Swinol®

Flunitrazepam 1 mg Tablets

swipha

Sleep-inducing agent

Composition:
Each film-coated tablet contains:
Flunitrazepam.....1 mg

Excipients: Avicel Ph 101, Lactose powder, Kollidon 90F, FD&C blue, hydroxypropyl methyl Cellulose, Croscarmellose sodium, Magnesium stearate and Green coating material.

Description:
Green oblong tablet embossed with breakscore above and **Swinol®** below.

Properties and effects:
Flunitrazepam is a full benzodiazepine agonist with a high affinity for the benzodiazepine central site.
It has anxiolytic, anticonvulsant and sedative effects, and induces slowing of psychomotor performance, amnesia, muscle relaxation and sleep.

Pharmacokinetics:
Absorption:
Following oral administration, flunitrazepam is almost entirely absorbed. 10-15% undergoes first-pass metabolism in the liver resulting in an absolute (vs. intravenous solution) bioavailability of 70-90%. The maximum plasma concentrations of flunitrazepam are 6-11 ng/ml and occur 0.75 -2 hours after administration of a single oral dose of 1 mg on an empty stomach. Food reduces the rate and extent of flunitrazepam absorption. The pharmacokinetics of flunitrazepam are linear in the 0.5–4 mg dose range. Repetitive daily oral administrations lead to a moderate accumulation of flunitrazepam in plasma (accumulation ratio 1.6-1.7).The steady state plasma concentration of flunitrazepam is reached after 5 days. The minimum plasma concentration of flunitrazepam at steady state is 3-4 ng/ml following multiple oral doses of 2 mg. The steady state plasma concentration of the pharmacologically active N-desmethyl metabolite is almost identical to that of the parent compound.

Distribution:
The distribution of flunitrazepam is rapid and extensive. The volume of distribution at steady state is 3-5 liters/kg.
Flunitrazepam is 78% bound to plasma proteins. There is a rapid uptake of flunitrazepam into human cerebrospinal fluid. Flunitrazepam crosses the human placenta and blood-milk barrier slowly and to a minor extent after a single dose.

Metabolism and Elimination:
Flunitrazepam is almost completely metabolized. About 80% and 10% of the radiolabel are found in urine and faeces, respectively. The principal plasma metabolites are 7-amino-flunitrazepam and N-desmethyl-flunitrazepam. The major urinary metabolite is 7-amino-flunitrazepam. Less than 2% of a dose is excreted renally as unchanged drug and as N-desmethyl-flunitrazepam. The N-desmethyl-flunitrazepam is pharmacologically active in man, though less than flunitrazepam, and plasma levels at steady state resulting from daily doses of 2 mg flunitrazepam are below the minimum effective concentration of the metabolite.
The elimination half-life of flunitrazepam is between 16 and 35 hours. The half-life of the active N-desmethyl-flunitrazepam is 28 hours. The total plasma clearance is 120-140 ml/min.

Pharmacokinetics in special populations:
Elderly:
There are no age-related changes in the pharmacokinetics of flunitrazepam.

Patients with renal impairment:
The pharmacokinetics of the active moieties of flunitrazepam is similar in patients with renal impairment to healthy subjects.

Patients with hepatic impairment:
The pharmacokinetics of flunitrazepam and N-desmethyl-flunitrazepam in patients with hepatic disease are similar to those in healthy volunteers.

Indications:
Short term treatment of insomnia.
Benzodiazepines are indicated only when the disorder is severe or disabling or subjects the individual to extreme stress.

Dosage and administration:
Standard dosage:
The recommended dosage for adult patients is 0.5-1 mg/day. In exceptional circumstances the dose may be increased to 2 mg.
Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded. The product should be taken just before going to bed.

Duration of treatment:
Treatment should be as short as possible. Generally, the duration of treatment varies from a few days to 2 weeks, with a maximum of 4 weeks including a tapering-off process.
In certain cases, extension beyond the maximum treatment period may be necessary; if so, it should not take place without a re-evaluation of the patient's status. It may be useful to inform the patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover, it is important that the patient be made aware of the possibility of rebound phenomena, thereby minimizing anxiety over such symptoms should they occur while the medicinal product is being discontinued. 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 (see Precautions).

Special dosage instructions:
Elderly:
The recommended dosage for elderly patients is 0.5 mg. In exceptional circumstances the dose may be increased to 1 mg.

Patients with hepatic impairment:
Patients with impaired liver function should receive a reduced dose.

Patients with chronic respiratory insufficiency:
A lower dose is recommended for patients with chronic respiratory insufficiency, due to the risk of respiratory depression (see Precautions).

Contraindications:
- myasthenia gravis
- use of this drug in patients with known hypersensitivity to flunitrazepam or to any of the components of the product
- hypersensitivity to benzodiazepines
- severe respiratory insufficiency
- sleep apnea syndrome
- children
- severe hepatic insufficiency

Precautions:
Benzodiazepines are not recommended for the primary treatment of psychotic illness. Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse. A lower dose is recommended for patients with chronic respiratory insufficiency, due to the risk of respiratory depression. (see Special dosage instructions).

Hypersensitivity:
Hypersensitivity reactions such as rash, angioedema or hypotension may occur in susceptible individuals.

Tolerance:
Some loss of efficacy to the hypnotic effects of benzodiazepines may develop after repeated use for a few weeks.

Dependence:
The use of benzodiazepines and benzodiazepine-like agents may lead to the development of physical and psychological dependence on these products. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of alcohol or drug abuse.

Withdrawal:
Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of 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.

Rebound insomnia:
A transient syndrome whereby the symptoms that led to treatment with a benzodiazepine or benzodiazepine-like agent recur in an enhanced form, rebound insomnia may occur on withdrawal of hypnotic treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness.
Since the risk of withdrawal and rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually.

Amnesia:
Benzodiazepines may induce anterograde amnesia. The condition most often occurs within the first few hours after ingesting the product, and therefore, to reduce the risk, patients should be able to ensure that they will be able to sleep undisturbed for 7-8 hours (see Undesirable effects).

Effects on ability to drive and use machinery:
Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or operate machinery. Insufficient sleep may increase the likelihood of impaired alertness.

Pregnancy, nursing mothers:
Insufficient data are available on flunitrazepam to assess its safety during pregnancy.
If the product is prescribed to a woman of childbearing potential, she should be advised to contact her physician regarding discontinuance of the product if she intends to become pregnant or suspects that she is pregnant. Although the placental transfer of flunitrazepam is small after a single dose, prolonged administration should be avoided in the last trimester of pregnancy. If, for compelling medical reasons, flunitrazepam is administered during the late phase of pregnancy or during labour, effects on the neonate such as hypothermia, hypotonia and moderate respiratory depression can be expected due to the pharmacological action of the product. Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk of developing withdrawal symptoms in the postnatal period (see Precautions).
Since benzodiazepines pass into breast milk, flunitrazepam should not be administered to breast-feeding mothers.

Undesirable effects:
The most commonly reported undesirable effects are drowsiness during the day, numbed emotions, reduced alertness, confusion, fatigue, headache, dizziness, muscle weakness, ataxia and double vision. These phenomena occur predominantly at the start of therapy and usually disappear with prolonged administration.
Other undesirable effects, including gastrointestinal disturbances, changes in libido and skin reactions, have been reported occasionally.
Hypersensitivity reactions, including rash, angioedema and hypotension, may occur.
Anterograde amnesia may occur with therapeutic dosages, the risk increasing at higher dosages. Amnestic effects may be associated with inappropriate behaviour (see Precautions).
Pre-existing depression may be unmasked during benzodiazepine use.

Psychiatric and 'paradoxical' reactions:
Paradoxical reactions such as restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behavior and other adverse behavioural effects are known to occur with benzodiazepines and benzodiazepine-like agents. These reactions may be quite severe with this product, and are more likely to occur in the elderly.
Should this occur, the use of the drug should be discontinued.
Chronic use (even at therapeutic doses) may lead to the development of physical dependence: abrupt discontinuation of therapy may result in withdrawal or rebound phenomena (see Precautions). Abuse has been reported.

Interactions:
Concomitant intake with alcohol should be avoided. The sedative and adverse effects of the product may be enhanced when it is used in combination with alcohol. This affects the ability to drive or use machines. Combination with CNS depressants may lead to enhancement of the central depressive effect (antipsychotics, neuroleptics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, antiepileptic drugs, anaesthetics and sedative antihistamines).
In the case of narcotic analgesics, enhancement of euphoria may also occur, leading to an increase in psychological dependence.
Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines and benzodiazepine-like agents.

Overdosage:
Symptoms:
Overdose of benzodiazepines is usually manifested by central nervous system depression, ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, coma (rarely) and death (very rarely). However, as with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol).

Treatment:
In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken. Following overdose oral benzodiazepines, vomiting should be induced (within 1 hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiac function in intensive care. Flumazenil may be useful as an antagonist (caution should be observed in the use of flumazenil in cases of mixed drug overdose and in epileptics treated with benzodiazepines).

Stability:
This medicine should not be used after the expiry date (EXP) shown on the pack.
See also outer pack for storage remark.

Presentation:
Packed in blisters of 3 x 10 tablets

Storage:
Store below 30°C.

This medicine is a benzodiazepine and has the risks for abuse, misuse, addiction, physical dependence, and withdrawal reactions. Do not drink alcohol with benzodiazepines. Alcohol can increase the risk of serious and life-threatening side effects.

Medicine: keep out of reach of children

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Manufactured in Nigeria by:
swiss pharma nigeria Ltd.,
5, Dopemu Road, Agege, Lagos.

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