165mm

155mm

DOSAGE:
As directed by the physician.

Instructions: Store below 30˚C in a dry place, protect from light. To be dispensed on the prescription of a registered medical practitioner only. Keep out of the reach of children.

خوراک : ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات : دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔

Kaizen Pharmaceuticals (Pvt.) Ltd.

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

DEXBUPRO

Dextromethorphan + Bupropion

45mg/105mg Tablets

ڈیکس بیوپرو

(ڈیکسٹرومیتھورفن + بیوپروپیون)

۴۵ ملی گرام / ۱۰۵ ملی گرام گولیاں

COMPOSITION:
Each film coated bi-layered tablet contains:
Dextromethorphan Hydrobromide 45mg
Eq. to Dextromethorphan Base ..... 32.98mg (as Immediate-Release Layer)
Bupropion Hydrochloride 105mg
Eq. to Bupropion..... 91.14mg (as Extended-Release Layer)

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and emergence of suicidal thoughts and behaviors. Dexbupro is not approved for use in pediatric patients

CLINICAL PHARMACOLOGY
Mechanism of Action:
Unlike traditional antidepressants that mainly act on the monoamine pathway by blocking the reuptake of serotonin, norepinephrine, or dopamine (or modulating their receptors), dextromethorphan works differently. The rate of dextromethorphan's rapid metabolism can be reduced with the use of CYP2D6 inhibitors such as quinidine or bupropion.

Dextromethorphan works as an uncompetitive NMDA receptor antagonist (increasing glutamate levels) & sigma-1 receptor agonist.
Bupropion may have noradrenergic and dopaminergic effects and increases plasma levels of dextromethorphan by inhibiting CYP2D6. Bupropion weakly inhibits norepinephrine and dopamine reuptake but does not inhibit monoamine oxidase or serotonin reuptake. Both dextromethorphan & bupropion increase the availability of norepinephrine by inhibiting its reuptake and also act as alpha-4-beta-2 nicotinic (nACh) antagonists. Bupropion also increases the availability of dopamine by blocking its reuptake. Dextromethorphan boosts serotonin levels by blocking its reuptake and increasing its action via sigma-1 agonism

PHARMACODYNAMICS:
Cardiac Electrophysiology
At the maximum recommended dose, DEXBUPRO does not prolong the QT interval to any clinically relevant extent.

PHARMACOKINETICS
DEXBUPRO is a combination of dextromethorphan and bupropion. Bupropion inhibits the metabolism of dextromethorphan via CYP2D6. Dextromethorphan when co-administered with bupropion displays nonlinear pharmacokinetics at steady state, with greater than dose-proportional changes in AUC and Cmax for varying doses of dextromethorphan [60 to 120 mg (0.67-1.33 times the maximum recommended dose of DEXBUPRO)] and less than dose-proportional changes for varying doses of bupropion [150 to 300 mg (0.71-1.43 times the maximum recommended dose of DEXBUPRO)].

Steady state plasma concentrations of dextromethorphan and bupropion when given as DEXBUPRO are achieved within 8 days. The accumulation ratios for dextromethorphan at steady state when given as DEXBUPRO are 20 and 32, respectively based on Cmax and

AUC0-12, compared to 1.3 and 1.4, respectively, for dextromethorphan given without bupropion. The accumulation ratios for bupropion at steady state are 1.1 and 1.5, respectively based on Cmax and AUC0-12.

SPECIAL POPULATION
- Lactation: Breastfeeding not recommended.
- Severe Renal Impairment: Avoid use.
- Severe Hepatic Impairment: Avoid use.

THERAPEUTIC INDICATIONS
DEXBUPRO is a combination of dextromethorphan, an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist, and bupropion, an aminoketone and CYP450 2D6 inhibitor, indicated for the treatment of major depressive disorder (MDD) in adults.

DOSAGE & ADMINISTRATION
Prior to initiating treatment with DEXBUPRO: assess blood pressure; screen patients for history of bipolar disorder, mania, or hypomania; and determine if patients are receiving any other medications that contain bupropion or dextromethorphan.
- Starting dosage is one tablet once daily in the morning. After 3 days, increase to the maximum recommended dosage of one tablet twice daily, separated by at least 8 hours. Do not exceed two doses within the same day.
- Swallow tablets whole, do not crush, divide, or chew.
- Moderate renal impairment: One tablet by mouth once daily in the morning.
- CYP2D6 poor metabolizers: One tablet by mouth once daily in the morning.

ROUTE OF ADMINISTRATION
For oral administration only.

ADVERSE REACTIONS
Most common adverse reactions (≥5% and more than twice as frequently as placebo): dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, and hyperhidrosis.

CONTRAINDICATIONS
- With a seizure disorder.
- With a current or prior diagnosis of bulimia or anorexia nervosa as a higher incidence of seizures was observed in such patients treated with the immediate-release formulation of bupropion.
- Undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs.
- Taking, or within 14 days of stopping, MAOIs due to the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome. Starting DEXBUPRO in a patient treated with reversible MAOIs such as linezolid or intravenous methylene blue is contraindicated.
- With known hypersensitivity to bupropion, dextromethorphan, or other components of DEXBUPRO. Anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported with bupropion. Arthralgia, myalgia, fever with rash, and other serum sickness-like symptoms suggestive of delayed hypersensitivity have also been reported with bupropion

PRECAUTIONS
- Seizure: Risk is dose-related. Discontinue if seizure occurs.
- Increased Blood Pressure and Hypertension: DEXBUPRO can increase blood pressure and cause hypertension. Assess blood pressure before initiating treatment and monitor periodically during treatment.
- Activation of Mania or Hypomania: Screen patients for bipolar disorder.

- Psychosis and Other Neuropsychiatric Reactions: Instruct patients to contact a healthcare provider if such reactions occur.
- Angle-Closure Glaucoma: Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants.
- Dizziness: DEXBUPRO may cause dizziness. Take precautions to reduce falls and use caution when operating machinery.
- Serotonin Syndrome: Use of DEXBUPRO with selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants increases the risk. Discontinue if occurs.
- Embryo-fetal Toxicity: May cause fetal harm. Advise pregnant females of the potential risk to a fetus. Discontinue treatment in pregnant females and use alternative treatment for females who are planning to become pregnant.

DRUG INTERACTIONS
Strong CYP2D6 inhibitors:
Recommended dosage is one tablet by mouth once daily in the morning.
- Strong CYP2B6 inducers: Avoid use.
- CYP2D6 Substrates: Increases the exposures of drugs that are substrates of CYP2D6.
- Digoxin: May decrease plasma digoxin levels. Monitor digoxin levels.
- Drugs that lower seizure threshold: Coadministration may increase risk of seizure.
- Dopaminergic drugs: Central Nervous System (CNS) toxicity can occur with concomitant use.
- Drug-laboratory test interactions: DEXBUPRO can cause false-positive urine test results for amphetamines.

OVERDOSAGE
There is limited clinical study experience regarding human overdosage with DEXBUPRO. Overdosage information is based on experience with the individual components, dextromethorphan and bupropion. Metabolism of the dextromethorphan component of DEXBUPRO is inhibited by the bupropion component, such that overdose due to DEXBUPRO might be more severe or more persistent compared to overdose of dextromethorphan alone.

Dextromethorphan
Symptoms of dextromethorphan overdose include nausea, vomiting, stupor, coma, respiratory depression, seizures, tachycardia, hyperexcitability, and toxic psychosis. Other adverse effects include ataxia, nystagmus, dystonia, blurred vision, and changes in muscle reflexes. Dextromethorphan may cause serotonin syndrome, and this risk is increased by overdose, particularly if taken with other serotonergic agents, SSRIs or tricyclic antidepressants.

Bupropion
Overdoses of up to 30 grams or more of bupropion (approximately 143 times the maximum recommended dose of DEXBUPRO) have been reported. Seizure was reported in approximately one-third of all cases. Other serious reactions reported with overdoses of bupropion alone included hallucinations, loss of consciousness, mental status changes, sinus tachycardia, ECG changes such as conduction disturbances (including QRS prolongation) or arrhythmias, clonus, myoclonus, and hyperreflexia. Fever, muscle rigidity, rhabdomyolysis, hypotension, stupor, coma, and respiratory failure have been reported mainly when bupropion was part of multiple drug overdoses.
Although most patients recovered without sequelae, deaths associated with overdoses of bupropion alone have been reported in patients ingesting large doses of the drug. Multiple uncontrolled seizures, bradycardia, cardiac failure, and cardiac arrest prior to death were reported in these patients.

How to supplied
Dexbupro 45mg/105mg Tablet available in pack size of 1x10's, 2x10's & 3x10's