Alprazolam is a white crystalline powder, which is soluble in methanol or ethanol but which has no appreciable solubility in water at physiological pH.

Each alprazolam tablet, for oral administration, contains 0.25, 0.5, 1 or 2 mg of alprazolam. Alprazolam tablets, 2 mg, are multi-scored and may be divided as shown below:

<table>
<thead>
<tr>
<th>Tablet strength</th>
<th>Segments</th>
<th>Segments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>0.5 mg</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1 mg</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2 mg</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Inactive ingredients: Canmoly ethylsulfate, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, sodium benzoate and sodium starch glycolate. In addition, the 2 mg tablets contain FD&C Blue No. 1 Aluminum Lake and the 1 mg tablet contains FD&C Blue No. 1 Aluminum Lake.


CENTRAL NERVOUS SYSTEM AGENTS

Diazepam (Valium) is the prototype benzodiazepine drug. benzodiazepine class of compounds that exhibit unique therapeutic and toxicologic properties. The development of this class of agents was begun in the 1950s with the introduction of the first benzodiazepine, chlordiazepoxide (Librium). Benzodiazepines are structurally related to the neurotransmitter, GABA (gamma-aminobutyric acid), and have affinity for the GABA receptor complex. Benzodiazepines have been shown to increase the inhibitory effects of GABA, and although benzodiazepines are known as anxiolytics, the mechanism of action for this benefit is not well understood.

Benzodiazepines are the most commonly prescribed drugs in the United States, with over 160 million prescriptions written annually. Benzodiazepines are indicated for the treatment of anxiety disorders, alcohol withdrawal syndrome, insomnia, and seizure disorders. Benzodiazepines are also used as premedications before surgery and as sedative-hypnotics in anesthesiology.

Benzodiazepines have been shown to be effective for the treatment of anxiety disorders, particularly generalized anxiety disorder (GAD). Benzodiazepines have been shown to reduce symptoms such as restlessness, lassitude, and cognitive impairment. Benzodiazepines have also been shown to be effective for the treatment of anxiety-related conditions such as panic disorder, social phobia, and post-traumatic stress disorder (PTSD).

Benzodiazepines are also used as premedications before surgery and as sedative-hypnotics in anesthesiology. Benzodiazepines are commonly used as anxiolytics for the treatment of alcohol withdrawal syndrome and as hypnotics for the treatment of insomnia. Benzodiazepines are also used as anticonvulsants for the treatment of seizures and as muscle relaxants for the treatment of muscle spasticity.

Benzodiazepines are metabolized by the liver and primarily excreted in the urine. Benzodiazepines are subject to significant first-pass metabolism, and therefore, the oral bioavailability of these drugs is variable. Benzodiazepines are typically dosed every 8 to 12 hours, and the half-life of these drugs ranges from 8 to 48 hours, depending on the specific benzodiazepine.

Benzodiazepines are subject to significant abuse and dependence, and therefore, they are classified as Schedule IV controlled substances. Benzodiazepines are associated with numerous adverse effects, including sedation, dizziness, and cognitive impairment. Benzodiazepines are also associated with withdrawal symptoms, including rebound anxiety and seizures, if the dose is abruptly discontinued.

Benzodiazepines are also associated with numerous drug interactions, including the potential for life-threatening interactions with other CNS depressants such as alcohol, opioids, and other benzodiazepines. Benzodiazepines are contraindicated in patients with a history of drug or alcohol dependence, as well as in patients with a history of suicidal ideation or behavior.

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In addition to the relatively common (i.e., greater than 1%) untoward events enumerated in the table above, the following adverse events have been reported in association with the use of benzodiazepines: drowsiness, dizziness, nausea, anorexia, vomiting, diarrhea, weight loss, vomiting, diarrhea, rebound insomnia, dream disturbances, pruritus, diaphoresis, changes in bowel, menstrual irregularity, incontinence and urinary retention.

### PANIC DISORDERS

#### Treatment-Emergent Symptom Incidence

<table>
<thead>
<tr>
<th>ALPRAZOLAM TABLETS</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>1980</td>
</tr>
<tr>
<td>% of Patients Reporting</td>
<td>30.2</td>
</tr>
</tbody>
</table>

### ADDITIONAL INFORMATION

- **DOSAGE AND ADMINISTRATION**

  - **Primary Therapeutic Indication**:

  - Lasting improvement of panic disorder, defined as a reduction of ≥50% in frequency of panic attacks and associated symptoms (e.g., autonomic symptoms, cognitive symptoms, and discomfort) compared to baseline.

  - **Suggested Dosage**:

    - Initial dosage: 0.5 mg or 1 mg, given in divided doses.
    - Titration rate: 1 mg or 2 mg per day, as tolerated, up to a maximum daily dose of 4 mg.

  - **Treatment Algorithm**:

    1. **Initial Dosing**:

       - Start with 0.5 mg or 1 mg, given in divided doses.

    2. **Titration**:

       - Titrate the dose by 1 mg or 2 mg per day, as tolerated, up to a maximum daily dose of 4 mg.

  - **Rapid Dosing**:

    - If a rapid decrease in dose is required, discontinue alprazolam 2 mg or more per day to avoid withdrawal symptoms.

### ADVERSE REACTIONS

- **Incidence of Treatment-Emergent Symptom Incidence**

<table>
<thead>
<tr>
<th>ALPRAZOLAM TABLETS</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>300</td>
</tr>
<tr>
<td>% of Patients Reporting</td>
<td>22.6</td>
</tr>
</tbody>
</table>

- **Events reported by 1% or more of alprazolam tablet patients included**:

  - **Somnolence**

  - **Other**

- **Events reported by at least 1% but less than 10% of patients receiving alprazolam included**:

  - **Somnolence**

  - **Other**

### CLINICAL STUDIES

- **Support for the Usefulness of Alprazolam Tablets in the Treatment of Panic Disorder**

  - A double-blind, placebo-controlled study in patients with panic disorder showed that alprazolam 0.5 mg, 1 mg, or 2 mg/day was significantly more effective than placebo in reducing the frequency of panic attacks and associated symptoms.

  - **Phase 3 Clinical Trials**

    - **Alprazolam Tablets**
      - In a double-blind, placebo-controlled study in patients with panic disorder, alprazolam 0.5 mg, 1 mg, or 2 mg/day was significantly more effective than placebo in reducing the frequency of panic attacks and associated symptoms.

### HOW SUPPLIED

- **Alprazolam Tablets**

  - **5 mg**
  - **2 mg**

### QUALIFIED PHARMACEUTICALS

- **Huntsville, AL 35801**

  - **213-822-2387**

  - **Ref 13/22**

  - **R2**