Read all of this leaflet carefully before you start taking this medicine:

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- If any of the side effects gets serious, or you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

IN THIS LEAFLET:
1. What Ativan Injection is and what it is used for.
2. Before you take Ativan Injection.
3. Receiving Ativan Injection.
4. Possible side effects.
5. How to store Ativan Injection.
6. Further information.

1. WHAT ATIVAN INJECTION IS AND WHAT IT IS USED FOR

The name of your medicine is Ativan Injection. The active ingredient in Ativan Injection is lorazepam, which is a member of a group of medicines called benzodiazepines. It helps to relieve anxiety and muscle tension.

Ativan Injection is usually prescribed as pre-medication to help you to relax before an operation or before uncomfortable or prolonged investigations. It may also be used to relieve short periods of anxiety, excitement or agitation, and in the control of convulsions.

2. BEFORE YOU TAKE ATIVAN INJECTION

You should not be given Ativan Injection if:

- You have severe breathing or chest problems.
- You are allergic to benzodiazepines or any of the ingredients in Ativan Injection (see Section 6 for a full list of ingredients).
- You have myasthenia gravis (a disease causing weakened muscles and excessive tiredness).
- You have serious liver problems.
- You suffer from sleep apnoea (breathing problems when you are asleep).

If you are an out-patient you should not be given Ativan Injection unless you have somebody to take you home.

Ativan Injection contains benzyl alcohol and should not be used in infants or young children up to 3 years old.

Tell your doctor or pharmacist if:

- You are pregnant or trying to become pregnant.
- You are breast-feeding, since the drug may pass into breast milk.
- You abuse or have in the past abused drugs or alcohol.
• You have a personality disorder. If so, you have a greater chance of becoming dependent on lorazepam.
• You have any kidney or liver problems.
• You have suffered from depression in the past since it could re-occur during treatment with lorazepam.
• You are currently suffering from depression, since lorazepam may increase any suicidal feelings, which you may have.
• You suffer from breathing problems.
• You suffer from an eye problem called glaucoma.
• You enter hospital for treatment.

Taking other medicines

You should tell your doctor or pharmacist if you are taking any other medicines, including those which have not been prescribed by a doctor, since they may affect the way Ativan Injection works. Ativan Injection may also affect the way other drugs work.

In particular, you should tell your doctor if you are taking any other sedative, anti-anxiety drugs, antidepressants, strong pain killers (e.g. methadone), drugs for epilepsy, antihistamines, drugs for mood or mental disorders (e.g. chlorpromazine, clozapine and haloperidol), drugs for respiratory diseases, drugs for gout (probenecid). The dose of these drugs may need to be reduced before you can take Ativan Injection. You should also tell your doctor if you are taking a drug called scopolamine, which may be used for gut problems or before an operation.

Taking Ativan Injection with food and drink

You should avoid alcohol for at least 24 to 48 hours after receiving Ativan Injection.

Pregnancy and breast-feeding

If you are pregnant or might become pregnant do not take this medicine without consulting your doctor first. Benzodiazepines, including Ativan Injection, may cause damage to the foetus if taken during early pregnancy. If you take this medicine during late pregnancy or during labour, your baby, when born, may be less active than other babies, have a low body temperature, be floppy or have breathing or feeding difficulties for a while. Your baby’s response to the cold might be temporarily impaired also. If this medicine is taken regularly in late pregnancy, your baby may develop withdrawal symptoms after birth.

Talk to your doctor or pharmacist if you are breast-feeding, since the drug may pass into breast milk.

Driving and using machines

Do not drive or use machinery within 24 to 48 hours of receiving Ativan Injection. The medicine can affect your ability to drive as it may make you sleepy or dizzy.
• Do not drive while taking this medicine until you know how it affects you.
• It is an offence to drive if this medicine affects your ability to drive.
• However, you would not be committing an offence if:
  o The medicine has been prescribed to treat a medical or dental problem and
  o You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
  o It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.
Important information about some of the ingredients of Ativan Injection

Toxic effects (including seizures) caused by the ingredients contained in Ativan Injection (polyethylene glycol and propylene glycol) have been reported following very high doses of Ativan Injection.

3. RECEIVING ATIVAN INJECTION

Your doctor will give you Ativan Injection, by injecting it into one of your veins (intravenously) or into one of your muscles. Ativan Injection may be diluted with water or saline just before it is given to you. The amount of Ativan Injection you are given will depend on how much you weigh and why it is being given to you:

- Before an operation or investigation, you will usually be given 0.05 mg of Ativan Injection for each kilogram that you weigh (e.g. if you weigh 70 kilograms you will receive 3.5 mg of Ativan Injection).

- For anxiety or excitement, the usual dose is 0.025 to 0.03 mg for each kilogram that you weigh (e.g. if you weigh 70 kilograms you will probably receive 1.75 to 2.1 mg of Ativan Injection).

- When Ativan Injection is used to control convulsions a dose of 4 mg is usually given intravenously to adults. A lower dose of 2 mg given intravenously is usually given to control convulsions in children.

Your doctor may prescribe a different dose or length of treatment, especially if you are elderly.

Some people feel sleepy after receiving Ativan Injection. Therefore, you may need to stay in hospital for at least 8 hours, or overnight, after receiving your injection. If you are to leave hospital shortly after receiving Ativan Injection you should have someone with you.

Ativan Injection is usually only prescribed for one or two doses, or for a short course of treatment. This reduces the risk of becoming dependent on Ativan Injection, or suffering unpleasant effects when you stop taking it (See ‘Stopping your medicine’, below).

Instructions for use:

Ativan ampoules are equipped with the OPC (One Point Cut) opening system and must be opened using the following instructions:

- hold with one hand the bottom part of the ampoule
- put the other hand on the top of the ampoule positioning the thumb above the coloured spot and press back using thumb and hand. Please see diagram below.

Stopping your medicine:
• After you have finished your prescribed treatment with Ativan Injection, your doctor will decide whether or not you need further treatment.

• Following a course of treatment your dose of Ativan Injection may be reduced slowly. This allows your body to get used to being without Ativan Injection, and reduces the risk of unpleasant effects.

• On stopping Ativan Injection, you may experience symptoms such as headaches, muscle or stomach pains, anxiety, tension, depression, restlessness, sweating, sleep problems, confusion or irritability. If these symptoms do occur, they do not usually last for long. If you suffer from any of these symptoms, ask your doctor for advice.

• If you suffer from any of the following symptoms; loss of the sense of reality, tinnitus (ringing sounds in your ears), numbness or tingling of your arms or legs, vomiting, twitching, hallucinations, convulsions, or effects on sight, hearing or touch, ask your doctor for advice immediately.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Ativan Injection can cause side effects, although not everybody gets them.

It is very important that you immediately contact your doctor if you develop any of the following symptoms:

• Anaphylactic (severe allergic) reactions
• A serious allergic reaction which causes swelling of your face or throat (angioedema)
• Develop signs of jaundice (yellowing of the skin or the whites of the eyes)
• Difficulty breathing
• Thoughts of harming or killing yourself
• Changes in your mental state.

Tell your doctor or pharmacist if you develop any of the following side effects:

Very common (affect more than 1 in 10 patients):

• Drowsiness, sedation
• Tiredness.

Common (affect more than 1 in 100 patients but less than 1 in 10 patients):

• Confusion, depression, unmasking of depression
• Lack of muscle coordination, dizziness
• Muscle weakness
• Lack of energy.

Uncommon (affect more than 1 in 1000 patients but less than 1 in 100 patients):

• Nausea
• Changes in sex drive, impotence, decreased orgasm.

The following side effects have also been reported with this class of medicine:
- Blood disorders which can include lower levels of red blood cells, white blood cells and platelets (known as blood dyscrasias). Symptoms of this include unexplained bruising, bleeding, pale skin, weakness and/or breathlessness, mouth ulcers and/or frequent infections.
- Allergic reactions
- Abnormally concentrated urine
- Low levels of sodium in the blood
- Loss of inhibitions, euphoria, thoughts or attempts of suicide
- Anxiety, agitation, excitation, hostility, aggression, rage, sleep disturbances/insomnia, sexual arousal, and hallucinations
- Involuntary trembling, vertigo, visual disturbances (including double vision and blurred vision), slurred speech, headache, vomiting, convulsions/seizures, memory loss, coma
- Low blood pressure
- Reduced breathing rate, shortness of breath, temporary cessation of breathing, including during sleep
- Worsening of chronic obstructive lung disease
- Constipation
- Increase in specific liver enzymes (bilirubin, liver transaminases and alkaline phosphatase)
- Allergic skin reactions, hair loss
- Hypothermia.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE ATIVAN INJECTION

Ativan Injection should be stored and transported refrigerated (2°C to 8°C).

Keep ampoule in the outer carton to protect from light.

Keep out of the reach and sight of children.

Do not use Ativan Injection after the expiry date, which is stated on the carton. The expiry date refers to the last day of that month.

6. FURTHER INFORMATION

What Ativan Injection contains

The active ingredient in Ativan Injection is lorazepam, and there are 4 mg of lorazepam in each 1 ml of the injection.

The other ingredients in Ativan Injection are polyethylene glycol, benzyl alcohol and propylene glycol.

What Ativan Injection looks like and contents of the pack

Ativan Injection is supplied in small clear glass bottles (called ampoules) and each ampoule contains 1 ml of Ativan Injection.

Ativan Injection is supplied in packs of 10 ampoules.

The Marketing Authorisation Holder is:
Pfizer Limited
Ramsgate Road
Sandwich
Kent,
CT13 9NJ
United Kingdom

The Manufacturer is:

Haupt Pharma Livron
1 rue Comte de Sinard
26 250 Livron Sur Drome
France

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This leaflet can be made available in large print, audio or Braille on request. Contact 0800 198 5000 to request this, quoting the following number: 00057/1279.

Ref: AT 6_1
1. NAME OF THE MEDICINAL PRODUCT
Ativan® Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Ativan Injection contains the active ingredient lorazepam at a concentration of 4 mg/ml.

Lorazepam (INN, BAN) is chemically defined as 7-chloro-5-(o-chlorphenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one.

3. PHARMACEUTICAL FORM
Solution for injection

Clear, colourless solution supplied in clear glass ampoules containing 4 mg lorazepam in 1 ml of solution.

4. CLINICAL PARTICULARS
4.1 Therapeutic Indications

Pre-operative medication or premedication for uncomfortable or prolonged investigations, e.g. bronchoscopy, arteriography, endoscopy.

The treatment of acute anxiety states, acute excitement or acute mania.

The control of status epilepticus.

4.2 Posology and method of administration

Dosage and duration of therapy should be individualised. The lowest effective dose should be prescribed for the shortest time possible.

Treatment in all patients should be withdrawn gradually to minimise possible withdrawal symptoms (See special warnings and precautions for use).

Route of administration

Ativan Injection can be given intravenously or intramuscularly. However, the intravenous route is to be preferred. Care should be taken to avoid injection into small veins and intra-arterial injection.

Absorption from the injection site is considerably slower if the intramuscular route is used and as rapid an effect may be obtained by oral administration of lorazepam.

Ativan should not be used for long-term chronic treatment.

Preparation of the injection
Ativan Injection is slightly viscid when cool.

**Intramuscular administration:**

A 1:1 dilution of Ativan Injection with normal saline or Sterile Water for Injection BP is recommended in order to facilitate intramuscular administration.

**Intravenous administration:**

For intravenous administration, Ativan Injection should always be diluted with saline or Sterile Water for Injection BP as a 1:1 dilution.

Ativan Injection is presented as a 1ml solution in a 2ml ampoule to facilitate dilution.

Ativan Injection should not be mixed with other drugs in the same syringe.

**Dosage:**

1. **Premedication:**

   **Adults:** 0.05mg/kg (3.5mg for an average 70kg man). By the intravenous route the injection should be given 30-45 minutes before surgery when sedation will be evident after 5-10 minutes and maximal loss of recall will occur after 30-45 minutes.

   By the intramuscular route the injection should be given 1-1 1/2 hours before surgery when sedation will be evident after 30-45 minutes and maximal loss of recall will occur after 60-90 minutes.

   **Children:** Ativan Injection is not recommended in children under 12.

2. **Acute Anxiety**

   **Adults:** 0.025-0.03mg/kg (1.75-2.1mg for an average 70kg man). Repeat 6 hourly.

   **Children:** Ativan Injection is not recommended in children under 12.

3. **Status epilepticus**

   **Adults:** 4mg intravenously

   **Children:** 2mg intravenously

   **Elderly:** The elderly may respond to lower doses and half the normal adult dose may be sufficient.

   **Patients with Renal or Hepatic impairment:**

   Lower doses may be sufficient in these patients *See special warnings and precautions for use*. Use in patients with severe hepatic insufficiency is contraindicated.

4.3 **Contra-indications**

- Acute pulmonary insufficiency
- Hypersensitivity to benzodiazepines, including Ativan Injection or any of the vehicle constituents (polyethylene glycol, propylene glycol, benzyl alcohol)
- Sleep apnoea syndrome
- Myasthenia gravis
• Severe hepatic insufficiency
• Ativan Injection contains benzyl alcohol and is contraindicated in infants or young children, up to 3 years old.

Ativan Injection is not recommended for out-patient use unless the patient is accompanied.

4.4 Special warnings and precautions for use

Prior to use, Ativan Injection may be diluted for IM administration and should always be diluted for IV administration with equal amounts of compatible diluent (see Posology and method of administration). Intravenous injection should be administered slowly except in the control of status epilepticus where rapid injection is required.

The possibility that respiratory arrest may occur or that the patient may have partial airway obstruction should be considered. Therefore, equipment necessary to maintain a patent airway and to support respiration/ventilation should be available and used where necessary.

The use of benzodiazepines, including lorazepam, may lead to physical and psychological dependence.

Severe anaphylactic/anaphylactoid reactions have been reported with the use of benzodiazepines. Cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of benzodiazepines. Some patients taking benzodiazepines have had additional symptoms such as dyspnoea, throat closing, or nausea and vomiting. Some patients have required medical therapy in the emergency department. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with a benzodiazepine should not be rechallenged with the drug.

It is recommended that patients receiving Ativan Injection should remain under observation for at least eight hours and preferably overnight. When Ativan Injection is used for short procedures on an outpatient basis, the patient should be accompanied when discharged.

Patients should be advised that their tolerance for alcohol and other CNS depressants will be diminished in the presence of Ativan Injection. Alcoholic beverages should not be consumed for at least 24 to 48 hours after receiving Ativan Injection.

Use of benzodiazepines, including lorazepam, may lead to potentially fatal respiratory depression. Extreme care must be taken in administering Ativan Injection to elderly or very ill patients and to those with limited pulmonary reserve or compromised respiratory function (e.g. chronic obstructive pulmonary disease [COPD]), because of the possibility that apnoea and/or cardiac arrest may occur. Care should also be exercised when administering Ativan Injection to a patient with status epilepticus, especially when the patient has received other central nervous system depressants.

There is no evidence to support the use of Ativan Injection in coma or shock.

Ativan is not intended for the primary treatment of psychotic illness or depressive disorders, and should not be used alone to treat depressed patients. The use of benzodiazepines may have a disinhibiting effect and may release suicidal tendencies in depressed patients.

Pre-existing depression may emerge during benzodiazepine use.

There are no clinical data available for Ativan Injection with regard to abuse or dependence. However, based upon experience with oral benzodiazepines, doctors should be aware that repeated doses of Ativan Injection over a prolonged period of time may lead to physical and psychological dependence. The risk of dependence on Ativan is low when used at the recommended dose and duration, but increases with higher doses and longer term use. The risk of dependence is further
increased in patients with a history of alcoholism or drug abuse, or in patients with significant personality disorders. Therefore, use in individuals with a history of alcoholism or drug abuse should be avoided.

Dependence may lead to withdrawal symptoms, especially if treatment is discontinued abruptly. Therefore, the drug should always be discontinued gradually - using the oral preparation if necessary.

Symptoms reported following discontinuation of oral benzodiazepines include headaches, muscle pain, anxiety, tension, depression, insomnia, restlessness, confusion, irritability, sweating, and the occurrence of "rebound" phenomena whereby the symptoms that led to treatment with benzodiazepines recur in an enhanced form. These symptoms may be difficult to distinguish from the original symptoms for which the drug was prescribed.

In severe cases the following symptoms may occur: derealisation; depersonalisation; hyperacusis; tinnitus; numbness and tingling of the extremities; hypersensitivity to light, noise, and physical contact; involuntary movements; vomiting; hallucinations; convulsions. Convulsions may be more common in patients with pre-existing seizure disorders or who are taking other drugs that lower the convulsive threshold, such as antidepressants.

It may be useful to inform the patient that treatment will be of limited duration and that it will be discontinued gradually. The patient should also be made aware of the possibility of "rebound" phenomena to minimise anxiety should they occur.

Withdrawal symptoms (e.g. rebound insomnia) can appear following cessation of recommended doses after as little as one week of therapy.

There are indications that, in the case of benzodiazepines with a short duration of action, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high.

When benzodiazepines with a long duration of action are being used, it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Abuse of benzodiazepines has been reported.

Anxiety or insomnia may be a symptom of several other disorders. The possibility should be considered that the complaint may be related to an underlying physical or psychiatric disorder for which there is more specific treatment.

Caution should be used in the treatment of patients with acute narrow-angle glaucoma.

As with all benzodiazepines, the use of lorazepam may worsen hepatic encephalopathy. Patients with impaired renal or hepatic function should be monitored frequently and have their dosage adjusted carefully according to patient response. Lower doses may be sufficient in these patients. The same precautions apply to elderly or debilitated patients and patients with chronic respiratory insufficiency.

As with all CNS-depressants, the use of benzodiazepines may precipitate encephalopathy in patients with severe hepatic insufficiency. Therefore, use in these patients is contraindicated.

Some patients taking benzodiazepines have developed a blood dyscrasia, and some have had elevations in liver enzymes. Periodic haematologic and liver-function assessments are recommended where repeated courses of treatment are considered clinically necessary.

Transient anterograde amnesia or memory impairment has been reported in association with the use of benzodiazepines. This effect may be advantageous when Ativan is used as a premedicant.
Paradoxical reactions have been occasionally reported during benzodiazepine use (see Undesirable effects). Such reactions may be more likely to occur in children and the elderly. Should these occur, use of the drug should be discontinued.

Although hypotension has occurred only rarely, benzodiazepines should be administered with caution to patients in whom a drop in blood pressure might lead to cardiovascular or cerebrovascular complications. This is particularly important in elderly patients.

Ativan Injection contains the excipients polyethylene glycol and propylene glycol. There have been reports of propylene glycol toxicity (e.g. lactic acidosis, hyperosmolality, hypotension) and polyethylene glycol toxicity (e.g. acute tubular necrosis) during administration of Ativan Injection, including at higher than recommended doses. Central nervous system toxicity, including seizures, as well as unresponsiveness, tachypnoea, tachycardia and diaphoresis have also been associated with propylene glycol toxicity. Those prone to propylene glycol accumulation and its potential adverse effects include patients with impaired alcohol and aldehyde dehydrogenase enzyme systems, those with renal or hepatic disease; and paediatric patients.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended: Concomitant intake with alcohol

The sedative effects may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

The benzodiazepines, including Ativan Injection, produce additive CNS depressant effects when co-administered with other medications which themselves produce CNS depression, e.g. barbiturates, antipsychotics, sedatives/hypnotics, anxiolytics, antidepressants, narcotic analgesics, sedative antihistamines, anticonvulsants and anaesthetics.

Concurrent administration of lorazepam with sodium valproate may result in reduced clearance (20 to 40%) and increased concentrations of lorazepam. Therefore clinical monitoring is advised and lorazepam dosage should be reduced when appropriate.

Concurrent administration of lorazepam with probenecid may result in reduced clearance, increased elimination half-life and increased concentrations of lorazepam. Therefore clinical monitoring is advised and lorazepam dosage should be reduced when appropriate.

An enhancement of the euphoria induced by narcotic analgesics may occur with benzodiazepine use, leading to an increase in psychic dependence.

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. To a lesser degree this also applies to benzodiazepines which are metabolised only by conjugation.

The addition of scopolamine to Ativan Injection is not recommended, since their combination has been observed to cause an increased incidence of sedation, hallucination and irrational behaviour.

Concomitant use of clozapine and lorazepam may produce marked sedation, excessive salivation, and ataxia.

Administration of theophylline or aminophylline may reduce the sedative effects of benzodiazepines, including lorazepam.

There have been reports of apnoea, coma, bradycardia, heart arrest and death with the concomitant use of lorazepam injection solution and haloperidol.

4.6 Pregnancy and Lactation
Ativan Injection should not be used during pregnancy, especially during the first and last trimesters, unless in the judgement of the physician such administration is clinically justifiable. Benzodiazepines may cause foetal damage when administered to pregnant women.

If the drug is prescribed to a woman of childbearing potential, she should be warned to contact her physician about stopping the drug if she intends to become, or suspects that she is, pregnant.

Use of Ativan Injection during the late phase of pregnancy may require ventilation of the infant at birth.

If, for compelling medical reasons, the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due to the pharmacological action of the compound.

Infants of mothers who ingested benzodiazepines for several weeks or more preceding delivery have been reported to have withdrawal symptoms during the postnatal period.

Symptoms such as hypotonia, hypothermia, respiratory depression, apnoea, feeding problems, and impaired metabolic response to cold stress have been reported in neonates born of mothers who have received benzodiazepines during the late phase of pregnancy or at delivery.

There are insufficient data regarding obstetrical safety of parenteral Ativan, including use in caesarean section. Such use, therefore, is not recommended.

Since benzodiazepines are found in breast milk, Ativan Injection should not be given to breast feeding mothers unless the expected benefit to the woman outweighs the potential risk to the infant.

4.7 Effects on Ability to Drive and Use Machines

This medicine can impair cognitive function and can affect a patient’s ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

• The medicine is likely to affect your ability to drive
• Do not drive until you know how the medicine affects you
• It is an offence to drive while under the influence of this medicine
• However, you would not be committing an offence (called “statutory defence”) if:
  o The medicine has been prescribed to treat a medical or dental problem and
  o You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
  o It was not affecting your ability to drive safely

Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or use machines. Therefore, patients should not drive or operate machinery within 24-48 hours of administration of Ativan Injection and should be advised not to take alcohol (see also Interactions).

4.8 Undesirable effects

Adverse reactions are listed in the table in CIOMS frequency categories:

<table>
<thead>
<tr>
<th>Frequency Category</th>
<th>CIOMS Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common:</td>
<td>≥ 10%</td>
</tr>
<tr>
<td>Common:</td>
<td>≥ 1% and &lt; 10%</td>
</tr>
<tr>
<td>Uncommon:</td>
<td>≥ 0.1% and &lt; 1%</td>
</tr>
<tr>
<td>Rare:</td>
<td>≥ 0.01% and &lt; 0.1%</td>
</tr>
<tr>
<td>System Organ Class and Frequency</td>
<td>Adverse Reaction</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Undetermined: Thrombocytopenia, agranulocytosis, pancytopenia.</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Undetermined: Hypersensitivity reactions, anaphylactic/oid reactions, angioedema.</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>Undetermined: Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Undetermined: Hyponatremia.</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Common: Confusion, depression, unmasking of depression. Undetermined: Disinhibition, euphoria, suicidal ideation/attempt. Paradoxical reactions, including anxiety, agitation, excitation, hostility, aggression, rage, sleep disturbances/insomnia, sexual arousal, and hallucinations.</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Undetermined: Hypotension.</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders†</td>
<td>Undetermined: Respiratory depression, apnoea, worsening of sleep Worsening of obstructive pulmonary disease.</td>
</tr>
</tbody>
</table>

* Benzodiazepine effects on the CNS are dose dependent, with more severe CNS depression occurring with higher doses.

† The extent of respiratory depression with benzodiazepines is dose dependent with more severe depression occurring with high doses.
System Organ Class and Frequency  
Gastrointestinal disorders

- **Uncommon:** Nausea.
- **Undetermined:** Constipation.

Hepatobiliary disorders

- **Undetermined:** Increase in bilirubin, increase in liver transaminases, increase in alkaline phosphatase.

Skin and subcutaneous tissue disorders

- **Undetermined:** Allergic skin reactions, alopecia.

Reproductive system and breast disorders

- **Uncommon:** Change in libido, impotence, decreased orgasm.

General disorders and administration site conditions

- **Very common:** Fatigue.
- **Common:** Muscle weakness, asthenia.
- **Undetermined:** Hypothermia.

Tolerance at the injection site is generally good although, rarely, pain and redness have been reported after Ativan Injection.

Transient anterograde amnesia or memory impairment may occur using therapeutic doses, the risk increasing at higher doses (see Special warnings and precautions for use).

Paradoxical reactions may be more likely to occur in children and the elderly (see Special warnings and precautions for use).

### 4.9 Overdose

In the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken.

Overdosage of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, and especially when other CNS-depressant drugs or alcohol are ingested, symptoms may include ataxia, hypotension, hypotonia, respiratory depression, cardiovascular depression, coma and, very rarely, death.

Propylene glycol toxicity and polyethylene glycol toxicity have been reported following higher than recommended doses of Ativan Injection (See Section 4.4 Special warnings and precautions for use).

Treatment of overdosage is mainly supportive including monitoring of vital signs and close observation of the patient. An adequate airway should be maintained and assisted respiration used as needed. Hypotension, though unlikely, may be controlled with noradrenaline. Lorazepam is poorly dialysable.

The benzodiazepine antagonist, flumazenil, may be useful in hospitalised patients for the management of benzodiazepine overdosage. Flumazenil product information should be consulted prior to use.
physician should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in tricyclic antidepressant overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ativan is a benzodiazepine with anxiolytic, sedative, hypnotic, anticonvulsant and muscle relaxant properties.

5.2 Pharmacokinetic Properties

Ativan Injection is readily absorbed when given intramuscularly. Peak plasma concentrations occur approximately 60-90 minutes following intramuscular administration.

Ativan is metabolised by a simple one-step process to a pharmacologically inactive glucuronide. There is minimal risk of accumulation after repeated doses, giving a wide margin of safety.

There are no major active metabolites. The elimination half-life is about 12-16 hours when given intramuscularly or intravenously.

5.3 Preclinical Safety Data

Nothing of relevance to the prescriber.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Polyethylene glycol 400
Benzyl alcohol
Propylene glycol

6.2 Incompatibilities

None known

6.3 Shelf Life

12 months

6.4 Special Precautions for Storage

Store and transport refrigerated (2°C to 8°C). Keep ampoule in the outer carton.

6.5 Nature and Contents of Container

1ml solution in 2ml ampoules (Type I glass) with a one-point-cut opening, position marked by red spot in pack sizes of 10.

6.6 Special precautions for disposal and other handling

None.
7. MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent,
CT13 9NJ
United Kingdom

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