REZAM®
(Mirtazapine)
Tablets U.S.P. 15mg 30mg 45mg

ریزام
(مِرٹازاپین)
ٹیبلٹس یو۔ایس۔پی۔
۱۵ ملی گرام ۳۰ ملی گرام ۴۵ ملی گرام

QUALITATIVE AND QUANTITATIVE COMPOSITION

Rezam® (Mirtazapine) Tablets U.S.P. 15mg
Each film-coated tablet contains:
Mirtazapine U.S.P……..15mg

Rezam® (Mirtazapine) Tablets U.S.P. 30mg
Each film-coated tablet contains:
Mirtazapine U.S.P……..30mg

Rezam® (Mirtazapine) Tablets U.S.P. 45mg
Each film-coated tablet contains:
Mirtazapine U.S.P……..45mg

WARNING

Suicidality and Antidepressant Drugs Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Rezam® (mirtazapine) Tablets or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Rezam® is not approved for use in pediatric patients.

DESCRIPTION

Rezam® (mirtazapine) Tablets are an orally administered drug. Mirtazapine has a tetracyclic chemical structure and belongs to the piperazino-azepine group of compounds. It is designated 1,2,3,4,10,14b-hexahydro- 2-methylpyrazino [2,1-a] pyrido [2,3-c] benzazepine and has the empirical formula of $C^{17}H^{19}N^3$. Its molecular weight is 265.36

CLINICAL PHARMACOLOGY

Pharmacodynamics: Mechanism of Action: The mechanism of action of Rezam® (mirtazapine) Tablets, as with other drugs effective in the treatment of major depressive disorder, is unknown.
Pharmacokinetics: Absorption: Rezam® (mirtazapine) Tablets are rapidly and completely absorbed following oral administration and have a half-life of about 20 to 40 hours. Peak plasma concentrations are reached within about 2 hours following an oral dose. The presence of food in the stomach has a minimal effect on both the rate and extent of absorption and does not require a dosage adjustment. **Distribution:**

Binding of mirtazapine to plasma proteins is approx. 85%.
Biotransformation: Mirtazapine is extensively metabolized after oral administration. Major pathways of biotransformation are demethylation and hydroxylation followed by glucuronide conjugation.
Elimination: It is eliminated predominantly via urine (75%) with 15% in feces. Several unconjugated metabolites possess pharmacological activity but are present in the plasma at very low levels

INDICATIONS AND USAGE

Rezam® (mirtazapine) Tablets are indicated for the treatment of major depressive disorder. A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least 5 of the following 9 symptoms: depressed mood, loss of interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt, or suicidal ideation. The effectiveness of Rezam® in hospitalized depressed patients has not been adequately studied.

CONTRAINDICATIONS

-Hypersensitivity Rezam® (mirtazapine) Tablets are contraindicated in patients with a known hypersensitivity to mirtazapine or to any of the excipients.
-Monoamine Oxidase Inhibitors The use of monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders with Rezam® Tablets or within 14 days of stopping treatment with 4. Rezam® is contraindicated because of an increased risk of serotonin syndrome. The use of Rezam® within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated. Starting Rezam® in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome.

INTERACTIONS

As with other drugs, the potential for interaction by a variety of mechanisms (e.g., pharmacodynamic, pharmacokinetic inhibition or enhancement, etc.) is a possibility. Drugs Affecting Hepatic Metabolism The metabolism and pharmacokinetics of Rezam® (mirtazapine) Tablets may be affected by the induction or inhibition of drug-metabolizing enzymes.
CYP Enzyme Inducers: When phenytoin, carbamazepine, or another inducer of hepatic metabolism (such as rifampicin) is added to mirtazapine therapy, the mirtazapine dose may have to be increased. If treatment with such a medicinal product is discontinued, it may be necessary to reduce the mirtazapine dose.
CYP Enzyme Inhibitors: Caution should be exercised when administering mirtazapine with potent CYP3A4 inhibitors, HIV protease inhibitors, azole antifungals, erythromycin, or nefazodone.
Other Drug-Drug Interactions: Amitriptyline: mirtazapine also did not cause relevant changes to the pharmacokinetics of amitriptyline. Warfarin: As at a higher dose of mirtazapine, a more pronounced effect cannot be excluded, it is advisable to monitor the INR in case of concomitant treatment of warfarin with mirtazapine. Lithium: The effects of higher doses of lithium on the pharmacokinetics of mirtazapine are unknown.
Alcohol, Diazepam: Accordingly, patients should be advised to avoid alcohol & Diazepam while taking Rezam®.
QTc-Prolonging Drugs: The risk of QT prolongation and/or ventricular arrhythmias (e.g., Torsades de Pointes) may be increased with concomi-

tant use of medicines which prolong the QTc interval (e.g., some antipsychotics and antibiotics) and in case of mirtazapine overdose.

USE IN SPECIFIC POPULATION

Pregnancy: There are no adequate and well-controlled studies in pregnant women, this drug should be used during pregnancy only if clearly needed.

Nursing mothers: Because some Rezam® may be excreted into breast milk, caution should be exercised when Rezam® (mirtazapine) Tablets are administered to nursing women.

Pediatric Use: Safety and effectiveness in pediatric patients under 18 years of age have not been established.

Geriatric use: Caution is indicated in administering Rezam® to elderly patients.

Renal Patients & Hepatic Patients: Mirtazapine clearance is decreased in patients with moderate [glomerular filtration rate (GFR)=11–39 mL/min/1.73 m^2] and severe [GFR <10ml/min/1.73m^2 renal impairment, and also in patients with hepatic impairment. Caution is indicated in administering Rezam® to such patients.

PRECAUTIONS

Akathisia/Psychomotor Restlessness: The use of antidepressants has been associated with the development of akathisia, characterized by a subjectively unpleasant or distressing restlessness and need to move, often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment.

Hyponatremia: has been reported very rarely with the use of mirtazapine. Caution should be exercised in patients at risk, such as elderly patients or patients concomitantly treated with medications known to cause hyponatremia.

Somnolence: Because of the potentially significant effects of Rezam® on impairment of performance, patients should be cautioned about engaging in activities requiring alertness until they have been able to assess the drug's effect on their own psychomotor performance.

Increased Appetite/Weight Gain: for long-term, open label treatment, 8% of patients receiving Rezam® discontinued for weight gain.

Cholesterol/Triglycerides: nonfasting cholesterol increases to ≥20% above the upper limits of normal in 15% of patients treated with Rezam®.

Transaminase Elevations: Rezam® should be used with caution in patients with impaired hepatic function.

Activation of Mania/Hypomania: Although the incidence of mania/hypomania was very low during treatment with mirtazapine, it should be used carefully in patients with a history of mania/hypomania.

Use in Patients with Concomitant Illness: Rezam® should be used with caution in patients with known cardiovascular or cerebrovascular disease that could be exacerbated by hypotension (history of myocardial infarction, angina, or ischemic stroke) and conditions that would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medication).

ADVERSE REACTIONS

- **Common or very common:** Anxiety. appetite increased. arthralgia. back pain. confusion. constipation. diarrhoea. dizziness. drowsiness. dry mouth. fatigue. headache (on discontinuation). myalgia. nausea. oedema. postural hypotension. sleep disorders. tremor. vomiting. weight increased
- **Uncommon:** Hallucination. mania. movement disorders. oral disorders. syncope
- **Rare or very rare:** Aggression. pancreatitis

- **Frequency not known:** Agranulocytosis. arrhythmias. bone marrow disorders . dysarthria . eosinophilia.
granulocytopenia. hyponatraemia. QT interval prolongation. rhabdomyolysis. seizure. serotonin syndrome. severe cutaneous adverse reactions (SCARs). SIADH. skin reactions. sudden death. suicidal tendencies. thrombocytopenia. urinary retention. withdrawal syndrome.

DRUG ABUSE AND DEPENDENCE

Physical and Psychologic Dependence: Patients should be evaluated carefully for history of drug abuse, and such patients should be observed closely for signs of Rezam® misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

DOSAGE AND ADMINISTRATION

BY MOUTH

Adult: Initially 15–30 mg daily for 2–4 weeks, dose to be taken at bedtime, then adjusted according to response to up to 45 mg once daily, alternatively up to 45 mg daily in 2 divided doses. Elderly and patients with renal or hepatic impairment. The clearance of mirtazapine is reduced in elderly patients and in patients with moderate to severe renal or hepatic impairment. Consequently, the prescriber should be aware that plasma mirtazapine levels may be increased in these patient groups, compared to levels observed in younger adults without renal or hepatic impairment.

OVERDOSAGE

Treatment should consist of those general measures employed in the management of overdose with any drug effective in the treatment of major depressive disorder. Ensure an adequate airway, oxygenation, and ventilation. Monitor ECG parameters (including cardiac rhythm) and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion, or in symptomatic patients. Activated charcoal should be administered. There is no experience with the use of forced diuresis, dialysis, hemoperfusion, or exchange transfusion in the treatment of mirtazapine overdosage. No specific antidotes for mirtazapine are known. In man-aging overdosage, consider the possibility of multiple-drug involvement.

INSTRUCTIONS

Dosage as directed by the physician. Store at 20°C-25°C, excursions permitted to 15°C-30°C. Protect from sunlight and moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION

Rezam® (Mirtazapine) Tablets U.S.P. 15mg are available in Alu-Alu blister pack of 2x10’s.
Rezam® (Mirtazapine) Tablets U.S.P. 30mg are available in Alu-Alu blister pack of 2x10’s.
Rezam® (Mirtazapine) Tablets U.S.P. 45mg are available in Alu-Alu blister pack of 2x10’s.

علامات / طریقہ استعمال

ریزام ٹیبلٹس ڈپریشن کے علاج کے لئے تجویز کردہ ہے۔

مضر اثرات

بھوک کا بڑھنا، کمر درد، سر درد، غنودگی، قبض، دست، چکر آنا۔

احتیاطی تدابیر

حاملہ خواتین اور دودھ پلانے والی مائیں ضرورت پڑنے کے پیشِ نظر صرف ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
بچے، بزرگ، جگر اور گردے کے مریض احتیاط سے استعمال کریں۔

ہدایات

۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
سورج کی روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

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ISO 14001:2015 CERTIFIED TÜV AUSTRIA — ISO 14001:2015
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