ADDICTION

We have requested that a statement which clearly defines the difference between physical dependency and addiction/abuse be added to all package inserts and accompanying drug literature. The term addiction is often used to mean physically dependent; this creates confusion regarding treatment for individuals who find themselves unwittingly physically dependent on the drug through no fault of their own. The grounds for this request are as follows:

OFTEN PHYSICAL DEPENDENCY ON BENZODIAZEPINES IS INCORRECTLY DIAGNOSED AND IMPROPER TREATMENT IS ADVISED.

We often come in contact on our group with members who were called "addicts" by their doctors when they went to a doctor in withdrawal and needed to get a refill of the drug to stabilize and taper slowly. Some of these members were not given a refill and were "cold turkeyed" because their doctor thought if they refilled the prescription they would be enabling a drug addict. This ignorance has caused seizures and a host of other severe withdrawal symptoms that could have been avoided had the doctor not confused physical dependency and addiction/abuse.

As therapeutic use benzodiazepine dependency differs from true drug addiction, the usual methods of drug treatment, such as referral to detox centers, are not an appropriate or effective solution for those in withdrawal or who wish to withdraw; this has caused much more harm than good. The detox protocols usually entail fairly rapid tapering and 12 step counseling to address addictive behaviors, which are not appropriate therapies and are harmful and demeaning to those suffering from physical dependency due to taking a drug in full compliance with their physician's orders. Terms like "sobriety" and "staying clean" do not apply to people suffering benzodiazepine withdrawal; their reason for seeking the drug is to stabilize withdrawal symptoms, not get high. Once these people are tapered carefully, spend time away from the drug, and are able to see withdrawal symptoms slowly diminish, the majority would never consider using a benzodiazepine again. True understanding by the doctors who prescribe the drug will enable the patients to taper off the drug more comfortably, while also supporting the patients emotionally.

a) **The following quote is from Dr. Ray Baker, Assistant Clinical Professor in the Faculty of Medicine at the University of British Columbia:**

"It is important not to confuse physical dependence, as evidenced by benzodiazepine withdrawal syndromes, with addiction or drug dependence (DSM-IV). The majority of people suffering with prolonged withdrawal syndromes from benzodiazepines do not meet sufficient criteria to make the diagnosis of addiction. They are NOT addicts.

Addiction is a biopsychosocial syndrome. Less than ten percent of the population is at risk. Although there are eight diagnostic criteria, three of which must be present for a year; the syndrome can best be described by 'the 3 Cs':

1. *Control: when the addicted person starts using their drug, they episodically lose control over their ingestion.*
2. *Compulsion: getting and using the drug takes on more and more importance or salience in the person's life, crowding out relationships and activities that were once important to them.*
3. *Consequences: they continue using the drug despite the drug causing problems at home, problems in relationships, medical problems, legal problems, emotional and psychiatric problems, and finally vocational problems.*

Physical dependence is simply a neurobiological phenomenon due to continued exposure to a drug. It happens to all human brains exposed to drugs such as benzodiazepines and opiates. It is not addiction."

Here are some quotes from the medical community regarding the difficulty one may face when becoming physically dependent on benzodiazepines:

b) Professor Malcolm H. Lader, Royal Maudesley Hospital, BBC Radio 4, 'Face The Facts', March 16, 1999:

"It is more difficult to withdraw people from benzodiazepines than it is from heroin. It just seems that the dependency is so ingrained and the withdrawal symptoms you get are so intolerable that people have a great deal of problem coming off. The other aspect is that with heroin, usually the withdrawal is over within a week or so. With benzodiazepines, a proportion of patients go on to long term withdrawal and they have very unpleasant symptoms for month after month, and I get letters from people saying this can go on for two years or more. Some of the tranquillizer groups can document people who still have symptoms ten years after stopping."

c) Professor Malcolm H. Lader, Professor of Clinical Psychopharmacology, Institute of Psychiatry, University of London. 'In Pills We Trust', Discovery Channel, December 4-18, 2002:

"We actually knew from some experiments back in the 1960s that you could have dependence... addiction to benzodiazepines but only on high dose. Later it became apparent that some people were having problems trying to stop and that they weren't on high doses; and then the whole question arose: can you actually get dependent - can you actually become addicted - to normal therapeutic doses? And then the alarm bells started to ring, quietly at first and then louder and louder. Doctors were not well equipped to deal with this. This was something new in their experience. They don't like dealing with chronic drug use or addiction anyway and here they were being confronted by hundreds in their practices - who they had put on the tranquillizers - and were now coming for help to come off. And I think they were bewildered by the numbers and severity of some of the reactions. The main characteristic of these dependent people was that when they tried to stop they didn't just get old symptoms back in an

exaggerated form; they developed new symptoms which they had not experienced before. Some people are put on to these tranquillizers not because they are anxious or have insomnia, they can't sleep, it's because they have muscle spasms - they've been injured in some way - they've had a skiing accident, or they've got a bad back. And they're put on and they've had no psychiatric history, they've had no anxiety, no insomnia, and yet they're just as likely to show dependence and withdrawal when they stop as those with a previous psychiatric history."

d) Caroline Adams, Political Office, 10 Downing Street, London SW1A 2AA, March 19, 2002:

"We regard dependence on benzodiazepines a very important issue and the Department of Health has taken a number of measures to tackle the problem. The main focus of the Department's action in this area has been to try and prevent addiction from occurring in the first place by warning GPs (and other prescribers) of the potential side-effects of the prescribed medicines and the dangers of involuntary addiction to benzodiazepines."

5. BENZODIAZEPINE EQUIVALENCIES

We have requested a statement be sent to providers at the time they are informed of the updates in this petition, which indicates the equivalency of each benzodiazepine. The grounds for this request are as follows:

VARIATION IN MILLIGRAM - TO - MILLIGRAM POTENCY CAUSES CONFUSION WITHIN THE MEDICAL COMMUNITY

There is a common perception that the newer classes of benzodiazepines (Klonopin, Xanax, Ativan, etc.) are "weaker", due to lower milligram strengths needed in dosing, and therefore "safer." The public is being prescribed what may appear like small doses of benzodiazepines based on milligram strengths, but in actuality are being over-medicated with large doses of these so called "minor tranquilizers." When patients present to their physicians with puzzling symptoms (tolerance/physical dependency/withdrawal), they are frequently told it cannot possibly be the medication as they are on very small doses. When physicians do not recognize the potency of the doses their patients are on, the patients are often told they can abruptly stop their doses without the need of a proper taper. This causes a whole new set of problems associated with a cold turkey withdrawal and possibly future protracted withdrawal syndrome.

Below is a table based on Dr. Ashton's work of the half-lives and equivalencies of Ativan, Klonopin, Valium and Xanax. Included as an attachment is an equivalency chart for all FDA-approved benzodiazepines.

Benzodiazepines	Half-life (hrs)² [active metabolite]	Amount (mg)³ Equivalent to 10mg Diazepam (Valium)	Potency compared with diazepam (Valium)
alprazolam (Xanax, Xanor, Tafil)	6-12	0.5	20X more potent per mg than diazepam (Valium)
Clonazepam (Klonopin, Rivotril)⁵	18-50	0.5	20X more potent per mg than diazepam (Valium)
diazepam (Valium)	20-100 [36-200]	10	Same potency per mg as diazepam (Valium)
lorazepam (Ativan, Temesta, Tavor)	10-20	1	10 times more potent than diazepam (Valium)

6. WITHDRAWAL METHODS

We have requested a statement indicating the best practice method of withdrawal be included in all benzodiazepine package inserts/labels and accompanying drug literature. The grounds for this request are as follows:

A. GRADUAL DOSE REDUCTION IS NOT DEFINED

Nearly all the benzodiazepine drug labels indicate that once tolerance and dependence have occurred, the drug must be withdrawn "slowly" or "gradually" but no indication is given as to what "slowly" and "gradually" mean specifically, and the perception of this term varies widely in the medical community. Understanding what is meant by "slowly" and giving specific recommendations on what "slowly" should look like is vital, as the brain needs time to adapt as the dose is lowered. This adaptation time varies from patient to patient. Not withdrawing a patient slowly can be a shock to the body physically dependent on this medication and greatly magnifies withdrawal symptoms, often making them intolerable.

HERE ARE QUOTES FROM THE ACTUAL DRUG LABELS THAT ARE NOT WELL DEFINED:

Valium states:

"It is advisable that they consult with their physician before either increasing the dose or abruptly discontinuing this drug."

"Since the risk of withdrawal phenomena and rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually."

Klonopin states:

"Therefore, when discontinuing Klonopin, gradual withdrawal is essential. While Klonopin is being gradually withdrawn, the simultaneous substitution of another anticonvulsant may be indicated."

*"Treatment should be discontinued gradually, with a decrease of 0.125 mg bid every 3 days, until the drug is completely withdrawn." **This would be considered a fast taper by most people who are physically dependent on the drug.***

"Consequently, after extended therapy, abrupt discontinuation should generally be avoided and a gradual dosage tapering schedule followed"

"However, there are not sufficient data from adequate and well-controlled long-term clonazepam studies in patients with panic disorder to accurately estimate the risks of withdrawal symptoms and dependence that may be associated with such use."

Xanax states

"Do not stop taking this medication abruptly or decrease the dose without consulting your physician, since withdrawal symptoms can occur."

"It is recommended that all patients on XANAX who require a dosage reduction be gradually tapered under close supervision."

"In all patients, dosage should be reduced gradually when discontinuing therapy or when decreasing the daily dosage. Although there are no systematically collected data to support a specific discontinuation schedule, it is suggested that the daily dosage be decreased by no more than 0.5 mg every 3 days. Some patients may require an even slower dosage reduction."

"For patients receiving doses greater than 4 mg/day, periodic reassessment and consideration of dosage reduction is advised. In a controlled postmarketing dose-response study, patients treated with doses of XANAX greater than 4 mg/day for 3 months were able to taper to 50% of their total maintenance dose without apparent loss of clinical benefit. Because of the danger of withdrawal, abrupt discontinuation of treatment should be avoided".

"In any case, reduction of dose must be undertaken under close supervision and must be gradual. If significant withdrawal symptoms develop, the previous dosing schedule should be reinstated and, only after stabilization, should a less rapid schedule of discontinuation be attempted."

"The slower schedule was associated with a reduction in symptoms associated with a withdrawal syndrome."

Ativan States:

"Abrupt discontinuation of product should be avoided and a gradual dosage-tapering schedule followed after extended therapy."

B. PATIENTS ARE OFTEN TOLD BY THEIR DOCTORS:

- They can simply stop taking the drug because they are on such a small dose. (This is a cold turkey situation).
- Some are told to reduce the amount they take by 50% every week until they are off. (This is often too rapid for many who are tolerant to or dependent upon these drugs and causes great suffering).
- Some are taken off abruptly and put on other drugs that do nothing to ease the pain of stopping cold turkey. In many cases this makes the situation much worse by adding more chemicals to a brain already compromised by benzodiazepines.
- Some are sent to detox where they are taken off cold turkey and then returned to the community 14 days later, more often than not in a high state of cold turkey withdrawal and unable to fend for themselves.

C. SURVEY FROM BENZOSUPPORT.ORG

A survey of 346 people showed seventy percent (70%) had tried to withdraw cold turkey at some stage, forty-seven percent (47%) had been subjected to an inpatient detox, and fifty-three percent (53%) had been subjected to a rapid taper.

(Note: members had often been subjected to a number of different withdrawal methods before they were introduced to the slow and more successful method).

D. THE FOLLOWING WITHDRAWAL METHODS, THOUGH RARELY KNOWN IN THE MEDICAL COMMUNITY, ARE THE MOST SUCCESSFUL STRATEGIES:

The only fully studied method of withdrawal from benzodiazepines is the protocol developed by Professor C. Heather Ashton, DM, FRCP, Emeritus Professor of Clinical Psychopharmacology at the University of Newcastle Upon Tyne, England. Dr. Ashton ran a benzodiazepine withdrawal clinic from 1982-1994 for people wanting to come off their tranquillisers. This protocol is detailed in the document 'Benzodiazepines: How They Work and How to Withdraw (aka 'The Ashton Manual'). The essential aspects of this protocol are:

- Gradually crossing patients on shorter-acting benzodiazepines to a longer-acting benzodiazepine, like diazepam, can help eliminate interdose withdrawal symptoms by keeping an even amount of the drug in the bloodstream while tapering. It is important to take the dose at the same time each day to keep blood levels even. (Note: there are cases where the patient does not stabilize because they have become very tolerant to the benzodiazepine).
- Subsequent cuts are made at a rate the patient is able to tolerate. The classic six week withdrawal period adopted by many clinics and doctors is much too fast for many long-term users. The rate of withdrawal, as long as it is slow enough, is not critical. Whether it takes 6 months, 12 months or 18 months is of little significance if one has taken benzodiazepines for a matter of years.
- The length of time between cuts can vary from one to four weeks or as tolerated by the patient. Nevertheless there is no magic rate of withdrawal and each person must find the pace that suits him/her best.
- It is important in withdrawal to always go forward. If one reaches a difficult point, they can stop there for a few weeks if necessary, but they should try to avoid going backwards and increasing their dosage again.
- Patients should avoid compensating for benzodiazepines by increasing their intake of alcohol, cannabis or non-prescription drugs. Occasionally doctors suggest other drugs for particular symptoms, but patients should not take the sleeping tablets zolpidem (Ambien), zopiclone (Zimovane, Imovane) or zaleplon (Sonata) as they have the same actions as benzodiazepines.

(It should be noted that Xanax states: *"To lessen the possibility of interdose symptoms, the times of administration should be distributed as evenly as possible throughout the waking hours, that is, on a three or four times per day schedule."* **This illustrates why Valium, with its longer half-life, is recommended for tapering.**

There are various tapering recommendations by others in the field which have helped achieve successful tapers, such as recommending cuts of no more than ten percent every three weeks as tolerated by the patient, direct tapering when a Valium cross-over is not an option, and using water titration and compounding to facilitate very small cuts. Some even prefer using water titration to make minute cuts on a daily basis versus larger cuts every few weeks.

E. THE ELEMENTS OF A WELL DESIGNED TAPER

The above are guidelines for a well-designed taper and must not be doctor-driven, but patient-driven; the idea is to keep symptoms to a minimum as the dose is lowered. Whatever method is used, it is vital for physicians and patients to have correct withdrawal terms and methods defined; this would prevent needless suffering and make patients as functional as possible during the withdrawal process. For many patients, withdrawal is a very daunting experience to go through regardless of the type of taper instituted.

Petitioners want to emphasize that even with a slow taper, many patients may still have a multitude of symptoms and be nonfunctional. Slow taper does not guarantee a symptom-free taper, or even a taper with only mild symptoms, particularly if the patient is already tolerant to benzodiazepines.

Xanax states:

"Some patients may prove resistant to all discontinuation regimens." (Xanax insert)

This is best avoided by physicians being very reticent to put patients on these drugs in the first place and prescribing them as a last resort after recommending other therapies to address issues patients may have; benzodiazepines should not be prescribed casually. Trying to design treatment plans after a patient is already tolerant to the drug and in withdrawal is a necessary evil, but one which could be avoided on the front end, with strictly enforced prescribing guidelines. Since physicians have no way of predicting which patients will develop physical dependency, they have a moral as well as a professional responsibility to treat every patient as though they have the same potential for this to occur in as little as one week to one month on the drug.

7. CLEAR INFORMATION NEEDS TO GET TO DOCTORS, PHARMACISTS AND PATIENTS

MEDICAL PROVIDERS AND PHARMACISTS MUST BE NOTIFIED OF THESE LABELING CHANGES (as per action requested):

We have requested the FDA contact all pharmacists and medical providers so they will be informed of the information detailed above, including a copy of the benzodiazepine equivalencies.

DRUG COMPANY WEBSITES:

It is important for both patients and doctors to be able to access the same information on a drug manufacturer's site.

PHARMACY LEAFLETS TO PATIENTS NEED TO BE MANDATORY WITH EVERY BENZODIAZEPINE PRESCRIPTION FILLED AND STATE:

In general, benzodiazepines should be prescribed for short periods only (e.g., 2-4 weeks). Extension of the treatment period should not take place without reevaluation of the need for continued therapy. Continued long-term use is not recommended. Withdrawal symptoms (e.g., rebound insomnia, dizziness, agitation, palpitations, etc.) can appear following cessation of the recommended dose after as little as one week of therapy. Abrupt discontinuation of product should be avoided and a gradual dosage-tapering schedule followed after extended therapy. Protracted withdrawal (symptoms lasting months or years after the drug is stopped) is a risk with this class of drug.

TOLL FREE PHONE NUMBERS:

We request a toll-free number and website address be given for all benzodiazepine manufacturers in the drug labeling and pharmacy leaflets.

8. A BLACK BOX WARNING IS APPLIED TO ALL FDA-APPROVED BENZODIAZEPINES

The misinformation regarding benzodiazepines is staggering. People have been seriously injured by this class of drug. People who were on the drug in some cases for only a few months have said that a few months or even a few years later they still had protracted lingering symptoms and are not back to the way they were pre-drug. We request that a Black Box Warning be placed on all FDA-approved benzodiazepines as a warning to doctors who casually prescribe this drug for longer than two to four weeks' use. This will also protect a patient who may wrongly believe if they take the drug at a low dose for a few months (or longer) they will not encounter life altering physical dependency or protracted withdrawal, which we have illustrated is a real risk when using benzodiazepines for over two to four weeks. Benzodiazepine physical dependency has seriously injured people. The kind of drug that can create such brain/CNS chemical injury and cause protracted withdrawal needs a Black Box Warning.

SUICIDE RISK AND DEPRESSION WITH BENZODIAZEPINES also warrants a Black Box Warning. People in our group who have used the drug over two to four weeks often complain they feel dead and hopeless; this is because benzodiazepines put the brain to sleep - they are tranquilizers/downers. In our group we have had members commit suicide because they were in tolerance withdrawal, sick, and unable to stabilize, and other drugs added by their doctor made them worse. We have members very sick with withdrawal symptoms and depressed because they can not function and keep up with their jobs or obligations. We had one member who was a professor at a prominent university but was having serious difficulty dealing with acute withdrawal symptoms. We later found out from his son that he hung himself. He had only been on Ativan a few months, initially prescribed for insomnia.

The benzodiazepine drug labels below state that depression and suicide are an issue with benzodiazepines. Benzodiazepines are also used as anti-seizure drugs and the risk of suicide from anti-seizure drugs has come under scrutiny because of the suicide issue.

Valium states:

"The usual precautions are indicated for severely depressed patients or those in whom there is any evidence of latent depression or anxiety associated with depression, particularly the recognition that suicidal tendencies may be present and protective measures may be necessary.

Psychiatric and paradoxical reactions are known to occur when using benzodiazepines (see ADVERSE REACTIONS). Should this occur, use of the drug should be discontinued. These reactions are more likely to occur in children and the elderly."

"As with other agents that have anticonvulsant activity, when Valium is used as an adjunct in treating convulsive disorders, the possibility of an increase in the frequency and/or severity of grand mal seizures may require an increase in the dosage of standard anticonvulsant medication."

Klonopin states:

"Anyone considering prescribing Klonopin or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness.

"Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers."

Xanax states:

Suicide

"As with other psychotropic medications, the usual precautions with respect to administration of the drug and size of the prescription are indicated for severely depressed patients or those in whom there is reason to expect concealed suicidal ideation or plans."

Ativan patient information states:

"If you are severely depressed or have suffered from severe depression, consult with your doctor before taking this medication. Not recommended for depressive or psychosis disorder"

"Pre-existing depression may emerge or worsen during use of benzodiazepines including lorazepam. Ativan (lorazepam) is not recommended for use in patients with a primary depressive disorder or psychosis."

Dr. Neil Capretto, Medical Director of the Gateway Rehabilitation Center in Pennsylvania, states:

"People were innocently put on benzodiazepines and in some instances it works out well. [But] there is a significant risk and we see it all of the time. Many people who have lost many years of their lives, who have lost jobs, been on the verge of suicide. I'm aware of cases where people have committed suicide. The drug can be dangerous, it can be fatal. During withdrawal the heart rate can go up, they may have a seizure, sometimes the body temperature can go up and in some instances its fatal."

Priest RG, Montgomery SA. Benzodiazepines and Dependence: A College Statement. Bulletin of the Royal College of Psychiatrists (p108) 1988;12:107-109.

"It is now acknowledged that the risks of benzodiazepines far outweigh the benefits in many cases and we would recommend that benzodiazepines should not be used in general for vague or mild disorders and should be prescribed for short-term relief when the problem is (i) disabling (ii) severe or (iii) subjecting the individual to unacceptable distress and even then should ideally be prescribed for no more than one month...The prescribing of benzodiazepines in cases of depression may have serious consequences and may precipitate suicide. Withdrawal from benzodiazepines in many cases may precipitate depression."

A Black Box Warning on this class of drug would bring attention to the serious life-altering issues regarding this drug.

PERSONAL IMPACT STATEMENTS

Most people were surprised and shocked when, having taken a benzodiazepine as prescribed, they realized they had become physically dependent and were suffering tolerance and withdrawal.

Below are just a handful of the thousands of stories e-mailed to our support group in the past couple of years regarding reactions to this drug. These are not isolated situations, but reflect circumstances commonly experienced from locations all over the US and abroad. Many stories we read are from people who took the drug for a few months to a year and at low doses.

(Note: Messages have not been corrected for spelling or grammatical errors; names have been deleted for privacy).

MEMBERS WHO TOOK BENZODIAZEPINES OVER TWO TO FOUR WEEKS, BUT LESS THAN A YEAR (often at low doses):

Group member: June 28, 2009

"I was on .5mg Klonopin daily for one year. Tapered off in four weeks - too fast? The past two days were not too bad, but then I had really no outside pressures. Last night I had bad night sweats all night and barely slept. I had gotten an email about a job fair tomorrow; maybe this is throwing me thinking about facing that. Also the ringing in the ears and trembling in the neck and hands, I am at wits end. Good days and bad days are normal? I have days where I think I'm on the other side of this process, then BAM. Is this normal? Does the dose that one takes before withdrawal make a difference in how bad the symptoms are? My dr. told me I shouldn't have a hard time because I was only taking .5, but I am having a hard time."

Group member: February 8, 2008

"I was unaware about the dangers of benzos, my doctor said benzos could be addictive but I thought that meant abuse, which I knew I would not do, I was not told about physical dependency or withdrawal. After a few months on .5 klonopin I started not feeling well, I started having symptoms I never had before, like floor moving, vibrating in skull, dizziness, none of the doctors I went to figured out it was the drug. It took me 11 months to figure out on my own, when I came across the Ashton manual on line at benzo.org.uk it all came together. I was only on .5 klonopin, but I went to a doctor to help me figure out how to taper, the doctor did not believe my symptoms were from the drug and told me I could just cold turkey since I never took the drug every day (I took 230 pills in 330 days (11 months) well the first 6 months off were hell, all sorts of weird neurological symptoms, could barely function or leave my house do to intense symptoms, slowly things began to lighten up but it was up and down in windows were I felt normal and waves where I would feel symptomatic. I am 22 months off now and feel a million times better then I did on benzos and the first year off, I can still get an odd symptom at times, but I am able to function now. It took a long time to get here and I had zero support from doctors who could not believe .5 klonopin could do what it did, BUT IT DID."

Group member: September 8, 2007

"11 months on 1mg of Lormetazepam, and got strong withdrawal symptoms when I tried to stop. Only found out about all this today. Overwhelmed and need more info / support."

Group member: October 22, 2007

"Was on benzo's for one year and it has destroyed my life. (been on disability from work since July) been off completely for the last 4 weeks and i am going crazy....need help and support."

Group member: January 15, 2007

"Only took 1.5mg of Ativan a day for six weeks—went into acute withdrawal when quit abruptly; ended up in two different ER's in one day with severe numbness in neck, arms, and back, extreme agitation, insomnia, felt like I was going to have a stroke, climbing the wall. Five different doctors didn't recognize the cause—I was told I was on a 'homeopathic dose' so it couldn't possibly be the Ativan.' Ended up having CT scan and left ER undiagnosed; was told to take Ambien. (While in the ER I was told to take another dose of Ativan, and I got quite a bit better, and still no one figured out was wrong!). A pharmacist I called later clued me in. Restarted the Ativan and am in the process of a very long difficult taper off, now two years later, because my doctor did not have good information on how to properly taper me off. Having extreme intestinal problems (bowels basically shut down), withdrawals between my very minute dose taken once a day—all kinds of horrible symptoms, lots of pain."

Group member: May 15, 2009

"I had no idea what was wrong with me and why I felt so horrible. I now believe I am one of those people that formed a dependency to this drug very early on, but I would take it and felt so much better....I thought it was a good thing. I never considered the drug could be the problem, but I realized a few weeks ago after I decided not to take the Ativan for two days in a row that the drug was the problem. On day two it was VERY apparent that the drug was causing me problems if I didn't have it. I now believe I have felt so terrible for over a year now because of inter-dose withdrawal. After such a long time of feeling terrible.... well...it's exhausting. I'm sure that's everyone's experience, I doubt I'm unique."

Group member: January 22, 2008

"Have been on Klonopin for one year. Quit taking drug six weeks ago and having a lot of scary symptoms."

Group member: *January 6, 2008*

"I have been taking Klonopin for about a year now and have been trying to slowly taper off, but have been having a tough time."

Group member: *February 11, 2008*

"I successfully tapered off benzos about 3 years ago. Stupidly, I took 10 xanax over a period of about 2.5 - 3 months and I'm now experiencing benzo w/d. I need help getting back off."

Group member: *April 4, 2008*

"Took Benzo's for about 1 month. Stopped cold turkey. I started experiencing severe symptoms."

Group member: *April 17, 2008*

"GP prescribed klonopin 1mg as a sleep aid. I stopped taking it after 3 weeks (when it stopped working) and I am now experiencing the withdrawal symptoms listed on this site."

Group member: *June 16, 2009*

(This member had all these tests before figuring out her symptoms were caused by benzodiazepine withdrawal)

"Just thinking out loud here.....Since going thru this ordeal these are the medical tests I have had:

- CT of my chest – it made my glands swell for some reason*
- x-rays – while in tolerance wd I developed pneumonia*
- 2 ct of the upper abdomen*
- upper gi and swallow test – couldn't swallow!*
- 3 endoscopies*
- colonoscopy*
- 2 stress tests*
- doppler of coronary artery – just paranoid*
- echo of heart*
- ct of heart*
- 3 24 hr. heart monitors*
- 1 30 day heart monitor*
- ct of sinuses-kept smelling amonia!*
- emg – neurological disturbances*
- test for parkinson's*
- an extra eye exam – blurry vision*

- small tube placed in tear duct to help with dry eyes
- endless, and I mean endless, blood tests!
- priceless wasted prescriptions – but I would not taken them!
- Thyroid underactive – this did pan out to be true

Love to you all! (9 months off Klonopin and a beta blocker to go!) Did I mention I just turned 37?"

MEMBERS WHOSE DOCTORS WERE NOT AWARE OF HOW TO TAPER THEIR PATIENTS OFF BENZODIAZEPINES (This is very common in the group):

Group member: August 4, 2009

"I have been on board since February 2008. I completed my taper on May 1, 2009. I have a family doctor who has been my doctor for almost 30 yrs. She was absolutely no help during my taper, tried to get me off in 5 days, lucky I found this group or I would not have survived it."

Group member: September 20, 2008

"I was advised to stop only .5mg of clonazepam in one month. I ended up in hospital with throat spasm, inability to swallow properly, and heart arrhythmias, not to mention all the other symptoms that come with - anxiety, irritability, insomnia, constant uneasiness, dizziness etc."

Group member: April 14, 2008

"Was told by my doctor that I could taper .5 klonopin in a week since it was a "low dose" at 5 weeks off was still sick as a dog with dizziness, vertigo, motion sickness, zero apatite, brain fog, tight band around head, no sleep, felt agitated like my body had trouble being still (not normal restlessness or butterflies), my head felt like I might have a seizure and other scary strange sensation like the floor seemed wobbly, I ended up going to the emergency room and was told I was having a panic attack and it was not the drug since it was out of my system after 30 days. I paid 1,600 out off pocket to go there and the doctors were clueless as to what I was going through and rather condescending to boot, they even suggested anti-depressants for my "panic attack", which I refused. After learning from this support group that it could take 18 months to heal I rode it out and by 6 months off I was seeing improvement, by 18 months off I was much better symptoms wise, I was functioning and working a full time job, what ever symptoms I still had I could deal with, they were no where near as debilitating felt normal most of the time."

PROTRACTED WITHDRAWAL - MEMBERS WITH SYMPTOMS LASTING MONTHS OR YEARS AFTER STOPPING THE DRUG:

Group member: August 4, 2009

"I have been feeling really despondent because I am still having some w/d problems at 26 months off".

Group member: August 3, 2009

"I rarely sign on here anymore, but I saw your post today and wish you all the best! It has been almost 3 yrs off ativan and lunesta for me and I am 95% healed now. Some residual symptoms remain, but they are not keeping me from living my life. If I can do it, anyone can. I wish you the best on your journey! 35 months benzo & lunesta free"

Group member: July 26, 2009

"5 years off all psychiatric medications. Mentally and physically doing pretty well, but still have some lingering symptoms that I never had before taking these medications."

Group member: July 25, 2009

"I was prescribed 10mgs of Klonopin for 16 years when a doctor- an 'addiction specialist'- had me discontinue the drug cold turkey at home, alone, with no other support. Despite being over 3-1/2 years off the drug, I still experience a number of lingering symptoms, including derealization/ depersonalization, insomnia, tinnitus, muscle tightness and jerking, fatigue, heightened anxiety and hyper-arousal, and a number of neurological symptoms. Though these symptoms are not constant, nor are they nearly as severe as they were during the first year or so off the drug, I still remain exquisitely sensitive to sound; a condition which severely limits the environments I can tolerate being in."

Group member: July 23, 2009

"3 years off today feel normal 95% of the time, but still have lingering symptoms, like dizziness, lightheaded or agitated feeling in head and body. Healing does happen, it just takes a long time."

Group member: January 29, 2009

"Detox c/t from xanax. Two visits to the hospital before figuring out it was benzo withdrawal. Reinstated on valium and completed a taper. Free almost going on 9 months and not fully recovered."

Group member: August 2, 2008

"I am at 11 months off (Xanax) and still not well. When I was c/t I had hallucinations, was delirious, thought I was dying. As time progressed I became very hostile, nasty, irritable etc. Then the physical symptoms kicked in, I had this feeling of wanting to come out of my skin (hard to explain), nausea, loss of appetite, could not sit still or sleep. My heart rate was at a steady 100-105 and I shook like a leaf. I went from hot to cold. I had vertigo. I began to experience depersonalization/derealisation badly. I stayed in my bed for months. I am able to get out of bed but I'm still not well. I have extreme fear, anxiety, and panic. I am still scared to leave the house but force myself when I need to. I had to resign from my job of 7 1/2 years. This is the most horrible thing someone can go through. At least in my case. Some people come off and they are fine. I thought I'd be well by now."

Group member: June 19, 2008

"I have been off benzos for over a year, and would like to join a community of people who understand how one can suffer after this long being off of benzos."

Group member: May 19, 2008

"I am benzo free for a year and a half. It was the hardest fight of my life. I now sleep and most of the time I am panic-free. I am very grateful to be benzo-free everyday."

Group member: April 24, 2008

"I was on this horrible drug for only a year and have had to go through 17 months of up and down hell after getting off, but now I can say that I feel much better now, although not symptom free."

Group member: February 16, 2008

"3 years ago I was prescribed Valium 10 mg for sleep-took it for 14 months and was told by my doctor to cold turkey-still sick after 14 months."

OPPOSITION

There are people that seem to go off benzodiazepines without issue. In those cases physical dependency has most likely not occurred....yet. Why some people seem to get physically dependent sooner than others we don't know. It could be genetic, although there have been people who went off the drug without issue the first time, but the second time got stuck with debilitating withdrawal. Doctors who give out the drug have no way of knowing who will have an issue and when, and this is why the drug should not be prescribed for longer than two to four weeks' use.

OUR PETITION IS BASED ON THE FOLLOWING PREMISES:

BENZODIAZEPINE FACTS:

The following are established benzodiazepine facts:

- Tolerance and physical dependency can occur in some people in as little as two to four weeks of continuous benzodiazepine use.
- Tolerance, physical dependency, and a withdrawal syndrome are significant problems associated with the use of benzodiazepines past two to four weeks of use.
- There are many symptoms associated with tolerance, physical dependency, and withdrawal.
- The withdrawal syndrome may affect 30%–40% of those who consume benzodiazepines past two to four weeks of continuous use.
- Once tolerance or physical dependency has developed, benzodiazepines should be withdrawn slowly.
- The only scientifically investigated method of withdrawing people from benzodiazepines is the Ashton protocol, detailed in the Ashton manual, recommending a very slow taper.
- There is a protracted withdrawal syndrome associated with getting off benzodiazepines; it affects 10% –15% of those who consume the drug for longer than four weeks.

We have taken each of these facts and presented evidence to support them. Any opponents to this petition would need to prove the above statements to be inaccurate. We are convinced that this would be impossible as they have been recognized by scientists and medical people specializing in the area of benzodiazepine research and dependency worldwide for a number of decades.

THE ABOVE FACTS ARE NOT WIDELY KNOWN BY MEDICAL CARE PROVIDERS

We have presented a range of information to show that benzodiazepine facts are not widely known by medical care providers:

- In excess of 100 million prescriptions were written for benzodiazepines in 2007 in the US; the US population for 2007 was approximately 304 million people. The number of prescriptions written in 2007 was greater than in 2006.
- As far back as 1990, 11 million Americans were given a prescription for benzodiazepines and it is estimated that about two percent (2%) of the adult population of the US (around four million people) appear to have used prescribed benzodiazepine hypnotics or tranquilizers regularly for five to ten years or more.
- Fifty percent (50%) of 348 people who participated in the www.benzosupport.org survey in 2007 had been prescribed benzodiazepines for more than five years; some had been prescribed them in excess of 20 years.
- Seventy percent (70%) of the 348 people who participated in the same survey in 2007 had tried to withdraw cold turkey from benzodiazepine at some stage; forty seven percent (47%) had been subject to an inpatient detox; and fifty three percent (53%) had been subject to a rapid taper.

These figures strongly suggest that something is very wrong with the knowledge base amongst physicians, pharmacists, and patients regarding benzodiazepines. Any opponent to this petition would need to present statistics establishing that there is not a problem in the knowledge base associated with benzodiazepines. Any opponent to this petition would need to establish that these problems are not occurring.

LACK OF KNOWLEDGE IS CAUSING HARM TO MANY PEOPLE

Following is a collection of quotes from members and their doctors. Some of them are funny and some of them show a frightening lack of understanding of benzodiazepines and withdrawal.

Comments confusing withdrawal and underlying diseases:

"The drugs are out of your system so this is the underlying anxiety and depression you're feeling right now."

"There is no way this is drug withdrawal. The drugs are out of your system. After a month, the underlying diseases show up."

The insulin comment:

"It's like insulin for diabetes - some people need these drugs to function"

Comments confusing addiction/dependency with the need to take benzodiazepines to function:

"You're confusing addiction with just needing the drugs. There's nothing wrong with needing them to function."

"Often only when you come off the drugs do people realize how much they really needed them."

"It's not an opinion, it's a fact - you were working and doing well while on the medications - now you're not working - you need them to function - nothing wrong with that."

"So what if you're 'dependent' on the drugs or you can't stop them quickly. If you were living a normal life, just deal with the side effects. They're not THAT bad and you're not functioning right now..."

"It's not physical dependence if you need the drugs."

Comments that underrate the difficulty of withdrawing from benzodiazepines:

"I've seen people go through true drug withdrawal and this isn't what is going on."

"Getting off the last .25mg of K is just psychological - just do it, you will be fine."

"This isn't acute withdrawal - just go out and have some fun and you will get better."

Patient: "Doctor you must have known that taking me off 3.5mg of K in three weeks was going to make me very ill." Doctor: "I just kind of hoped it wouldn't."

"You are being oversensitive to these symptoms - just get on with your life and everything will feel better."

"The tranquilizers haven't done this to you, all you need to do is go out and buy a new red sports car and you will be fine!"

Therapist: " You need to accept that your withdrawal symptoms are 100% psychological or you will get nowhere." Patient: "Benzo withdrawal is mostly a physical phenomenon." Therapist: "You are hopelessly in denial and no amount of therapy will help you."

Comments that were just wrong:

Patient: "Is K addictive?" Doctor: "Not if you are not taking it for anxiety - you will have no trouble getting off it if you need to."

"You can go off today (cold turkey). However, I think that a good amount of your nausea and lightheadedness is stress-related, and not entirely attributed to Klonopin withdrawal. Some people have mild withdrawal symptoms for a few weeks"

"My doctor said in regard to the extreme muscle pain I am having in my legs from withdrawal that "Its your varicose veins."

Comments about the length of the withdrawal syndrome:

"Most people get better after two months -- I'm not sure why it's taking you so long."

"This is not withdrawal - it is out of your system after 30 days."

"Withdrawal only occurs to people that have taken high doses for a long time."

Comments from those who just want to add more drugs:

"We need to approach this taper from a place of strength -- have you tried Effexor?"

"I think this is not just withdrawal from the Klonopin, but a cycle of anxiety/stress that requires Lexapro to be broken."

"Trust me, if you will just take Paxil as I tell you, you will be fine."

Other Comments:

"Wow, you're having the worst withdrawal of anyone I've ever seen."

"Trust me, I'm a doctor."

"Don't worry you don't have an addicting type of personality."

And the best: "Huh."

IT IS THE FDA'S RESPONSIBILITY TO RECTIFY THE SITUATION

The FDA's mission statement is as follows:

"The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health."

No opponent to this petition could reasonably argue that the FDA is not responsible for assuring that all relevant parties receive accurate information about these drugs.

The makers of Ativan have already updated their literature to contain much of the needed detail. It would seem logical that all other manufacturers be required to do the same.

Many of the medical authorities in the western world have communicated the dangers associated with benzodiazepines directly to their healthcare providers so there is no doubt about proper benzodiazepine protocols. The World Health Organization has also issued statements on this subject. The FDA should be taking the lead in this matter.

Opponents to this petition might argue that the measures suggested are not the most efficient ways of solving the problems detailed. If this is suggested, alternative proposals capable of achieving the same results need to be put forth.

CONCLUSION

The thousands of e-mails the petitioners have received from our support group illustrate that people all over the world have been negatively affected by benzodiazepine use. Even short-term, low dose users have reported taking months or even years to heal after the drug has been stopped. Involuntary benzodiazepine dependency is a life-altering experience, and is not a result of illicit use or abuse. The fact that patients were not informed of the risks before starting this drug, or received little support or awareness from their doctors and pharmacists when they started having issues while on the drug, compounds the problem. Some seek out support from on-line websites; but, sadly, many fall through the cracks. Accurate, consistent, and comprehensive product information by all benzodiazepine manufacturers is a fairly simple yet crucial step in preventing future iatrogenic benzodiazepine sufferers.

Citizens rightfully expect the FDA to take appropriate action in such matters, and should not have to resort to a desperate search for information from outside the established healthcare system. They deserve what is already legally mandated - accurate information from their healthcare providers who prescribed these drugs in the first place. Benzodiazepines require stronger pharmacovigilance. Consumers deserve to know every effort is being made to ensure their safety through rigorous testing and ongoing monitoring of pharmaceuticals, all done to prevent adverse effects. Current benzodiazepine product information does not clearly communicate to providers or patients the potential known risks with use of this class of drug, nor does it provide advice on how to avoid/reduce such risks.

Class IV drugs such as benzodiazepines should never be casually prescribed. The FDA has the power to initiate education and help stop this problem from the start, which would prevent patients from being harmed.

The FDA should be at the helm of providing accurate product labeling. There are many cases where the FDA has taken swift action to get products off the market (for example, Zicam Cold Remedy/Zicam zinc nasal spray) that have harmed far fewer people than those affected by benzodiazepines due to inappropriate prescribing. The problems of physical dependency and withdrawal from benzodiazepines have been known for years, yet no productive action has yet been taken by the FDA to protect consumers.

We urge the FDA to review this issue and take action to make the requested changes of requiring accurate package inserts and accompanying drug literature in all FDA-approved benzodiazepine products. Our desire is that in the future, support groups such as ours will no longer be necessary, due to the FDA taking the action requested in this petition.

ENVIRONMENTAL IMPACT STATEMENT

No environmental impact analysis is required in support of this petition, and the granting of this petition would not have any environmental impact.

However, it should be noted that disposal of benzodiazepines and other prescription drugs should not take place in the home (e.g., flushed down the toilet) as these drugs make their way into the waterways. This not only poses a threat to our drinking water, but is destroying our ecosystem.

THE ATHENS DECLARATION as unanimously voted on August 3rd, 2007 at the 2nd International Conference on Environment in the City of Athens Cultural Center is as follows:

We, an international group, support the following six reasons to address citizen unused drug disposal:

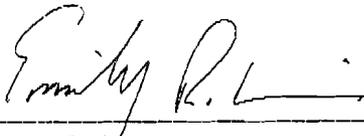
1. To curtail childhood overdoses
2. To restrict household drug theft
3. To limit accumulation of drugs by the elderly
4. To protect our physical environment
5. To restrain improper international drug donations
6. To eliminate waste in the international health care systems of all countries

We call upon governments, NGO's, and citizens everywhere to correct policies and practices that foster waste in the health care systems of all countries and endanger humans, animals, and our physical environment.

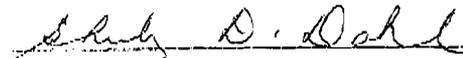
CERTIFICATION

The undersigned certifies that, to the best of his/her knowledge and belief, this petition includes all information and views on which the petition relies, and it includes representative data and information known to petitioner, which is unfavorable to the petition.

PETITIONERS' SIGNATURE PAGE

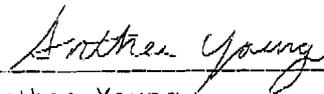


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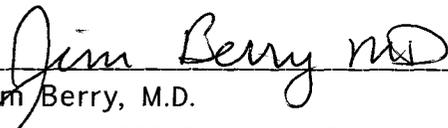
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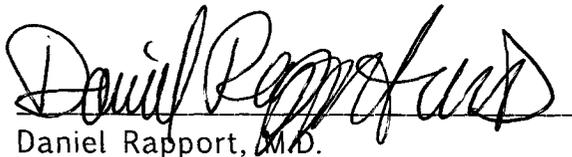
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Enclosures 2,3,5, and 6