
Contraindications
- Known allergy to benzodiazepines.
- Decompensated respiratory insufficiency.
- Sleep apnea.
- Children: 10 mg capsules are not suitable for prescription to children. 5 mg capsules should not be used in children under the age of 30 months.

Side Effects
These are related to the dose taken and the individual sensitivity of the patient:
- anterograde amnesia (see Precautions).
- dizziness, asthenia, drowsiness (particularly in elderly), bradypsychia, muscle hypotonia, in certain patients (in particular, in children and elderly) paradoxical reactions may be observed: irritability, aggressivity, excitation, oniric confusion syndrome, hallucinations, maculopapular and pruriginous skin rash.

Rebound syndrome may occur with exacerbation of anxiety which motivated the treatment. Prolonged use (in particular, at high dosages) may lead to the development of physical dependence, and then treatment discontinuation leads to a withdrawal syndrome (see Precautions). This may occur more rapidly with benzodiazepines with a short half-life than with benzodiazepines with a long half-life (several days).

Precautions
Depression: benzodiazepines essentially act on the anxiety component of depression. Used alone, they do not represent a treatment of depression and may even disguise its signs. (Depressive condition may justify antidepressant therapy).
Alcohol: absorption of alcoholic beverages is not advised throughout the duration of treatment. In children, more particularly, treatment duration should be short. In the elderly or in case of renal failure, dosage adjustment may be necessary. In case of liver failure, the use of a benzodiazepine may cause encephalopathy. In patients with respiratory failure, the depressant effect of benzodiazepine should be taken into account (exacerbation of hypoxia may itself cause anxiety justifying the patient’s admission into an Intensive Care Unit). Treatment discontinuation: discontinuation of treatment may lead to the development of withdrawal symptoms. The patient should be warned and progressive discontinuation of treatment is advised with dosage being reduced over several weeks, in particular after prolonged therapy or if drug dependence is suspected.

The combination of several benzodiazepines is of no utility and may, whether the indication is anxiolytic or hypnotic, increase drug dependence.

Myasthenia: treatment with a benzodiazepine exacerbates the symptoms. It is recommended that it is used exceptionally and under particularly careful monitoring.

Pregnancy and Lactation

Pregnancy

In humans, the teratogenic risk, if any, is probably extremely slight. A teratogenic effect has been suggested but not confirmed for certain benzodiazepines, from epidemiological studies. Therefore, it seems better to avoid prescription of these drugs during the first three months of pregnancy. High doses should not be prescribed during the last three months of pregnancy as neonatal hypotonia and respiratory distress may occur in the newborn. After a few days or a few weeks of age, withdrawal syndrome may occur.

Lactation

Breastfeeding is not recommended during the use of benzodiazepines.

Effects on Ability to Drive and Operate Machinery

Attention should be drawn, in particular in vehicle drivers and machine operators, to the risk of drowsiness associated with the use of this drug. Combinations may potentiate this sedative effect. (See Drug Interactions).

Overdosage

In cases of massive intake, deep sleep is the main sign of overdosage and it may even become a coma, depending on the dose taken. The prognosis is positive, at least in the absence of a combination with other psychotropic agents and as long as the subject is treated. Special attention should be paid to respiratory and cardiovascular functions, in an intensive care unit. The outcome is positive. Administration of flumazenil may be useful for diagnosis and/or treatment of intentional or accidental overdosage with benzodiazepines.

Shelf Life: 36 months.

Storage

Tranxene capsules must be kept at room temperature, in a dry place and protected from light.

Warnings

Dependence: any treatment with benzodiazepines may lead to the development of physical and psychic drug dependence. Several factors seem to promote the development of dependence: duration of treatment, dosage, combination with other drugs: psychotropics, anxiolytics, hypnotics, combination with alcohol, history of other drug or non-drug dependencies. This may lead to withdrawal symptoms when treatment is discontinued, including insomnia, headaches, marked anxiety, myalgia, muscle tension, occasionally irritability, agitation and even confusion. In exceptional cases, the following may be observed: trembling, hallucinations, seizures. It can be useful to warn the patient immediately about the limited length of the treatment that should not exceed 4 to 12 weeks - and about the precise way the treatment should be progressively decreased (over a few days to a few weeks).
Tolerance may also develop during prolonged use. Anterograde amnesia may occur, more particularly when the benzodiazepine drug is used at bed time and when sleep duration is short (early awakening due to an outside event).

Anxiolytic benzodiazepines should not be used to treat depressive condition and psychotic disorders (see Precautions).

**Drug Interactions**

Additive synergy with neuromuscular depressants (curare-like drugs, muscle relaxants). The risk of development of a withdrawal syndrome is increased by combination with benzodiazepines prescribed as anxiolytics or hypnotics.

The following combination is not recommended:

Alcohol: intake of alcohol beverages and drugs containing alcohol should be avoided.

Increase of the sedative effect of benzodiazepines due to alcohol. The decrease in alertness can make driving vehicles and operating machines dangerous.

The following interactions should be taken into account:

*Other central nervous system depressants*: morphine derivatives (analgesics and antitussives), barbiturates, certain antidepressants, H1 sedative antihistamines, tranquilizers other than benzodiazepines, neuroleptics, clonidine and related substances. Increase in central depression which could have serious consequences, in particular if driving vehicles and operating machines.

*Cisapride*: Transient increase in the sedative effect of benzodiazepines due to a faster speed of absorption. The decrease in alertness can make driving vehicles and operating machines dangerous.

*Clozapine*: The risk of collapses with respiratory and/or cardiac arrest is increased by the combination of clozapine and benzodiazepines.

**Dosage and Administration**

**Administration**

*Treatment duration*: The duration of treatment should be as short as possible and should not exceed 4 to 12 weeks, including tapering off (see Warnings and Precautions).

Reactional anxiety, adjunctive therapy for anxiety in neuroses, anxiety associated with severe or painful somatic disorders: 4 to 12 weeks, including tapering off.

*Generalized anxiety*: long-term treatment upon specialist’s advice.


*Prevention and treatment of delirium tremens*: a few days.

*Alcohol withdrawal*: treatment lasting 3 to 6 weeks surrounding the withdrawal period.

*Treatment Discontinuation*: progressive, with reduction over several weeks (see Warnings and Precautions).

**Children**: The use should be recommended only in exceptional cases; the dosage is about 0.5 mg/kg/day, using 5 mg capsules of Tranxene, several divided doses.

**Elderly, Patients with Renal Insufficiency**: reduced dosage is recommended; for example, half of the mean dosage may be enough.

**Packaging**

ca: 5 mg, 10 mg.