LUVOX® (fluvoxamine maleate) 25 ma TABLETS, 50 mg and 100 mg SCORED TABLETS

Brief Summary (For full Prescribing Information and Patient Information, refer to package insert.)

INDICATIONS AND USAGE

LUYOX** Toblets are indicated for the treatment of obsessions and compulsions in adults and children and adolescents (ages 8-17) with Obsessive Compulsive Disorder (OCD), as defined in the DSMHIPR.

UNIQUE (U.U.), as derived in the DAMPIN.

CONTRAINDICATIONS

Coadministration of befenodine, astemizale, or asoptide with LUVOX*Tablets is contraindicated (see WARNINGS and PRECAUTIONS).

LUVOX® Tablets are contraindicated in patients with a history of hypersensitivity to fluvoxamine male

TRANCINOS
In patients receiving another serotonin reuptake inhibitor drug in combination with monoamine oxidase inhibitors (MAOI),
there have been reports of serious, sometimes fatal, reactions. Some cases presented with features resembling neurolepiti
malignant syndrome. Therefore, it is recommended that LUVOX° Tablets not be used in combination with a MAOI, or within
14 days of discontinuing treatment with a MAOI. After stopping LUVOX° Tablets, at least 2 weeks should be allowed before

notignant syndrome. Therefore, it is recommended that LUVOX* Tablets, at least 2 weeks should be allowed before starting a MAOI.

Terlenadine, astemizale and cisapride are all metabolized by the cytochrome P450IIIA4 iscenzyme. Increased plasma concentrations of terlenadine, astemizale and cisapride are all metabolized by the cytochrome P450IIIA4 iscenzyme. Increased plasma concentrations of terlenadine, astemizale and cisapride cause QT prolongation and have been associated with torsides de pointes-type ventricular tachycardia, sometimes fatal. Although it has not been definitively demonstrated that fluvoxamine is a potent IIIA4 inhibitor, it is likely to be. Consequently, it is recommended that fluvoxamine not be used in combination with either terfenadine, astemizale, or disapride.

Other Patentially Important Drug Interactions
(Abo see PRCALIMINS. 5- Dug Interactions) Bezacidiazepines: Benzodiazepines metabolized by phonic oxidation (e.g., diprazolom, miczolom, http://doi.org/10.1009/10.1

PRECAUTIONS

General

General Activation of Mania/Hypomania: During premarketing studies involving primarily depressed patients, hypomania or monia occurred in approximately 2% of patients treated with fluoroscensine. Activation of monia/hypomania has also been reported in a small proportion of patients with major affective disorder with were neared with other marketed antidepressons. As with all antidepressons, LUVOX® Tablets should be used contiously in potients where the properties of the properties with a bistory of transia. Seizures: Inshould be descrimined in any potient who develops servers. Surface! The possibility objects the standard in independent in patients with the depressive symptoms, whether these occur in primary depression or in association with another primary disorder such as QCD. Close supervision of high risk patients should accompany initial drug therapy. Prescriptions for LUVOX® Tables should be written for the smallest rought quantity of totalests consistent with good potient management in order to reduce the risk of overdose. Use in Parlients with Concomitant Illness; Closely monitored clinical experience with LUVOX® Tables in potients with concomitant systemic lines is limited. Coulton is advised in administering LUVOX® Tables to make the description of the smallest transition with diseases or conditions that could didn'the theorytenic responses or metables. ILluVOX® Tablest have not been evidented or used to any appreciable extent in potients with a secent history of myocardial infortion or unstable heart disease. Patients with these diagnoses were systematically excluded from many clinical studies during the product's permutaking testing. Evolution of the electrocologisms for potients with depression or COV 600 Mportipated in permaketing studies revealed no differences between fluorosmic and placebook in the emerger of initiative important EG changes. In patients with liver dysfunction fluorosmic and offerences betw

Information for Patients

Information for Patients
Physicians are advised to discuss the following issues with patients for whom they prescribe LUVOX* Toblets: Interference with Cognitive or Motor
Performance: Since any psychoactive drug may impair judgement, thinking, or motor skills, patients should be continued about operating hazardous
machinery, including automobiles, until they are sertain that LUVOX* Toblets therapy does not obversely offset their ability to engage in such activates.
Pergenancy: Patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during therapy with LUVOX*
Toblets. Nursing: Patients receiving LUVOX* Toblets should be advised to notify their physicians if they are bicking, or plan to take, any prescription
or over-the-counter drugs, since there is a potential for clinically important interactions with LUVOX Toblets. Alorshot: As with other psychotropic medications,
patients should be advised to notify their physicians if they
develop or rosh, hives, or a related allergic phenomenon during therapy with LUVOX* Toblets.

Laboratory Tests
There are no specific laboratory tests recommended.

Drug Interactions

Potential interactions with drugs that inhibit or are Metabolized by Cytochrome P450 Isozymes: Multiple hepatic cytochrome P450 (CY450) enzymes: Multiple hepatic cytochrome P450 (CY450) enzymes are involved in the axidative biotransformation of a large number of structurally different drugs and endogenous campounds. The axidatic knowledge concerning the relationship of fluoroximine and the CY450 enzyme system has been obtained mostly from phermacokinetic interaction studies conducted in healthy volunteers, but some periminary in with data are also available. Based on a finding of substantial interactions of luoroximine with tention of these and limited in with data for the IMA4 is everyme, in appears that fluoroximine inhibits iscenzymes that are known to be involved in the metabolism of drugs such as wordnin, theophyline and proparolal. A clinically significant fluoroximine inhibits iscenzymes that are known to be involved in the metabolism of drugs such as surfacing, the control, evantarin, theraphylline, certain benerodizegations and phenyllom. If UMXD's Polisto are to be administred together with a drug that is eliminated via axidative metabolism and has a narrow therapeutic window, plasma levels and/or pharmacodynamic effects of the latter drug should be monitored closely, at least until standy-state considience are noted. Also Active Drugs: Please see complete esecucing information for recommendations regarding USX drugs and can amonamie axidates withintox, observation, divergent, achieve, durbanazepine, clozopine, lithium, lorazeporm, methodone, sumotripton, torine, trickic antidepressans, hystophara and other drugs such as theophyline, evant in the relabolisms, proponallo and that belabolisms. Effects of Smoklang on Fluoroximine Metabolisms. Smoklers biod 25% increase in the nebbolisms, fluoropamine and fluoroximine moletter.

Cardioagenesis, Mutagenesis, Implairment of Fertility

of combined use of ECT and fluvoxomine molecute.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis; There is no evidence of corcinogenicity, mutagenicity or impairment of fertility with fluvoxomine molecute. There was no evidence of corcinogenicity in tast treated analy with fluvoxomine molecute for 20 months or harmsters treated analy with fluvoxomine molecute for 20 months. The daily doses in the high dose groups in these studies were increased over the course of the study from a minimum of 130 mg/kg to a maximum of 240 mg/kg in studies. The maximum makes of 740 mg/kg is approximately 6 times the maximum human aduly dose on a mg/m² basis. Mutagenesis: No evidence of mutagenic potential was observed in a mouse microaucless test, an in wino chromosome observation test, or the Ames microbial mutagen test with or without metabolic cultivation. Impairment of Fertility: In Entility studies of make and female rats, up to 80 mg/kg/doy ordity of fluvoxomine molecute. (approximately 2 times the maximum human daily dose on a mg/m² basis) had no effect an mating performance, duration of gestation, or pregnancy rate.

only dose on a mg/m basis; hod no effect on instrup performance, ourotion of gestionar, or pregionary rate.

Perspansory

Labor and Delivery
The effect of fluvoxamine on labor and delivery in humans is unknown

Nursing Mothers

As far many other drugs, fluvoxamine is secreted in human breast milk. The decision of whether to discontinue nursing or to discontinue the drug should take into account the potential for serious adverse effects from exposure to fluvoxamine in the nursing infant as well as the potential benefits of LIVOX* (fluvoxamine maleate) Tablets therapy to the mother.

Pediatry of fluvoxamine molecte for the treatment of Obsessive Compulsive Disorder was demonstrated in a 10-week multicenter placebo controlled study with 120 outpotients ages 8-17. The odverse event profile observed in that study was generally similar to that observed in adult studies with fluvoxamine (see ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION).

Decreased appetite and weight loss have been observed in association with the use of fluvoxomine as well as other SSRIs. Consequently, reguler monitoring of weight and growth is recommended if treatment of a child with an SSRI is to be continued long term.

Geriatric Use

Oction 16 Section 200 patients participating in controlled premarketing studies with LUYOX¹⁰ Tablets were 65 years of age or over. No overall differences in safety were observed between these patients and younger patients. Other reported clinical experience has not identified differences in response between the elderly and younger patients. However, the clearance of fluxosamine is decreased by about 50% in elderly compared to younger patients (see Pharmacokinerias under CUNICAL

PHARMACOLOGY), and greater sensitivity of some older individuals also cannot be ruled out. Consequently, LUVOX® Tablets should be slowly titrated during initiation

ADVERSE REACTIONS

Associated with Discontinuation of Treatment
Of the 1087 OCD and depressed patients mented with fluvoxamine maleate in controlled clinical trials conducted in North America, 22% discontinued trentment due to an infrerse event

Incidence in Controlled Trials - Commonly Observed Adverse Events in Controlled Clinical Trials: LUVOX® Tablets have been studied Incidence in Controlled Trials - Commonly Observed Adverse Events in Controlled Clinical Trials: LINOVE Tolds have been studied in controlled trials of OCD (H=320) and depression (H=1350). In general, observed event rates were similar in the two data sets as well as in the pediatric OCD study. The most commonly observed otherse events associated with the use of LINOVE Toldsets and likely to the drug-petrated facindative of 5% or geneter and at least twice that for placebol derived from Tolds 1 were: somnolence, insomnia, nervousness, tremor, noussea, dyspepsia, nonrexia, vomiting, obnormal ejacutation, astherial, and sweating, in a pool of two studies involving only patients with OCD, the following additional events were identified using the above rate; dry mouth, decreased skidus, unionsy frequency, amaginari, shinks and totals pervension. In study of pediatric swith OCD, the following additional events were identified using the above rule: agritation, depression, dysmenorihea, flotolence, hyperkinesia, and rash.

**Adverse Events Occurring at an Incidence of 1%: Tolds I enumerates observe events that occurred at a frequency of 1% or more, and were a forested that in the backer, more, appeals operation treated with UNION which is two between before a frequent through and and a supplementations are supplementations.

Adverse Events Occurring at an Incidence of 1%: toble I enumericies obverse events that occurred at a frequency of 1% of more, and were frequent than in the placets group, among polemats reader with UNOV Tobles in two shorterm placets controlled COD this (10 week) and depression trials (6 week) in which patients were dosed in a range of generally 100 to 300 mg/day. This toble shows the percentage of potents in each group who had at least one occurrence of an event at some time during their treatment. Reported odverse events were classified using a standard COSIATE and of Costa of the control of the do provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the side-effect incidence rate in

the population studied.

Table 1: Treatment-emergent adverse event (incidence rates by Body System in adult ocd and depression Populations Combined) (floroximine (N-892) vs. placeho (N-778) by potients-percentage): Body as whole: Heodoche (22 vs. 20); Asthenia (14 vs. 6); Flu Syndrome (3 vs. 2); Chills (2 vs. 1), Cardiovascular: Polyintinos (3 vs. 2), Digestive System: Nousea (40 vs. 14); Asherian (14 vs. 6); the Syndrome (3 vs. 2); (hills (2 vs. 1). CARDIOVASCULAR: Polytetions (3 vs. 2). DIGESTIVE SYSTEM: Nousen (40 vs. 14); Diorthea (11 vs. 7); Contaption (10 vs. 8); Dysepselo (10 vs. 5); Ancreas (6 vs. 2); Ventrian (6 vs. 2); Polyteting (7 vs. 6); Polyteting (7 vs. 7); Polyteting (7 vs.

Events for which fluvoramine malectic incidence was equal to or less than placebo are not listed in the table above, but include the following abdominal ani, abnormal dreams, appetite increase, back pain, chest pain, confusion, dysmenorthea, fever, infection, leg aromps, migraine, myoligia, pain, possession, pharyngilis, perturn lytpoersion, putths, sost, thinks, thirst and limitus. Includes "toothache," "tooth extraction and adsress," and "caies." Mostly "delayed ejaculation." "Incidence based on number of male patient and Adverse Events in OCD Placebo Controlled Studies Which are Markedly Different (defined as at least a two-fold difference) in Rate from the Pooled Event Rates in OCD and Depression Placebo Controlled Studies: The events in OCD studies with the world decrease in rate compared to event rates in OCD and depression studies were dysphagia and analytopia (norshy blurred vision). Additionally, there was proproximate 25% decrease in nousean. The events in OCD studies with to two-fold increase in inter compared to event rates in OCD and depression studies were: asthenia, obnormal ejaculation (mostly delayed ejaculation), amiety, infaction, thinitis, anargasmia (in males), depression, hibide decreased, pharyngifis, agritation, impolence, myoclosus/hiniti, thist, weight less, leg camps, myolgia and uninary retention. These events are listed in order of decreasing rates in the OCD trials.

Other Adverse Events in OCD Pediatric Population. In Pediatric pointents (N=57) treated with LUVOX® Tablets, the overall profile of adverse events is similar to that seen in adult studies. Other reactions which have been reported in two or more pediatric patients, and were more frequent than in the placebo group were: abnormal thinking, cough increase, dysmenorthea, enchymosis, emotional ability, epistaxis, hyperkinesia, infection, maint reaction, resh, sinusifis, and

weight decrease.

Virtal Sign Changes

Comparisons of throwarmine malerate and placebo groups in separate pools of short-term OCD and depression trials on (1) median change from baseline on various what signs variables and on (2) incidence of patients meeting critaria for potentially important changes from baseline on various what signs variables revealed no important differences between fluovoxamine malerate and piacebo.

Laboratory Changes

Comparisons of fluovoxamine maleate and placebo groups in separate pools of shart-term OCD and depression trials on (1) median change from baseline on various serum emistry, hematology, and uninalysis variables and on (2) incidence of patients meeting criteria for potentially important changes from baseline on various serum chemistry, hematology, and uninalysis variables revealed no important differences between fluovoxamine maleate and placebo. ECG Changes

Comparisons of Theoroamine maleute and placebo groups in separate pools of short-term OCD and depression trials on (1) mean change from boseline on various ECG variables and on (2) incidence of patients meeting criteria for patentially important changes from boseline on various ECG variables revealed no important differences between fluvoxomine maleate and placebo.

The high productive served noncommental interests of the present of the trents Observed During the Premarketing Evaluation of LUVOX® Tablets

During premarketing clinical trials conducted in North America and Europe, multiple doses of fluoroamine maleate were administered for a combined total of 2737 patient exposures in patients suffering OCD or Major Depressive Disorder. Unnoward events associated with this exposure were recorded by clinical Other Events Observed During the Premarketing Evaluation of LUVOX* Tablets
During premarking cinical trials conducted in North America and Europe, multiple doses of throxamine maleate were administered for a combined total
of 2737 potient exposures in patients suffering OCD or Major Depressive Disorder. Untroward events associated with this exposure were recorded by chical
investigators using descriptive terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of
individuals experiencing adverse events without first grouping similar types of untrowed events into a limited (i.e., reduced) number of standard event
and considers. In the bublishors which follow, a standard COSIARFbased Dictionary terminology has been used to dassily reported adverse events. If the
COSIARF term for an event was so general as to be uninformative, it was replaced with a more informative them. The frequencies prevented, theelone,
represent the proportion of the 2737 patient exposures to multiple doses of flyworamine molecute who experienced an event of the type cited and not exposures the proportion of the 2737 patient exposures to multiple doses of flyworamine molecute who experienced an event of the type cited and not exposures the proportion of the 2737 patient exposures to multiple doses of flyworamine molecute, and to day good was excracised remote (i.e., neoplasta, gastrointesthal accuration, the proportion of the type cited and a day cover was excracised remote (i.e., neoplasta, gastrointesthal accuration, the proportion of the proportion of the continuous proportion of

Based on the number of females, 'Based on the number of males,

hoses of the funder of melanes. Dose of the funder of most of adverse events in partients taking UNVOX." Itables that have been received since makes introduction and are of unknown coosal relationship to UNVOX." Tables use include: toxic epidermal nearolysis, Stevens-Johnson syndrome, Henach-Schoenlein purpura, bullous eruption, pringism, againulocytoss, neuropethy, adolstic anemia, anapythydratic reaction, hypometremia, acute renal failure, liepatitis, and severe admissio with fever when ne was co-administered with antipsychotic medication

Refer to package insert (11E Rev 3/98) for overdosage information. DOSAGE AND ADMINISTRATION

Refer to package insert (11E Rev 3/98) for dosage and administration information.

Rev 10/98 (11E-5)

Reference: 1. Data on fife, Solvay Pharmaceuticals, Inc.

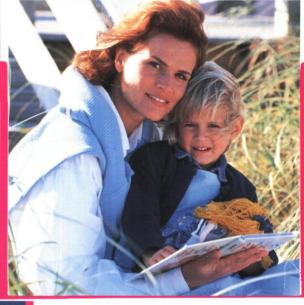
Solvay Pharmaceuticals Marietta, GA 30062

Pharmacia&Upjohn

Solvay **Pharmaceuticals** OCD IS AN
ANXIETY DISORDER

from the profound anxiety of OCD





VISIT THE OCD WEB SITE AT http://www.ocdresource.com

SIGNIFICANTLY IMPROVES OBSESSIVE-COMPULSIVE SYMPTOMS¹ LOW INCIDENCE OF AGITATION IN ADULTS¹

▼ 2% vs 1% for placebo

LOW INCIDENCE OF SEXUAL DYSFUNCTION¹

▼ LUVOX® Tablets vs placebo*: decreased libido 2% vs 1%; delayed ejaculation 8% vs 1%; anorgasmia 2% vs 0%; impotence 2% vs 1%

FAVORABLE TOLERABILITY PROFILE¹

- ▼ For adults, the most commonly observed adverse events compared to placebo were somnolence 22% vs 8%; insomnia 21% vs 10%; nervousness 12% vs 5%; nausea 40% vs 14%; asthenia 14% vs 6%
- ▼ Adverse events in children and adolescents were similar to those observed in adult studies. The most commonly observed adverse events compared to placebo were: agitation 12% vs 3%; hyperkinesia 12% vs 3%; depression 5% vs 0%; dysmenorrhea 7% vs 3%; flatulence 5% vs 0%; rash 7% vs 3%
- ▼ Concomitant use of LUVOX® Tablets and monoamine oxidase inhibitors is not recommended
- ▼ Fluvoxamine should not be used in combination with terfenadine, astemizole, or cisapride

^{*}Parameters occurring ≥1% with fluvoxamine maleate.



Please see brief summary of prescribing information on adjacent page."

fluvoxamine maleate 25 mg TABLETS 50 mg & 100 mg SCORED TABLETS

THE #1 SSRI PRESCRIBED BY PSYCHIATRISTS FOR OCD¹