PATIENT INFORMATION LEAFLET

SLEEPGABA 3 (ESZOPICLONE TABLETS USP 3MG)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, or pharmacist, or nurse
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Eszopiclone Tablets is and what it is used for

Eszopiclone Tablets is indicated for the treatment of insomnia. In controlled outpatient and sleep laboratory studies, Eszopiclone Tablets administered at bedtime decreased sleep latency and improved sleep maintenance.

The clinical trials performed in support of efficacy were up to 6 months in duration. The final formal assessments of sleep latency and maintenance were performed at 4 weeks in the 6-week study (adults only), at the end of both 2-week studies (elderly only) and at the end of the 6-month study (adults only).

2. What you need to know before you take Eszopiclone Tablets

Eszopiclone Tablets is contraindicated in patients who have experienced complex sleep behaviours after taking Eszopiclone Tablets [see Warnings and Precautions].

Eszopiclone Tablets is contraindicated in patients with known hypersensitivity to Eszopiclone. Hypersensitivity reactions include anaphylaxis and angioedema [see Warnings and Precautions].

Special warnings and precautions for use

Complex Sleep Behaviors

Complex sleep behaviors including sleep-walking, sleep-driving, and engaging in other activities while not fully awake may occur following the first or any subsequent use of Eszopiclone Tablets.

Patients can be seriously injured or injure others during complex sleep behaviors. Such injuries may result in a fatal outcome. Other complex sleep behaviors (e.g., preparing and eating food, making phone calls, or having sex) have also been reported. Patients usually do not remember these events. Post-marketing reports have shown that complex sleep behaviors may occur with Eszopiclone Tablets alone at recommended dosages, with or without the concomitant use of alcohol or other CNS depressants [see Drug Interactions]. Discontinue Eszopiclone Tablets immediately if a patient experiences a complex sleep behavior.

CNS Depressant Effects and Next-Day Impairment

Eszopiclone Tablets is a CNS depressant and can impair daytime function in some patients at the higher doses (2 mg or 3 mg), even when used as prescribed. Prescribers should monitor for excess depressant effects, but impairment can occur in the absence of symptoms (or even with subjective improvement), and impairment may not be reliably detected by ordinary clinical exam (i.e., less than formal psychomotor testing). While pharmacodynamic tolerance or adaptation to some adverse depressant effects of Eszopiclone Tablets may develop, patients using 3 mg Eszopiclone Tablets should be cautioned against driving or engaging in other hazardous activities or activities requiring complete mental alertness the day after use.

Additive effects occur with concomitant use of other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol), including daytime use. Downward dose adjustment of Eszopiclone Tablets and concomitant CNS depressants should be considered.

The use of Eszopiclone Tablets with other sedative-hypnotics at bedtime or the middle of the night is not recommended.

The risk of next-day psychomotor impairment is increased if Eszopiclone Tablets is taken with less than a full night of sleep remaining (7- to 8 hours); if higher than the recommended dose is taken; if coadministered with other CNS depressants; or coadministered with other drugs that increase the blood levels of Eszopiclone

Because Eszopiclone Tablets can cause drowsiness and a decreased level of consciousness, patients, particularly the elderly, are at higher risk of falls.

Need to Evaluate for Comorbid Diagnoses

Because sleep disturbances may be the presenting manifestation of a physical and/or psychiatric disorder, symptomatic treatment of insomnia should be initiated only after a careful evaluation of the patient. The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder. Such findings have emerged during the course of treatment with sedative/hypnotic drugs, including Eszopiclone Tablets. Because some of the

important adverse effects of Eszopiclone Tablets appear to be dose related, it is important to use the lowest possible effective dose, especially in the elderly.

Severe Anaphylactic and Anaphylactoid Reactions

Rare cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of sedative-hypnotics, including Eszopiclone Tablets. Some patients have had additional symptoms such as dyspnea, throat closing, or nausea and vomiting that suggest anaphylaxis. 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 Eszopiclone Tablets should not be rechallenged with the drug.

Abnormal Thinking and Behavioral Changes

A variety of abnormal thinking and behavior changes have been reported to occur in association with the use of sedative/hypnotics. Some of these changes may be characterized by decreased inhibition (e.g., aggressiveness and extroversion that seem out of character), similar to effects produced by alcohol and other CNS depressants. Other reported behavioral changes have included bizarre behavior, agitation, hallucinations, and depersonalization. Amnesia and other neuropsychiatric symptoms may occur unpredictably.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is drug induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Nonetheless, the emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

Withdrawal Effects

Following rapid dose decrease or abrupt discontinuation of the use of sedative/hypnotics, there have been reports of signs and symptoms similar to those associated with withdrawal from other CNS-depressant drugs [see Drug Abuse and Dependence].

Timing of Drug Administration

Eszopiclone Tablets should be taken immediately before bedtime. Taking a sedative/hypnotic while still up and about may result in short-term memory impairment, hallucinations, impaired coordination, dizziness, and lightheadedness.

Special Populations

Use in Elderly and/or Debilitated Patients

Impaired motor and/or cognitive performance after repeated exposure or unusual sensitivity to sedative/hypnotic drugs is a concern in the treatment of elderly and/or debilitated patients. The dose should not exceed 2 mg in elderly or debilitated patients.

Use in Patients with Concomitant Illness

Clinical experience with Eszopiclone in patients with concomitant illness is limited. Eszopiclone should be used with caution in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

A study in healthy volunteers did not reveal respiratory-depressant effects at doses 2.5-fold higher (7 mg) than the recommended dose of Eszopiclone. Caution is advised, however, if Eszopiclone Tablets is prescribed to patients with compromised respiratory function.

The dose of Eszopiclone Tablets should not exceed 2 mg in patients with severe hepatic impairment, because systemic exposure is doubled in such subjects. No dose adjustment appears necessary for subjects with mild or moderate hepatic impairment. No dose adjustment appears necessary in subjects with any degree of renal impairment, since less than 10% of Eszopiclone is excreted unchanged in the urine.

The dose of Eszopiclone Tablets should be reduced in patients who are administered potent inhibitors of CYP3A4, such as ketoconazole, while taking Eszopiclone Tablets. Downward dose adjustment is also recommended when Eszopiclone Tablets is administered with agents having known CNS-depressant effects.

Use in Patients with Depression

In primarily depressed patients treated with sedative-hypnotics, worsening of depression, including suicidal thoughts and actions (including completed suicides), have been reported in association with the use of sedative/hypnotics.

Sedative/hypnotic drugs should be administered with caution to patients exhibiting signs and symptoms of depression. Suicidal tendencies may be present in such patients, and protective measures may be required. Intentional overdose is more common in this group of patients; therefore, the least amount of drug that is feasible should be prescribed for the patient at any one time.

3. How to take Eszopiclone Tablets

Use the lowest effective dose for the patient.

Dosage in Adults

The recommended starting dose is 1 mg. Dosing can be raised to 2 mg or 3 mg if clinically indicated. In some patients, the higher morning blood levels of Eszopiclone Tablets following use of the 2 mg or 3 mg dose increase the risk of next day impairment of driving and other activities that require full alertness [*see Warnings and Precautions (5.1)*]. The total dose of Eszopiclone Tablets should not exceed 3 mg, once daily immediately before bedtime [*see Warnings and Precautions*].

Geriatric or Debilitated Patients

The total dose of Eszopiclone Tablets should not exceed 2 mg in elderly or debilitated patients.

Patients with Severe Hepatic Impairment, or Taking Potent CYP3A4 Inhibitors

In patients with severe hepatic impairment, or in patients co-administered Eszopiclone Tablets with potent CYP3A4 inhibitors, the total dose of Eszopiclone Tablets should not exceed 2 mg [*see Warnings and Precautions*].

Use with CNS Depressants

Dosage adjustments may be necessary when Eszopiclone Tablets is combined with other central nervous system (CNS) depressant drugs because of the potentially additive effects *[see Warnings and Precautions]*.

Administration with Food

Taking Eszopiclone Tablets with or immediately after a heavy, high-fat meal results in slower absorption and would be expected to reduce the effect of Eszopiclone Tablets on sleep latency *[see Clinical Pharmacology]*.

4. Possible side effects

The following are described in more detail in the Warnings and Precautions section of the label:

- Complex Sleep Behaviours
- CNS Depressant Effects and Next-Day
- Need to Evaluate for Comorbid Diagnoses
- Severe Anaphylactic and Anaphylactoid Reactions
- Abnormal Thinking and Behavioural Changes
- Withdrawal Effects
- Timing of Drug Administration
- Special Populations

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The premarketing development program for Eszopiclone Tablets included Eszopiclone exposures in patients and/or normal subjects from two different groups of studies: approximately 400 normal subjects in clinical pharmacology/pharmacokinetic studies, and approximately 1550 patients in placebo-controlled clinical effectiveness studies, corresponding to approximately 263 patient-exposure years. The conditions and duration of treatment with Eszopiclone Tablets varied greatly and included (in overlapping categories) open-label and double-blind phases of studies, inpatients and outpatients, and short-term and longer-term exposure. Adverse reactions were assessed by

collecting adverse events, results of physical examinations, vital signs, weights, laboratory analyses, and ECGs.

The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, adverse reaction of the type listed. A reaction was considered treatment-emergent if it occurred for the first time or worsened while the patient was receiving therapy following baseline evaluation.

Clinical Trials Experience

Adverse Reactions Resulting in Discontinuation of Treatment

In placebo-controlled, parallel-group clinical trials in the elderly, 3.8% of 208 patients who received placebo, 2.3% of 215 patients who received 2 mg Eszopiclone Tablets, and 1.4% of 72 patients who received 1 mg Eszopiclone Tablets discontinued treatment due to an adverse reaction. In the 6-week parallel-group study in adults, no patients in the 3 mg arm discontinued because of an adverse reaction. In the long-term 6-month study in adult insomnia patients, 7.2% of 195 patients who received placebo and 12.8% of 593 patients who received 3 mg Eszopiclone Tablets discontinued due to an adverse reaction. No reaction that resulted in discontinuation occurred at a rate of greater than 2%.

Adverse Reactions Observed at an Incidence of ≥2% in Controlled Trials

TABLE 1 shows the incidence of adverse reactions from a Phase 3 placebo-controlled study of Eszopiclone Tablets at doses of 2 or 3 mg in nonelderly adults. Treatment duration in this trial was 44 days. The table includes only reactions that occurred in 2% or more of patients treated with Eszopiclone Tablets 2 mg or 3 mg in which the incidence in patients treated with Eszopiclone Tablets was greater than the incidence in placebo-treated patients.

Table 1: Incidence (%) of Adverse Reactions in a 6-Week Placebo-Controlled Study in Nonelderly Adults with Eszopiclone Tablets 1mg.

Adverse Reaction	Placebo (n=99)	Eszopiclone Tablets 2 mg (n=104)	Eszopiclone Tablets 3 mg (n=105)
Body as a Whole			
Headache	13	21	17
Viral Infection	1	3	3
Digestive System			
Dry Mouth	3	5	7
Dyspepsia	4	4	5
Nausea	4	5	4

Vomiting	1	3	0
Nervous System			
Anxiety	0	3	1
Confusion	0	0	3
Depression	0	4	1
Dizziness	4	5	7
Hallucinations	0	1	3
Libido Decreased	0	0	3
Nervousness	3	5	0
Somnolence	3	10	8
Respiratory System			
Infection	3	5	10
Skin and Appendages			
Rash	1	3	4
Special Senses			
Unpleasant Taste	3	17	34
Urogenital System			
Dysmenorrhea *	0	3	0
Gynecomastia **	0	3	0

Reactions for which the Eszopiclone Tablets incidence was equal to or less than placebo are not listed on the table, but included the following: abnormal dreams, accidental injury, back pain, diarrhea, flu syndrome, myalgia, pain, pharyngitis, and rhinitis.

* Gender-specific adverse reaction in females

** Gender-specific adverse reaction in males

Adverse reactions from Table 1 that suggest a dose-response relationship in adults include viral infection, dry mouth, dizziness, hallucinations, infection, rash, and unpleasant taste, with this relationship clearest for unpleasant taste.

TABLE 2 shows the incidence of adverse reactions from combined Phase 3 placebo-controlled studies of Eszopiclone Tablets at doses of 1 or 2 mg in elderly adults (ages 65-86). Treatment duration in these trials was 14 days. The table includes only reactions that occurred in 2% or more of patients treated with Eszopiclone Tablets 1 mg or 2 mg in which the incidence in patients treated with Eszopiclone Tablets was greater than the incidence in placebo-treated patients.

Table 2: Incidence (%) of Adverse Reactions in Elderly Adults (Ages 65-86 Years) in 2-Week Placebo-Controlled Trials with Eszopiclone Tablets 1 mg.

Adverse Reactions	Placebo (n=208)	Eszopiclone Tablets 1 mg (n=72)	Eszopiclone Tablets 2 mg (n=215)
Body as a Whole			
Accidental Injury	1	0	3
Headache	14	15	13
Pain	2	4	5
Digestive System			
Diarrhea	2	4	2
Dry Mouth	2	3	7
Dyspepsia	2	6	2
Nervous System			
Abnormal Dreams	0	3	1
Dizziness	2	1	6
Nervousness	1	0	2
Neuralgia	0	3	0
Skin and Appendages			
Pruritus	1	4	1
Special Senses			
Unpleasant Taste	0	8	12
Urogenital System			
Urinary Tract Infection	0	3	0

Reactions for which the Eszopiclone Tablets incidence was equal to or less than placebo are not listed on the table, but included the following: abdominal pain, asthenia, nausea, rash, and somnolence.

Adverse reactions from Table 2 that suggest a dose-response relationship in elderly adults include pain, dry mouth, and unpleasant taste, with this relationship again clearest for unpleasant taste.

These figures cannot be used to predict the incidence of adverse reactions in the course of usual medical practice because patient characteristics and other factors may differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contributions of drug and nondrug factors to the adverse reaction incidence rate in the population studied.

Other Reactions Observed During the Premarketing Evaluation of Eszopiclone Tablets

Following is a list of modified COSTART terms that reflect adverse reactions as defined in the introduction to the ADVERSE REACTIONS section and reported by approximately 1550 subjects treated with Eszopiclone Tablets at doses in the range of 1 to 3.5 mg/day during Phase 2 and 3 clinical trials throughout the United States and Canada. All reported reactions are included except those already listed in Tables 1 and 2 or elsewhere in labeling, minor reactions common in the general population, and reactions unlikely to be drug related. Although the reactions reported occurred during treatment with Eszopiclone Tablets, they were not necessarily caused by it.

Reactions are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse reactions are those that occurred on one or more occasions in at least 1/100 patients; infrequent adverse reactions are those that occurred in fewer than 1/100 patients but in at least 1/1,000 patients; rare adverse reactions are those that occurred in fewer than 1/1,000 patients. Gender-specific reactions are categorized based on their incidence for the appropriate gender.

Body as a Whole: Frequent: chest pain; Infrequent: allergic reaction, cellulitis, face edema, fever, halitosis, heat stroke, hernia, malaise, neck rigidity, photosensitivity.

Cardiovascular System: Frequent: migraine; Infrequent: hypertension; Rare: thrombophlebitis.

Digestive System: Infrequent: anorexia, cholelithiasis, increased appetite, melena, mouth ulceration, thirst, ulcerative stomatitis; Rare: colitis, dysphagia, gastritis, hepatitis, hepatomegaly, liver damage, stomach ulcer, stomatitis, tongue edema, rectal hemorrhage.

Hemic and Lymphatic System: Infrequent: anemia, lymphadenopathy.

Metabolic and Nutritional: Frequent: peripheral edema; Infrequent: hypercholesteremia, weight gain, weight loss; Rare: dehydration, gout, hyperlipemia, hypokalemia.

Musculoskeletal System: Infrequent: arthritis, bursitis, joint disorder (mainly swelling, stiffness, and pain), leg cramps, myasthenia, twitching; Rare: arthrosis, myopathy, ptosis.

Nervous System: Infrequent: agitation, apathy, ataxia, emotional lability, hostility, hypertonia, hypesthesia, incoordination, insomnia, memory impairment, neurosis, nystagmus, paresthesia, reflexes decreased, thinking abnormal (mainly difficulty concentrating), vertigo; Rare: abnormal gait, euphoria, hyperesthesia, hypokinesia, neuritis, neuropathy, stupor, tremor.

Respiratory System: Infrequent: asthma, bronchitis, dyspnea, epistaxis, hiccup, laryngitis.

Skin and Appendages: Infrequent: acne, alopecia, contact dermatitis, dry skin, eczema, skin discoloration, sweating, urticaria; Rare: erythema multiforme, furunculosis, herpes zoster, hirsutism, maculopapular rash, vesiculobullous rash.

Special Senses: Infrequent: conjunctivitis, dry eyes, ear pain, otitis externa, otitis media, tinnitus, vestibular disorder; Rare: hyperacusis, iritis, mydriasis and photophobia.

Urogenital System: Infrequent: amenorrhea, breast engorgement, breast enlargement, breast neoplasm, breast pain, cystitis, dysuria, female lactation, hematuria, kidney calculus, kidney pain, mastitis, menorrhagia, metrorrhagia, urinary frequency, urinary incontinence, uterine hemorrhage, vaginal hemorrhage, vaginitis; Rare: oliguria, pyelonephritis, urethritis.

Postmarketing Experience

In addition to the adverse reactions observed during clinical trials, dysosmia, an olfactory dysfunction that is characterized by distortion of the sense of smell, has been reported during postmarketing surveillance with Eszopiclone Tablets. Because this event is reported spontaneously from a population of unknown size, it is not possible to estimate the frequency of this event.

5. How to store Eszopiclone

Store below 30°C.

6. Contents of the pack and other information

Tablets core:

Lactose Monohydrate USP-NF (Pharmatose 200 M), Microcrystalline Cellulose, USP-NF (Avicel PH 102), Anhydrous Dibasic Calcium Phosphate, USP (A-Tab), Croscarmellose Sodium, USP-NF (Ac-Di-SoL), Colloidal Silicon Dioxide, USP-NF (Aerosil 200), Magnesium Stearate, USP-NF (LIGAMED MF-2-V),

Tablet coating

Coating agent composition: Opadry blue 03G505018, IH

%w/w	Ingredients/Compendial Reference	Grade/Dye Strength	E Number	CFR Reference	CI Number
62.500	HPMC 2910/HYPROMELLOSE (USP, Ph.Eur, JP)	6 cP	E464	172.874	-
14.850	TITANIUM DIOXIDE (USP,FCC, Ph.Eur, JP)	-	E171	73.575,73.15 75	77891
8.000	MACROGOL/PEG (NF, FCC, Ph.Eur, JECFA, JP)	MW 3350, MACROGO L 4000 JP	E1521	172.820	-
7.000	FD&C BLUE #2/INDIGO CARMINE ALUMINUM LAKE	11%-14%	E132	82.51,82.102	73015:1
6.250	TRIACETIN (USP, FCC, Ph.Eur, JPE)	-	-	184.1901	-
1.400	FD&C BLUE #2/INDIGO CARMINE ALUMINUM LAKE	30%-36%	E132	82.51,82.102	73015:1

What Eszopiclone Tablets looks like and contents of the pack

Dark blue to blue, round, biconvex, film-coated tablets debossed with ‘H’ on one side and ‘E16’ on the other side.

The Tablets are packed in

Blister pack: **10’s Alu/Alu Blister**

Supplier and Manufacturer:

Supplier	**Manufacturer**
Hetero Labs Limited 7-2-A2, Hetero Corporate Industrial Estates Sanath Nagar, Hyderabad-500 018 Telangana, India Tel. No.: +91 40 23704923/ 24/25 Fax:+91 40 23704035, 23813359 Email:contact@heterodrugs.com	HETERO LABS LIMITED UNIT-V, TSIIC Formulation SEZ, Survey No. 411, 425, 435 & 458, Polepally village, Jadcherla Mandal, Mahaboob Nagar (Dist) – 509301, Telangana. India. ANNORA PHARMA PRIVATE LIMITED, Sy. No. 261, Annaram Village, Gummadidal Mandal, Sangareddy District. Telangana State – 502313, India