xxxxxxxx-5343

MIRTAZAPINE

MENELAT 30

30 mg Film-Coated Tablet

Antidepressant

Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders and those considering use of these agents must balance risk with the clinical need."

FORMULATION:
Each film-coated tablet contains:
Mirtazapine, USP ..... 30 mg

PRODUCT DESCRIPTION:
Mirtazapine (Menelat 30) 30 mg Film-Coated Tablet is a pink coloured, round, biconvex, film coated tablet plain on one side and break line on other side.
Mirtazapine has a tetracyclic chemical structure unrelated to selective serotonin reuptake inhibitors (MAOI). Mirtazapine belongs to the piperazanoazepine group of compounds and is an analogue of Mianserin. It is designated 1,2,3,4,10,14b-hexahydro-2-methylpyrazino [2,1-a] pyrido [2,3-c] benzazepine and has the emipirical formula of $C_{17}H_{19}Cl_3$. Its molecular weight is 265.36.
Mirtazapine is a white to creamy white crystalline powder which is slightly soluble in water.

PHARMACOKINETICS:
Mirtazapine is rapidly and completely absorbed following oral administration and has a half-life of about 20 to 40 hours. Peak plasma concentrations are reached within about 2 hours following an oral dose. Mirtazapine is approximately 85% bound to plasma proteins over a concentration range of 0.01 to 10 mcg/mL and is extensively metabolized after oral administration. Major pathways of biotransformation are demethylation and hydroxylation followed by glucuronide conjugation. In vitro, data from human liver microsomes indicate the cytochrome 2D6 and 1A2 are involved in the formation of the 8-hydroxy metabolite of Mirtazapine, whereas cytochrome 3A is considered to be responsible for the formation of the N-desmethyl and N-oxide metabolite. Mirtazapine has an absolute bioavailability of about 50%. Elimination is predominantly via urine (75%) with 15% in feces. Several unconjugated metabolite possess pharmacological activity but are present in the plasma at very low levels. The (-) enantiomer has an elimination half life that is approximately twice as long as the (+) enantiomer and therefore achieves plasma levels that are about 3 times high as that of the (+) enantiomer.

PHARMACODYNAMICS:
Mirtazapine enhances central noradrenergic and serotonergic activity. These studies have shown that Mirtazapine acts as an antagonist at central presynaptic α2 adrenergic inhibitory autoreceptors and heteroreceptors, an action that is postulated to result in an increase in central noradrenergic and serotonergic activity.Mirtazapine is a potent antagonist of 5-HT2 and 5-HT3 receptors and has no significant affinity for the 5-HT1A & 5-HT1B receptors. Mirtazapine is a potent antagonist of histamine (H1) receptors (prominent sedative effects), moderate peripheral α1 adrenergic antagonist (occasional orthostatic hypotension reported in association with its use) and as a moderate antagonist at muscarinic receptors (relatively low incidence of anticholinergic side effects associated with its use)

INDICATION:
Mirtazapine is indicated for the treatment of major depressive disorder.

DOSAGE AND ADMINISTRATION:
Initial dose is 15 or 30 mg, taken preferably in the evening. The maintenance dose is usually between 15 mg to 45 mg per day.

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.

Switching Patients to Mirtazapine from a Monoamine Oxidase Inhibitor (MAOI): At least 14 days should elapse between discontinuation of a MAOI and initiation of therapy with Mirtazapine tablets. In addition, at least 14 days should be allowed after stopping Mirtazapine before starting a MAOI. Mirtazapine has an elimination half-life of approximately 20 to 40 hours; therefore, dose changes should not be made at intervals of less than 1 to 2 weeks in order to allow sufficient time for evaluation of the therapeutic response to a given dose.

CONTRAINDICATIONS:
It is contraindicated in patients with known hypersensitivity to Mirtazapine or any of its excipients.

PRECAUTIONS:
Mirtazapine should be used with caution in patients with epilepsy, hepatic or renal impairment and cardiac disorders such as conduction disturbances, angina pectoris and recent myocardial infarction, and also in patients with hypotension, diabetes mellitus, psychoses and those with history of bipolar disorder. Treatment should be stopped if jaundice develops. Although Mirtazapine has only weak antimuscarinic activity, caution should nevertheless be exercised in patients with micturition disturbances, angle-closure glaucoma and raised intra-ocular pressure.

Patients should be advised to report any of the following symptoms during treatment: fever, sore throat, stomatitis or other signs of infection; treatment should be stopped and blood count performed. Drowsiness is often experienced at the start of therapy and patients, if affected, should not drive or operate machinery.

Patients should be closely monitored during early therapy until improvement in depression is observed because suicide is an inherent risk in depressed patients. Mirtazapine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

DRUG INTERACTIONS:
Mirtazapine should not be used with or within 2 weeks of stopping a MAOI; at least one week should elapse between stopping Mirtazapine and starting any drug liable to provoke a serious reaction (e.g. phenelzine) The use of Mirtazapine with alcohol or benzodiazepines may potentiate sedative effects.

ADVERSE REACTIONS:
Adverse effects commonly reported with Mirtazapine are increase in appetite and weight; drowsiness or sedation generally occurs during the first few weeks of treatment. Dizziness, headache, edema and increase in liver enzyme levels have been reported less commonly; jaundice may occur. Other rarely reported adverse effects include postural hypotension, exanthema, nightmares, agitation, mania, hallucinations, paraesthesia, convulsions, tremor, myoclonus, restless leg syndrome, arthalgia, myalgia, and reversible agranulocytosis, leucopenia, and granulocytopenia.

Hyponatremia, possibly due to inappropriate secretion of antidiuretic hormone, has been associated with the use of antidepressants, particularly in the elderly.

Extrapyramidal effects: Akathisia that developed in 2 patients given Mirtazapine 30 mg at night resolved in one after being treated with Clonazepam and in the other patient after reducing the dose of Mirtazapine to 15 mg at night.

Serotonin Syndrome: The serotonin syndrome is most commonly due to the additive adverse effects of two or more drugs that enhance serotonin activity at central receptors; rarely, a single serotonergic drug has caused the syndrome. One such case occurred in an elderly patient given Mirtazapine 15 mg daily; he was also taking Salbutamol, Ipratropium and Nimodipine; although none of these are known to have serotonergic effects.

"For suspected adverse drug reaction, report to FDA: www.fda.gov.ph or to TORRENT: www.torrentpharma.com".
Patient to seek medical attention immediately at the first sign of any adverse drug reaction shall appear.

STORAGE CONDITION:
Store at temperatures not exceeding 30^{o}C. Protect from light & moisture.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
Mirtazapine (Menelat 30) 30 mg Film-Coated Tablet - Alu-Alu Blister pack of 10's (Box of 30's) – DRP-2896

DATE OF FIRST AUTHORIZATION
December 21, 2009

DATE OF REVISION
June 2016

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
Units 3 & 4, 34th Floor, Zuellig Building
Makati Avenue Corner Paseo de Roxas
Makati City, PHILIPPINES

PRODUCT NAME :	Menelat	**COUNTRY :** Philippines	**LOCATION :** Indrad	**Supersedes A/W No.:**			
ITEM / PACK :	Insert	**NO. OF COLORS:** 1	**REMARK :**				
DESIGN STYLE :	Front Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE :	xxxxxxxxx-5343		**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM) (LxWxH) :	150 x 180		Prepared By	**Pkg.Dev**			
ART WORK SIZE :	S/S		Reviewed By	**Pkg.Dev**			
DATE :	17-06-2016	Black	Approved By	**Quality**			