Imovane®

Zopiclone BP

50016

SANOFI

DESCRIPTION
Active Ingredient: Zopiclone
Therapeutic or Pharmacological Class: Hypnotics and sedatives, benzodiazepine related drugs
Pharmaceutical Form: Tablet

PRESENTATION
White or almost white, film-coated, elliptical tablets with break line on one face and with the other face plain. Each tablet contains Zopiclone BP 7.5 mg. The tablet also contains lactose.

INDICATIONS
Imovane is indicated for the short-term treatment of insomnia in adults.

DOSAGE AND ADMINISTRATION

General
Use the lowest effective dose. Imovane should be taken in a single intake and not to be re administered during the same night.

Adults
The recommended dose is 7.5 mg Imovane by the oral route shortly before retiring. This dose of 7.5 mg should not be exceeded.
As with all hypnotics, long-term use of zopiclone is not recommended. Treatment should be as short as possible and should not exceed four weeks including the period of tapering off. Extension beyond the maximum treatment period should not take place without re-evaluation of the patient's status, since the risk of abuse and dependence increases with the duration of treatment (see PRECAUTIONS).

Special Populations

Pediatric patients
The safe and effective dose of Imovane has not been established in children and young adults less than 18 years.

Elderly patients
In elderly a starting dose of 3.75 mg Imovane is recommended initially. The dosage subsequently may be increased to 7.5 mg.

Hepatic impairment
In patients with impaired liver function: a starting dose of 3.75 mg Imovane is recommended initially. The dosage subsequently may be increased to 7.5 mg.

Renal Impairment
In patients with renal insufficiency: it is recommended that patients with impaired renal function should start treatment with 3.75 mg.

Chronic respiratory insufficiency
In patients with chronic respiratory insufficiency, a starting dose of 3.75 mg Imovane is recommended initially. The dosage subsequently may be increased to 7.5 mg.

Administration
For oral use only

CONTRAINDICATIONS

Imovane is contraindicated in patients with:
- **Myasthenia gravis**
- **Hypersensitivity to zopiclone or any of the excipients**
- **Respiratory failure**
- **Severe sleep apnoea syndrome**
- **Severe hepatic insufficiency.**

WARNINGS
Respiratory depression:
As hypnotics have the capacity to depress respiratory drive, precautions should be observed if zopiclone is prescribed to patients with compromised respiratory function (see ADVERSE REACTIONS).
Psychomotor impairment:
Like other sedative/hypnotic drugs, zopiclone has CNS-depressant effects.
The risk of psychomotor impairment, including impaired driving ability, is increased if: zopiclone is taken within 12 hours of performing activities that require mental alertness, a dose higher than the recommended dose is taken, or zopiclone is co-administered with other CNS depressants, alcohol, or with other drugs that increase the blood levels of zopiclone (See INTERACTIONS). Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motor coordination such as operating machinery or driving a motor vehicle following administration of zopiclone and in particular during the 12 hours following that administration (see DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS).

Risks from concomitant use with opioids:
Concomitant use of opioids with benzodiazepines or other sedative-hypnotic drugs, including zopiclone, may result in sedation, respiratory depression, coma, and death.
Because of these risks, reserve concomitant prescribing of opioids and benzodiazepines for use in patients for whom alternative treatment options are inadequate.
If a decision is made to prescribe zopiclone concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation (see INTERACTIONS).

PRECAUTIONS
The cause of insomnia should be identified wherever possible and the underlying factors treated before a hypnotic is prescribed

Dependence
Use of zopiclone may lead to the development of abuse and/or physical and psychological dependence.
The risk of dependence increases with dose and duration of treatment. Cases of dependence have been reported more frequently in patients treated with Imovane for longer than 4 weeks. The risk of abuse and dependence is also greater in patients with a history of psychiatric disorders and/or alcohol or drug abuse. Imovane should be used with extreme caution in patients with current or a history of alcohol or drug abuse.
Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms.

Rebound insomnia
A transient syndrome whereby the symptoms that led to treatment with sedative/hypnotic agents recur in an enhanced form, may occur on withdrawal of hypnotic treatment. Since the risk of such phenomena is greater after abrupt discontinuation of Imovane, especially after prolonged treatment, it is, therefore, recommended to decrease the dose gradually and to advise the patient accordingly (see ADVERSE REACTIONS).

Amnesia
Anterograde amnesia may occur, especially when sleep is interrupted or when retiring to bed is delayed after the intake of the tablet.
To reduce the possibility of anterograde amnesia, patients should ensure that they:
- **take the tablet strictly when retiring for the night.**
- **are able to have a full night sleep.**

Other psychiatric and paradoxical reactions:
Other psychiatric and paradoxical reactions (see ADVERSE REACTIONS) are known to occur when using sedative/hypnotic agents like zopiclone. These reactions are more likely to occur in the elderly.

Somnambulism and associated behaviours:
Sleep walking and other associated behaviours such as "sleep driving", preparing and eating food, or making phone calls, with amnesia for the event, have been reported in patients who have taken zopiclone and were not fully awake. The use of alcohol and other CNS-depressants with zopiclone appears to increase the risk of such behaviours, as does the use of zopiclone at doses exceeding the maximum recommended dose. Discontinuation of zopiclone should be strongly considered for patients who report such behaviours (SeeINTERACTIONS: Alcohol, andADVERSE REACTIONS; Psychiatric Disorders).

Suicidality and Depression
Several epidemiological studies show an increased incidence of suicide and suicide attempt in patients with or without depression, treated with benzodiazepines and other hypnotics, including zopiclone. A causal relationship has not been established.
Imovane should be administered with caution in patients exhibiting symptoms of depression. Suicidal tendencies may be present, therefore the lowest possible quantity of Imovane that should be supplied to these patients to reduce the risk of intentional overdosage by the patient. Pre-existing depression may be unmasked during use of Imovane.

Use in children
The safe and effective dose of Imovane has not been established in children and young adults less than 18 years.

INTERACTIONS

Association not recommended:
Alcohol
Concomitant intake with alcohol is not recommended. The sedative effect of Imovane may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

Associations to be taken into account:
Combination with CNS depressants
Enhancement of the central depressive effect may occur in cases of concomitant use with neuroleptics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, antiepileptic drugs, anesthetics and sedative anti-histaminics. In the case of narcotic analgesics, enhancement of euphoria may also occur leading to an increase in psychic dependence.

CYP450 inhibitors and inducers
The AUC of Imovane is increased by 80% in presence of erythromycin which indicates that erythromycin can inhibit the metabolism of drugs metabolized by CYP 3A4. As a consequence, the hypnotic effect of Imovane may be enhanced.

Plasma levels of zopiclone may be increased when co-administered with CYP3A4 inhibitors, such as erythromycin, clarithromycin, ketoconazole, itraconazole, and ritonavir. A dose reduction for zopiclone may be required when it is co-administered with CYP3A4 inhibitors. Conversely, plasma levels of zopiclone may be decreased when co-administered with CYP3A4 inducers, such as rifampicin, carbamazepine, phenobarbital, phenytoin, and St. John's wort. A dose increase for zopiclone may be required when it is co-administered with CYP3A4 inducers.

Opioids
The concomitant use of benzodiazepines and other sedative-hypnotic drugs, including zopiclone, and opioids increases the risk of sedation, respiratory depression, coma, and death because of additive CNS depressant effect.

PREGNANCY
The use of Imovane is not recommended during pregnancy.
Cases of reduced fetal movement and fetal heart rate variability have been described after administration of benzodiazepines during the second and/or third trimester of pregnancy
Administration of Imovane during the late phase of pregnancy or during labour has been associated with effects on the neonate, such as hypothermia, hypotonia, feeding difficulties and respiratory depression.
Infants born to mothers who took sedative/hypnotics agents chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.
Appropriate monitoring of the newborn in the postnatal period is recommended.

If Imovane is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuation of the product if she intends to become or suspects that she is pregnant.

LACTATION
Although the concentration of zopiclone in the breast milk is very low, Imovane should not be used by nursing mothers.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS

Because of its pharmacological properties and its effects on central nervous system, Imovane may adversely affect the ability to drive or to use machines. The risk of psychomotor impairment, including impaired driving ability, is increased if:
zopiclone is taken within 12 hours of performing activities that require mental alertness,
a dose higher than the recommended dose is taken, or
zopiclone is co-administered with other CNS depressants, alcohol, or with other drugs that increase the blood levels of zopiclone.
Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness or motor coordination such as operating machinery or driving a motor vehicle following administration of zopiclone and in particular during the 12 hours following that administration.

ADVERSE REACTIONS
Immune system disorders
Very rare: **angiooedema**, **anaphylactic reaction**
Psychiatric disorders
Uncommon: **nightmare, agitation**
Rare: **confusional state, libido disorder, irritability, aggression, hallucination**
Not known: **restlessness, delusion, anger, abnormal** behaviour **(possibly associated with amnesia) and somnambulism** (see PRECAUTIONS: Somnambulism and associated behaviour), **dependence** (see Abuse and Dependence), and **withdrawal syndrome** (see below)

Nervous system disorders
Common: **dysgeusia** (Bitter taste), **somnolence (residual)**
Uncommon**: dizziness, headache**
Rare: **anterograde amnesia**
Not known: **ataxia, paresthesia, cognitive disorders such as memory impairment, disturbance in attention, speech disorder**

Eye disorders
Not known: **diplopia**

Respiratory, thoracic and mediastinal disorders
Rare: **dyspnea** (see WARNINGS)
Not known: **respiratory depression** (see WARNINGS)

Gastrointestinal disorders
Common: **dry mouth**
Uncommon: **nausea**
Not known: **dyspepsia**

Hepatobiliary disorders
Very rare: **transaminases increased and/or blood alkaline phosphatase increased (mild to moderate)**

Skin and subcutaneous tissue disorders
Rare: **rash, pruritus**

Musculoskeletal and connective tissue disorders
Not known: **muscular weakness**

General disorders and administration site conditions
Uncommon: **fatigue**

Injury, poisoning and procedural complications
Rare: **fall** (predominantly in elderly patients)

Withdrawal syndrome has been reported upon discontinuation of Imovane (see PRECAUTIONS). Withdrawal symptoms vary and may include rebound insomnia, muscle pain anxiety, tremor, sweating, agitation, confusion, headache, palpitations, tachycardia, delirium, nightmares, irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations, In very rare cases, seizures may occur.

OVERDOSE

Signs and Symptoms
Overdose is usually manifested by varying degrees of central nervous system depression ranging from drowsiness to coma according to the quantity ingested. In mild cases, symptoms include drowsiness, confusion, and lethargy; in more serious cases, symptoms may include ataxia, hypotonia, hypotension, methaemoglobinaemia, respiratory depression, and coma. Overdose should not be life threatening unless combined with other CNS depressants, including alcohol. Other risk factors, such as the presence of concomitant illness and the debilitated state of the patient, may contribute to the severity of symptoms and very rarely can result in fatal outcome.

Management
Symptomatic and supportive treatment in adequate clinical environment is recommended, attention should be paid to respiratory and cardiovascular functions. Gastric lavage or activated charcoal is only useful when performed soon after ingestion. Hemodialysis is of no value due to the large volume of distribution of zopiclone. Flumazenil may be a useful antidote.

STORAGE CONDITIONS
- Store below 30°, protect from light
- Keep out of the reach of children.
- Drugs to be only dispensed according to registered physician's prescription

PACKAGE QUANTITY
Imoven Tablet: Each box contains 3 X 10 X 7.5mg in blister packs

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