NEANXETIN® Capsules
Fluoxetine hydrochloride

1. Description
Fluoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI). Each capsule contains:
1.1 *Active ingredient*: Fluoxetine hydrochloride equivalent to 20 mg fluoxetine.
1.2 *Excipients*: Starch flowable, dimethicone, patent blue V, yellow iron oxide, titanium dioxide, gelatin, pharmaceutical grade edible printing ink.

2. Clinical Information
2.1 Therapeutic Indications
Depression with or without associated anxiety symptoms.
Obsessive-compulsive disorder (OCD).
Bulimia nervosa: Fluoxetine is indicated for the reduction of binge-eating and purging activity.
Pre-menstrual Dysphoric Disorder (PMDD): Fluoxetine is indicated for the treatment of pre-menstrual dysphoric disorder.
Diagnosis of PMDD: The essential diagnostic features of PMDD are clear and established cyclicity (occurring during the last week of the luteal phase in most menstrual cycles) of symptoms such as depressed mood, anxiety, affective lability, accompanied by impairment in social and/or occupational function and physical symptoms (such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of bloating, weight gain) -all of which must be severe. This syndrome should be distinguished from the commoner pre-menstrual tension (distinguished from PMDD by milder symptoms and less impact on normal activities) and from any co-existing psychiatric disorder.
Panic disorder
2.2 Posology/dosing and method of administration
Depression with or without associated anxiety symptoms: 20 mg per day is the recommended dose -adults and the elderly.
Bulimia nervosa: 60 mg per day is the recommended dose for a reduction in binge eating and purging activity.-adults and the elderly.
Obsessive-compulsive disorder: 20 mg to 60 mg per day is the recommended dose.-adults and the elderly.
Premenstrual dysphoric disorder: 20 mg per day given continuously (every day of the menstrual cycle) or intermittently (defined as starting a daily dose 14 days prior to the anticipated onset of menstruation through the first full day of menses and repeating with each cycle) is the recommended dose.
Panic disorder: Treatment is recommended to be initiated with a dose of 10 mg per day. After one week on 10 mg per day, the dose should be increased to the recommended dose of 20 mg per day. The dose can be further titrated as needed up to 60 mg per day.
All indications: The recommended dose may be increased or decreased. Doses above 80 mg/day have not been systematically evaluated.
Administration with food: Fluoxetine may be administered with or without food.
Age: There are no data to suggest that alternative dosing is required on the basis of age alone.
Use in children: Safety and effectiveness in children (ages 7 to < 18) have been established for depression and OCD. A lower starting dose should be considered. Doses above 60 mg/day have not been systematically evaluated in children (ages 7 to < 18).
Concurrent disease and/or concomitant therapy: A lower or less frequent dose should be considered in patients with hepatic impairment, concurrent diseases, or who are taking multiple medications.

2.3 Contraindications
Hypersensitivity: Fluoxetine is contraindicated in patients known to be hypersensitive to it.
Monoamine oxidase inhibitors (MAOIs): Fluoxetine should not be used in combination with a monoamine oxidase inhibitor (MAOI). Fluoxetine should not be used within a minimum of 14 days of discontinuing therapy with an MAOI. At least 5 weeks should elapse between discontinuation of fluoxetine and initiation of therapy with an MAOI. If fluoxetine has been prescribed chronically and/or at a high dose, a longer interval should be considered.
Serious and fatal cases of serotonin syndrome (which may resemble and be diagnosed as neuroleptic malignant syndrome) have been reported in patients treated with fluoxetine and an MAOI in close temporal proximity.
2.4 Warnings
Rash: Rash, anaphylactoid events, and progressive systemic events, sometimes serious and involving skin, kidney, liver, or lung have been reported in patients taking fluoxetine.
Upon the appearance of rash, or of other possibly allergic phenomena for which an alternative aetiology cannot be identified, fluoxetine should be discontinued.
2.5 Precautions
Seizures: As with other antidepressants, fluoxetine should be introduced cautiously in patients who have a history of seizures.
Hepatic / renal function: Fluoxetine is extensively metabolized by the liver and excreted by the kidneys. A lower dose, e.g., alternate day dosing, is recommended in patients with significant hepatic dysfunction. When given fluoxetine 20mg per day for 2 months, patients with severe renal failure (GFR < 10 ml/min) requiring dialysis showed no difference in plasma levels of fluoxetine or norfluoxetine compared to controls with normal renal function.
Hyponatremia: Cases of hyponatremia (some with serum sodium lower than 110 mmol/L) have been reported. The majority of these cases occurred in elderly patients & in patients treated with diuretics or otherwise volume- depleted.
Glycemic control: In patients with diabetes, treatment with an SSRI may alter glycemic control. Hypoglycemia has occurred during therapy with fluoxetine and hyperglycaemia has developed following discontinuation. Insulin and/or oral hypoglycaemic dosage may need to be adjusted when fluoxetine therapy is initiated or discontinued.
2.6 Drug interactions :
Monoamine oxidase inhibitors: (see "Contraindications")
Drugs metabolized by cytochrome P450IID6 isoenzyme: Because fluoxetine has the potential to inhibit the cytochrome P450IID6 isoenzyme, therapy with medications that are predominantly metabolized by the P450IID6 system and that have a relatively narrow therapeutic index should be initiated at the low end of the dose range if a patient is receiving fluoxetine concurrently or has taken it in the previous 5 weeks. If fluoxetine is added to the treatment regimen of a patient already receiving such a drug, the need for decreased dose of the original medication should be considered.
CNS active drugs: Changes in blood levels of phenytoin, carbamazepine, haloperidol, clozapine, diazepam, alprazolam, lithium, imipramine and desipramine, and in some cases, clinical manifestations of toxicity have been observed. Consideration should be given to using conservative titration schedules of the concomitant drug and monitoring of clinical status.
Protein binding: Because fluoxetine is tightly bound to plasma protein, the administration of fluoxetine to a patient taking another drug that is tightly bound to protein may cause a shift in plasma concentrations of either drug.
Warfarin: Altered anti-coagulant effects (laboratory values and/or clinical signs and symptoms), with no consistent pat-

tern, but including increased bleeding, have been reported uncommonly when fluoxetine is co-administered with warfarin. As is prudent in concomitant use of warfarin with many other drugs, patients receiving warfarin therapy should receive careful coagulation monitoring when fluoxetine is initiated or stopped.

Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g. atypical antipsychotic such as clozapine, phenothiazines, most TCAs, aspirin, NSAIDs) , as well as in patients with a history of bleeding disorders

Alcohol: The combination of SSRI treatment and alcohol is not advisable. However, in formal testing, fluoxetine did not raise blood alcohol levels or enhance the effects of alcohol.

Electroconvulsive therapy (ECT): There have been rare reports of prolonged seizures in patients on fluoxetine receiving ECT treatment.

Elimination half-life: The long elimination half-lives of fluoxetine and its principal metabolite, norfluoxetine, are of potential consequence when drugs are prescribed which might interact with either substance following the discontinuation of fluoxetine.

2.7 Carcinogenesis, mutagenesis, impairment of fertility

There is no evidence of carcinogenicity, mutagenicity, or impairment of fertility from in vitro or animal studies.

2.8 Use during pregnancy and lactation

Pregnancy: Experimental animal studies do not indicate direct or indirect harmful effects, with respect to the development of the embryo or foetus or the course of gestation. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation: Fluoxetine is secreted in human milk; therefore, caution should be exercised when fluoxetine is administered to nursing women.

Labour and delivery: The effect of fluoxetine on labour and delivery in humans is unknown.

2.9 Undesirable effects

As with other SSRIs , the following undesirable effects have been seen:

Body as a whole: autonomic symptoms[1], hypersensitivity[2] (see Contraindications and Warnings), serotonin syndrome[3], photosensitivity.

Cardiovascular system: None.

Digestive system: gastrointestinal disorders[4] , very rare idiosyncratic hepatitis.

Endocrine system: inappropriate secretion of ADH.

Hemic and lymphatic system: ecchymosis.

Metabolic and nutritional disorders: None.

Musculoskeletal system: None.

Nervous system: abnormal movement/tremor[5], anorexia[6], anxiety and associated symptoms[7], dizziness, fatigue[8], impairment of concentration or thought process[9], manic reaction, sleep abnormalities[10].

Respiratory system: yawn.

Skin and appendages: alopecia.

Special senses: abnormal vision[11].

Urogenital system: abnormalities of micturition[12], priapism/prolonged erection, sexual dysfunction[13].

Children: headache.

2.10 Overdose

Symptoms: Cases of overdose of fluoxetine alone usually have a mild course. Symptoms of overdose have included nausea, vomiting, seizures, cardiovascular dysfunction ranging from asymptomatic arrhythmias to cardiac arrest, pulmonary dysfunction, and signs of altered CNS status ranging from excitation to coma. Fatality attributed to overdose of fluoxetine alone has been extremely rare.

Management: Cardiac and vital signs monitoring is recommended, along with general symptomatic and supportive measures. No specific antidote is known. Forced diuresis, dialysis, haemoperfusion, and exchange transfusion are unlikely to be of benefit. In managing overdosage, consider the possibility of multiple drug involvement.

2.11 Effects on ability to drive and use machines

Psychoactive drugs may impair judgement, thinking, or motor skills. Patients should be advised to avoid driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected.

3. Pharmacodynamic Properties

Fluoxetine has practically no affinity to other receptors such as alpha 1-, alpha 2- and beta adrenergic; serotonergic; dopaminergic; histaminergic1; muscarinic; and GABA receptors.

3.1 Pharmacokinetic Properties

Absorption and distribution: Fluoxetine is well absorbed after oral administration. Peak plasma concentration is reached in 6 to 8 hours. Fluoxetine is extensively bound to plasma proteins. Fluoxetine is widely distributed. Steady-state plasma concentrations are achieved after dosing for several weeks. Steady-state concentrations after prolonged dosing are similar to concentrations seen at 4 to 5 weeks.

Metabolism and excretion: Fluoxetine is extensively metabolized in the liver to norfluoxetine and a number of other, unidentified metabolites which are excreted in urine. The elimination half-life of fluoxetine is 4 to 6 days and that of its active metabolite is 4 to 16 days.

3.2 Preclinical Safety Data

There is no evidence of carcinogenicity, mutagenicity, or impairment of fertility from in vitro or animal studies.

4. Storage Conditions

Store in a dry place below 30°C, protected from light.
Do not refrigerate.

Do not use after expiry date

5. Presentation

Capsules 20 mg in blister pack of 14's.

THIS IS A MEDICAMENT

- A Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

KEEP MEDICAMENT OUT OF REACH OF CHILDREN

Manufactured in Zouk Mosbeh, Lebanon, by
ALGORITHM S.A.L.

1 includes: dry mouth, sweating, vasodilatation, chills
2 includes: pruritus, rash, urticaria, anaphylactoid reaction, vasculitis, serum sickness-like reaction
3 characterized by the clustering of clinical features of changes in mental state and neuromuscular activity, in combination with autonomic nervous system dysfunction.
4 includes: diarrhea, nausea, vomiting, dysphagia, dyspepsia, taste perversion
5 includes: twitching, ataxia, buccoglossal syndrome, myoclonus, tremor
6 includes: anorexia, weight loss
7 includes: palpitation, anxiety, nervousness, psychomotor restlessness
8 includes: somnolence, asthenia
9 includes: concentration impaired, thought process impaired, depersonalisation
10 includes: abnormal dreams, insomnia
11 includes: blurred vision, mydriasis
12 includes: urinary frequency, urination impaired
13 includes: libido decreased, delayed or absent ejaculation, anorgasmia, impotence

Rev. No. 05/05