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

Brief Summary of prescribing information (based on 8E1252 Rev 3/97)

INDICATIONS AND USAGE

LUVOX Tablets are indicated for the treatment of obsessions and compulsions in patients with Obsessive Compulsive Disorder (OCD), as defined in the DSM-III-R. Obsessive Compulsive Disorder is characterized by recurrent and persistent ideas, thoughts, impulses or images (obsessions) that are ego-dystonic and/or repetitive, purposeful, and intentional behaviors (compulsions) that are recognized by the person as excessive or unreasonable.

CONTRAINDICATIONS

Co-administration of terfenadine, astemizole, or cisapride with LUVOX Tablets is contraindicated (see WARNINGS and PRECAUTIONS).

LUVOX Tablets are contraindicated in patients with a history of hypersensitivity to fluvoxamine maleate.

WARNINGS

In patients receiving another serotonin reuptake inhibitor drug in combination with monoamine oxidase inhibitors (MAOIs), there have been reports of serious, sometimes fatal, reactions. 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. In addition, after stopping LUVOX® Tablets, at least 2 weeks should be allowed before starting a MAOI.

Terfenadine, astemizole and cisapride are all metabolized by the cytochrome P450IIIA4 isoenzyme. Increased plasma concentrations of terfenadine, astemizole and cisapride cause QT prolongation and have been associated with torsades de points-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, astemizole, or cisapride.

Other Potentially Important Drug Interactions

(Also see PRECAUTIONS - Drug Interactions) ***Benzodiazepines:*** Benzodiazepines metabolized by hepatic oxidation (e.g., alprazolam, midazolam, triazolam, etc.) should be used with caution because the clearance of these drugs is likely to be reduced by fluvoxamine. The clearance of benzodiazepines metabolized by glucuronidation (e.g., lorazepam, oxazepam, temazepam) is unlikely to be affected by fluvoxamine. ***Alprazolam-*** When fluvoxamine maleate (100 mg qd) and alprazolam (1 mg qid) were co-administered to steady state, plasma concentrations and other pharmacokinetic parameters (AUC, C_{max}, $T_{1/2}$) of alprazolam were approximately twice those observed when alprazolam was administered alone; oral clearance was reduced by about 50%. The elevated plasma alprazolam concentrations resulted in decreased psychomotor performance and memory. This interaction, which has not been investigated using higher doses of fluvoxamine, may be more pronounced if a 300 mg daily dose is co-administered, particularly since fluvoxamine exhibits non-linear pharmacokinetics over the dosage range 100-300 mg. If alprazolam is co-administered with LUVOX Tablets, the initial alprazolam dosage should be at least halved and titration to the lowest effective dose is recommended. No dosage adjustment is required for LUVOX Tablets. ***Diazepam-*** The co-administration of LUVOX Tablets and diazepam is generally not advisable. Because fluvoxamine reduces the clearance of both diazepam and its active metabolite, N-desmethyldiazepam, there is a strong likelihood of substantial accumulation of both species during chronic co-administration. Evidence supporting the conclusion that it is inadvisable to co-administer fluvoxamine and diazepam is derived from a study in which healthy volunteers taking 150 mg/day of fluvoxamine were administered a single oral dose of 10 mg of diazepam. In these subjects (n=8), the clearance of diazepam was reduced by 65% and that of N-desmethyldiazepam to a level that was too low to measure over the course of the 2 week long study. It is likely that this experience significantly underestimates the degree of accumulation that might occur with repeated diazepam administration. Moreover, as noted with alprazolam, the effect of fluvoxamine may even be more pronounced when it is administered at higher doses. Accordingly, diazepam and fluvoxamine should not ordinarily be co-administered. ***Theophylline:*** The effect of steady-state fluvoxamine (50 mg bid) on the pharmacokinetics of a single dose of theophylline (375 mg as 442 mg aminophylline) was evaluated in 12 healthy non-smoking, male volunteers. The clearance of theophylline was decreased approximately 3-fold. Therefore, if theophylline is co-administered with fluvoxamine maleate, its dose should be reduced to one third of the usual daily maintenance dose and plasma concentrations of theophylline should be monitored. No dosage adjustment is required for LUVOX Tablets. ***Warfarin:*** When fluvoxamine maleate (50 mg tid) was administered concomitantly with warfarin for two weeks, warfarin plasma concentrations increased by 98% and prothrombin times were prolonged. Thus patients receiving oral anticoagulants and LUVOX Tablets should have their prothrombin time monitored and their anticoagulant dose adjusted accordingly. No dosage adjustment is required for LUVOX Tablets.

PRECAUTIONS

General

Activation of Mania/Hypomania: During premarketing studies involving primarily depressed patients, hypomania or mania occurred in approximately 1% of patients treated with fluvoxamine. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, LUVOX Tablets should be used cautiously in patients with a history of mania. ***Seizures:*** During premarketing studies, seizures were reported in 0.2% of fluvoxamine-treated patients. LUVOX Tablets should be used cautiously in patients with a history of seizures. It should be discontinued in any patient who develops seizures. ***Suicide:*** The possibility of a suicide attempt is inherent in patients with depressive symptoms, whether these occur in primary depression or in association with another primary disorder such as OCD. Close supervision of high risk patients should accompany initial drug therapy. Prescriptions for LUVOX Tablets should be written for the smallest quantity of tablets consistent with good patient management in order to reduce the risk of overdose. ***Use in Patients with Concomitant Illness:*** Closely monitored clinical experience with LUVOX Tablets in patients with concomitant systemic illness is limited. Caution is advised in administering LUVOX Tablets to patients with diseases or conditions that could affect hemodynamic responses or metabolism. LUVOX Tablets have not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were systematically excluded from many clinical studies during the product's premarketing testing. Evaluation of the electrocardiograms for patients with depression or OCD who participated in premarketing studies revealed no differences between fluvoxamine and placebo in the emergence of clinically important ECG changes. In patients with liver dysfunction, fluvoxamine clearance was decreased by approximately 30%. LUVOX Tablets should be slowly titrated in patients with liver dysfunction during the initiation of treatment.

Information for Patients

Physicians are advised to discuss the following issues with patients for whom they prescribe LUVOX Tablets: ***Interference with Cognitive or Motor Performance:*** Since any psychoactive drug may impair judgement, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain that LUVOX Tablets therapy does not adversely affect their ability to engage in such activities. ***Pregnancy:*** Patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during therapy with LUVOX Tablets. ***Nursing:*** Patients receiving LUVOX Tablets should be advised to notify their physicians if they are breast feeding an infant. (See PRECAUTIONS - Nursing Mothers.) ***Concomitant Medication:*** Patients should be advised to notify their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for clinically important interactions with LUVOX Tablets. ***Alcohol:*** As with other psychotropic medications, patients should be advised to avoid alcohol while taking LUVOX Tablets. ***Allergic Reactions:*** Patients should be advised to notify their physicians if they develop a rash, hives, or a related allergic phenomenon during therapy with LUVOX Tablets.

Laboratory Tests

There are no specific laboratory tests recommended.

Drug Interactions

There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline) is clinically warranted, appropriate observation of the patient is advised. ***Potential interactions with drugs that inhibit or are Metabolized by Cytochrome P450 Isozymes:*** Based on a finding of substantial interactions of fluvoxamine with certain drugs and limited *in vitro* data for the IIIA4 isoenzyme, it appears that fluvoxamine inhibits isoenzymes that are known to be involved in the metabolism of drugs such as warfarin, theophylline and propranolol. A clinically significant fluvoxamine interaction is possible with drugs having a narrow therapeutic ratio such as terfenadine, astemizole cisapride, warfarin, theophylline, certain benzodiazepines and phenytoin. If LUVOX® Tablets are to be administered together with a drug that is eliminated via oxidative metabolism and has a narrow therapeutic window, plasma levels and/or pharmacodynamic effects of the latter drug should be monitored closely, at least until steady state conditions are reached. Please see complete prescribing information for recommendations regarding CNS drugs such as monoamine oxidase inhibitors, alprazolam, diazepam, lorazepam, lithium, tryptophan, clozapine, alcohol, tricyclic antidepressants, carbamazepine, methadone; and other drugs such as theophylline, propranolol and other beta-blockers, warfarin, digoxin, and diltiazem. ***Effects of Smoking on Fluvoxamine Metabolism:*** Smokers had a 25% increase in the metabolism of fluvoxamine compared to nonsmokers. ***Electroconvulsive Therapy (ECT):*** There are no clinical studies establishing the benefits or risks of combined use of ECT and fluvoxamine maleate.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: There is no evidence of carcinogenicity, mutagenicity or impairment of fertility with fluvoxamine maleate.There was no evidence of carcinogenicity in rats treated orally with fluvoxamine maleate for 30 months or hamsters treated orally with fluvoxamine maleate for 20 (females) or 26 (males) months. The daily doses in the high dose groups in these studies were increased over the course of the study from a minimum of 160 mg/kg to a maximum of 240 mg/kg in rats, and from a minimum of 135 mg/kg to a maximum of 240 mg/kg in hamsters. The maximum dose of 240 mg/kg is approximately 6 times the maximum human daily dose on a mg/m^2 basis. ***Mutagenesis:*** No evidence of mutagenic potential was observed in a mouse micronucleus test, or an vitro chromosome aberration test, or the Ames microbial mutagen test with or without metabolic activation. ***Impairment of Fertility:*** In fertility studies of male and female rats, up to 80 mg/kg/day orally of fluvoxamine maleate, (approximately 2 times the maximum human daily dose on a mg/m^2 basis) had no effect on mating performance, duration of gestation, or pregnancy rate.

Pregnancy

Teratogenic Effects - Pregnancy Category C: In teratology studies in rats and rabbits, daily oral doses of fluvoxamine maleate of up to 80 and 40 mg/kg, respectively (approximately 2 times the maximum human daily dose on a mg/m^2 basis) caused no fetal malformations. However, in other reproduction studies in which pregnant rats were dosed through weaning there was (1) an increase in pup mortality at birth (seen at 80 mg/kg and above but not at 20 mg/kg), and (2) decreases in postnatal pup weights (seen at 160 but not at 80 mg/kg) and survival (seen at all doses; lowest dose tested = 5 mg/kg). (Doses of 5, 20, 80, and 160 mg/kg are approximately 0.1, 0.5, 2, and 4 times the maximum human daily dose on a mg/m^2 basis.) While the results of a cross-fostering study implied that at least some of these results likely occurred secondarily to maternal toxicity, the role of a direct drug effect on the fetuses or pups could not be ruled out. There are no adequate and well-controlled studies in pregnant women. Fluvoxamine maleate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

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

Nursing Mothers

As for 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 LUVOX® (fluvoxamine maleate) Tablets therapy to the mother.

Pediatric Use

The efficacy of fluvoxamine maleate for the treatmernt of Obsessive Compulsive Disorder was demonstrated in a 10-week multicenter placebo controlled study with 120 outpatients ages 8-17. The adverse event profile observed in that study was generally similar to that observed in adult studies with fluvoxamine (see ADVERSE REACTIONS).

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

Geriatric Use

Approximately 230 patients participating in controlled premarketing studies with LUVOX 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 fluvoxamine is decreased by about 50% in elderly compared to younger patients (see Pharmacokinetics under CLINICAL PHARMACOLOGY), and greater sensitivity of some older individuals also cannot be ruled out. Consequently, LUVOX Tablets should be slowly titrated during initiation of therapy.

ADVERSE REACTIONS

Associated with Discontinuation of Treatment

Of the 1087 OCD and depressed patients treated with fluvoxamine maleate in controlled clinical trials conducted in North America, 22% discontinued treatment due to an adverse event.

Adverse events in OCD Pediatric Population

In pediatric patients (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 of the pediatric patients, and were more frequent than in the placebo group (N=63) were: abnormal thinking, cough increase, dysmenorrhea, ecchymosis, emotional lability, epistaxis, hyperkinesia, infection, manic reaction, rash, sinusitis, and weight decrease.

Events for which the incidence in fluvoxamine maleate was equal to or less than the incidence in placebo (N=63) and involved two or more of the pediatric study patients were: abdominal pain, abnormal dreams, fever, headache, nausea, nervousness, pain, pharyngitis and rhinitis.

Incidence in Controlled Trials - *Commonly Observed Adverse Events in Controlled Clinical Trials:* LUVOX Tablets have been studied in controlled trials of OCD (n=320) and depression (n=1350). In general, adverse event rates were similar in the two data sets. The most commonly observed adverse events associated with the use of LUVOX Tablets and likely to be drug-related (incidence of 5% or greater and at least twice that for placebo) derived from Table 2 were: *somnolence, insomnia, nervousness, tremor, nausea, dyspepsia, anorexia, vomiting, abnormal ejaculation, asthenia,* and *sweating*. In a pool of two studies involving only patients with OCD, the following additional events were identified using the above rule: *dry mouth, decreased libido, urinary frequency, anorgasmia, rhinitis* and *taste perversion.* ***Adverse Events Occurring at an Incidence of 1%:*** Table 2 enumerates adverse events that occurred at a frequency of 1% or more, and were more frequent than in the placebo group, among patients treated with LUVOX Tablets in two short-term placebo controlled OCD trials (10 week) and depression trials (6 week) in which patients were dosed in a range of generally 100 to 300 mg/day. This table shows the percentage of patients in each group who had at least one occurrence of an event at some time during their treatment. Reported adverse events were classified using a standard COSTART-based Dictionary terminology. The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors may differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, 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. ***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 a two-fold decrease in rate compared to event rates in OCD and depression studies were dysphagia and amblyopia (mostly blurred vision). Additionally, there was an approximate 25% decrease in nausea. The events in OCD studies with a two-fold increase in rate compared to event rates in OCD and depression studies were: *asthenia, abnormal ejaculation (mostly delayed ejaculation), anxiety, infection, rhinitis, anorgasmia (in males), depression, libido decreased, pharyngitis, agitation, impotence, myoclonus/twitch, thirst, weight loss, leg cramps, myalgia* and *urinary retention.* These events are listed in order of decreasing rates in the OCD trials.

Vital Sign Changes

Comparisons of fluvoxamine maleate and placebo groups in separate pools of short-term OCD and depression trials on (1) median change from baseline on various vital signs variables and on (2) incidence of patients meeting criteria for potentially important changes from baseline on various vital signs variables revealed no important differences between fluvoxamine maleate and placebo.

Laboratory Changes

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

ECG Changes

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

Table 2: TREATMENT-EMERGENT ADVERSE EVENT INCIDENCE RATES BY BODY SYSTEM IN OCD AND DEPRESSION POPULATIONS COMBINED[1] (fluvoxamine [n=892] vs. placebo [n=778] by patients–percentage): **BODY AS WHOLE:** Headache (22 vs. 20); Asthenia (14 vs. 6); Flu Syndrome (3 vs. 2); Chills (2 vs. 1). **CARDIOVASCULAR:** Palpitations (3 vs. 2). **DIGESTIVE SYSTEM:** Nausea (40 vs. 14); Diarrhea (11 vs. 7); Constipation (10 vs. 8); Dyspepsia (10 vs. 5); Anorexia (6 vs. 2); Vomiting (5 vs. 2); Flatulence (4 vs. 3); Tooth Disorder[2] (3 vs. 1); Dysphagia (2 vs. 1). **NERVOUS SYSTEM:** Somnolence (22 vs. 8); Insomnia (21 vs. 10); Dry Mouth (14 vs. 10); Nervousness (12 vs. 5); Dizziness (11 vs. 6); Tremor (5 vs. 1); Anxiety (5 vs. 3); Vasodilatation[3] (3 vs. 1) Hypertonia (2 vs. 1) Agitation (2 vs. 1); Decreased Libido (2 vs. 1); Depression (2 vs. 1); CNS Stimulation (2 vs. 1). **RESPIRATORY SYSTEM:** Upper Respiratory Infection (9 vs. 5); Dyspnea (2 vs. 1); Yawn (2 vs. 0). **SKIN:** Sweating (7 vs. 3). **SPECIAL SENSES:** Taste Perversion (3 vs. 1); Amblyopia[4] (3 vs. 2). **UROGENITAL:** Abnormal Ejaculation[5,6] (8 vs. 1); Urinary Frequency (3 vs. 2); Impotence[6] (2 vs. 1); Anorgasmia (2 vs. 0); Urinary Retention (1 vs. 0).[7]

[1]Events for which fluvoxamine maleate incidence was equal to or less than placebo are not listed in the table above, but include the following: abdominal pain, abnormal dreams, appetite increase, back pain, chest pain, confusion, dysmenorrhea, fever, infection, leg cramps, migraine, myalgia, pain, paresthesia, pharyngitis, postural hypotension, pruritus, rash, rhinitis, thirst and tinnitus. [2]Includes "toothache," "tooth extraction and abscess," and "caries." [3]Mostly feeling warm, hot, or flushed. [4]Mostly "blurred vision." [5]Mostly "delayed ejaculation." [6]Incidence based on number of male patients.

Other Events Observed During the Premarketing Evaluation of LUVOX Tablets

During premarketing clinical trials conducted in North America and Europe, multiple doses of fluvoxamine maleate were administered for a combined total of 2737 patient exposures in patients suffering OCD or Major Depressive Disorder. Untoward events associated with this exposure were recorded by clinical 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 untoward events into a limited (i.e., reduced) number of standard event categories.In the tabulations which follow, a standard COSTART-based Dictionary terminology has been used to classify reported adverse events. If the COSTART term for an event was so general as to be uninformative, it was replaced with a more informative term. The frequencies presented, therefore, represent the proportion of the 2737 patient exposures to multiple doses of fluvoxamine maleate who experienced an event of the type cited on at least one occasion while receiving fluvoxamine maleate. All reported events are included in the list below, with the following exceptions: 1) those events already listed in Table 2, which tabulates incidence rates of common adverse experiences in placebo-controlled OCD and depression clinical trials, are excluded; 2) those events for which a drug cause was considered remote (i.e., neoplasia, gastrointestinal carcinoma, herpes simplex, herpes zoster, application site reaction, and unintended pregnancy) are omitted; and 3) events which were reported in only one patient and judged to not be potentially serious are not included. It is important to emphasize that, although the events reported did occur during treatment with fluvoxamine maleate, a causal relationship to fluvoxamine maleate has not been established. Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring between 1/100 and 1/1000 patients; and rare adverse events are those occurring in less than 1/1000 patients. ***Body as a Whole:*** *Frequent:* accidental injury, malaise; *Infrequent:* allergic reaction, neck pain, neck rigidity, overdose, photosensitivity reaction, suicide attempt; *Rare:* cyst, pelvic pain, sudden death. ***Cardiovascular System:*** *Frequent:* hypertension, hypotension, syncope, tachycardia; *Infrequent:* angina pectoris, bradycardia, cardiomyopathy, cardiovascular disease, cold extremities, conduction delay, heart failure, myocardial infarction, pallor, pulse irregular, ST segment changes; *Rare:* AV block, cerebrovascular accident, coronary artery disease, embolus, pericarditis, phlebitis, pulmonary infarction, supraventricular extrasystoles. ***Digestive System:*** *Frequent:* elevated liver transaminases; *Infrequent:* colitis, eructation, esophagitis, gastritis, gastroenteritis, gastrointestinal hemorrhage, gastrointestinal ulcer, gingivitis, glossitis, hemorrhoids, melena, rectal hemorrhage, stomatitis; *Rare:* biliary pain, cholecystitis, cholelithiasis, fecal incontinence, hematemesis, intestinal obstruction, jaundice. ***Endocrine System:*** *Infrequent:* hypothyroidism; *Rare:* goiter. ***Hemic and Lymphatic Systems:*** *Infrequent:* anemia, ecchymosis, leukocytosis, lymphadenopathy, thrombocytopenia; *Rare:* leukopenia, purpura. ***Metabolic and Nutritional Systems:*** *Frequent:* edema, weight gain, weight loss; *Infrequent:* dehydration, hypercholesteroiemia; *Rare:* diabetes mellitus, hyperglycemia, hyperlipidemia, hypoglycemia, hypokalemia, lactate dehydrogenase increased. ***Musculoskeletal System:*** *Infrequent:* arthralgia, arthritis, bursitis, generalized muscle spasm, myasthenia, tendinous contracture, tenosynovitis; *Rare:* arthrosis, myopathy, pathological fracture. ***Nervous System:*** *Frequent:* amnesia, apathy, hyperkinesia, hypokinesia, manic reaction, myoclonus, psychotic reaction; *Infrequent:* agoraphobia, akathisia, ataxia, CNS depression, convulsion, delirium, delusion, depersonalization, drug dependence, dyskinesia, dystonia, emotional lability, euphoria, extrapyramidal syndrome, gait unsteady, hallucinations, hemiplegia, hostility, hypersomnia, hypochondriasis, hypotonia, hysteria, incoordination, increased salivation, increased libido, neuralgia, paralysis, paranoid reaction, phobia, psychosis, sleep disorder, stupor, twitching, vertigo; *Rare:* akinesia, coma, fibrillations, mutism, obsessions, reflexes decreased, slurred speech, tardive dyskinesia, torticollis, trismus, withdrawal syndrome. ***Respiratory System:*** *Frequent:* cough increased, sinusitis; *Infrequent:* asthma, bronchitis, epistaxis, hoarseness, hyperventilation; *Rare:* apnea, congestion of upper airway, hemoptysis, hiccups, laryngismus, obstructive pulmonary disease, pneumonia. ***Skin:*** *Infrequent:* acne, alopecia, dry skin, eczema, exfoliative dermatitis, furunculosis, seborrhea, skin discoloration, urticaria. ***Special Senses:*** *Infrequent:* accommodation abnormal, conjunctivitis, deafness, diplopia, dry eyes, ear pain, eye pain, mydriasis, otitis media, parosmia, photophobia, taste loss, visual field defect; *Rare:* corneal ulcer, retinal detachment. ***Urogenital System:*** *Infrequent:* anuria, breast pain, cystitis, delayed menstruation[1], dysuria, female lactation[1], hematuria, menopause[1], menorrhagia[1], metrorrhagia[1], nocturia, polyuria, premenstrual syndrome[1], urinary incontinence, urinary tract infection, urinary urgency, urination impaired, vaginal hemorrhage[1], vaginitis[1]; *Rare:* kidney calculus, hematospermia[2], oliguria.

[1]Based on the number of females. [2]Based on the number of males.

Non-US Postmarketing Reports

Voluntary reports of adverse events in patients taking LUVOX Tablets that have been received since market introduction and are of unknown causal relationship to LUVOX Tablets use include: toxic epidermal necrolysis, Stevens-Johnson syndrome, Henoch-Schoenlein purpura, bullous eruption, priapism, agranulocytosis, neuropathy, aplastic anemia, anaphylactic reaction, hyponatremia, acute renal failure, hepatitis, and severe akinesia with fever when fluvoxamine was co-administered with antipsychotic medication.

CAUTION: Federal law prohibits dispensing without prescription.

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

Pharmacia&Upjohn

Solvay Pharmaceuticals

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