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 Computisve 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

Condiministration of terfenodine, asternizole, or cisapside with LUVOX Tablets is contraindicated (see WARNINGS and PRECAUTIONS). LUVOX Tablets are contraindicated in patients with a history of hypersensitivity to fluvoxamine moleate.

WARNINGS

WAKNINGS
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 depoints-type ventricular tackyrodia, 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, ostemizole, or cisapride.

Other Patentially Impactable Typu Interactions

with either Tetrakodina, astemizael, or Casapride.

Other Potentially Important Drug Interactions:
(Ako see PRECAUTIONS - Drug Interactions). Benzodiazepiness: Benzodiazepines metabolized by hepotic oxidation (e.g., alprazolam, midazolam, midazolam, etc.) should be used with courtin because the clearance of these drugs is likely to be reduced by Huvorannine. The clearance of benzodiazepine metabolized by Quorandotion (e.g., lorazepom, covazepom, terrazepom) is utilizely to be officed by Huvorannine. Alprazolam-When Huvorannine maleate (100 mg qil) and alprazolam (1 mg qid) were opadmiristered to sleady state, plasmo concentrations and other pharmacokinetic parameters (AUC, makeute (100 mg od) and alprazolam (1 mg gid) were condiministeed to steady stree, plasmo concentrations and other pharmacokinetic parameters (ALC,
—, 1) of alprazolam were approximately hvice those observed when alprazolam was administered alone; and clearance was reduced by about 50%. The
elevated plasmo alprazolam concentrations resulted in deversed psychomotro performance and memory. This interaction, which has not been investigated
using higher doses of flavoramine, may be more pronounced if a 500 mg daily dose is co-administered, princludiny since flavoramonie exhibits non-inear
pharmacokinetics worthe dosage range 100.300 mg. If objectored in is co-administered with UVIX foldes, the initial oliprazolam dosage has been always and alternative and interaction to the lowest effective dose is recommended. No desage adjustment is required for LUVOX foldes. Diazopam—The co-administration
of LUVOX foldes and discagen is generally not advisable. Because flavoramine reduces the clearance of both biazopam and its active metabolite, No
desamethyldizappim, there is a strong fischhood of substantial occurribation of both species during dranic condiministration. Evidence in proporting the
conclusion that it is indivisable to co-diministration furched and diazopem is derived from a study in which healthy valunteers taking 150 mg/day of
flavoramine used redistration of a diazopem is derived from a study in which healthy valunteers taking 150 mg/day of
the second of the condiministration. Evidence of this propriets the second of the second bus 65% and conclusion that it is nodivisable to co-diministe fluvoramine and diszepem is derived from a study in which healthy valantees taking 150 mg/dio pf fluvoramine were administered a single and dose of 10 mg of diazepam. In these subjects (n=8), the clearance of diazepam was reduced by 6% and that of N-desmethyldrazepam 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. Marcever, as noted with adjacrolum, the effort diazepam owners are subject to the fluvoramine mount of the mountained of the produced of the production of the effect of steady-state fluvoxamine (50 mg bid) on the pharmacokinetics of a single dose of theophylline is of the subject of the produced of 12 healthy non-smaking, make valunteers. The clearance of theophylline was decreased approximately 3-fold. Herefore, if theophylline is coordinated with fluvoxamine moletale, its doses should be required to one third of the susual daily material establishment of the subject of the control of the control of the support of the supp

PRECAUTIONS

General

Activation of Mania/Hypomania: During premarketing studies involving primarily depressed potients, hypomania or mania occurred in approximately 1% of patients treated with fluvoromine. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were heated with other marketed antidepressants. As with all antidepressants, LUVOX Toblets should be used counticusly in patients with a history of mania. Setzures: 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 potients with depressive symptoms, whether these accur in primary depression or in association with continue to the potient with depressive symptoms, whether these accur in primary depression or in association with continue primary depression of high risk potients should accompany inflat drug therapy. Prescriptions for LIVOX Tables should be written for the smallest quantitative to the state of the primary depression of high risk potients should accompany inflat drug therapy. Prescriptions for LIVOX Tables is should be written for the smallest quantitative to the primary depression of high risk potients with concomitant flaness; Closely monitored clinical experience with LIVOX Tables is potients with concomitant systemic illness is limited. Caution is oxived in ordinalisating LIVOX tables to no ordinalisating LIVOX Tables have not been envaluant to use the only appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were systematically special and the service of the servi dysfunction during the initiation of heatment Information for Patients

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 psychocribe drug may impain judgement, thinking, or motor skills, patients should be counted about operating hazardous
machinery, including automobiles, until they are certain that LUVOX Tablets therapy does not adversely affect their ability to engage in such activation.

Pergenancy: Collents should be advised to notify their physicians if they become pregnant or intend to become pregnant during therapy with LUVOX Tablets.

Norsing: Planets seeking LUVOX Tablets should be advised to notify their physicians if they are beast feeding on intain. See PREAUTIONS - Nursing
Mothers): Concomitant Medication: Patients should be advised to notify their physicians if they are backing, or plan to take, any prescriptions or overtherecounter days, since there is a pertain for clinically important interactions with LUVOX Tablets. Alchook Lev, with other psychotromic medications,
patients should be advised to avoid alchol while taking LUVOX Tablets. Alchook Lev. See with other psychotromic medications,
patients should be advised to avoid alchol while taking LUVOX Tablets. Alchook Lev. See with other psychotromic medications,
patients should be advised to notify their physicians if they
develop a rish, hove, or a related ellergic phenomenon during therapy with LUVOX Tablets.

Laboratory Tests

There are no specific laboratory tests recommended.

There have been one postmarketing reports describing patients with weakness, hyperreflexing, and incoordination following the use of a selective sentoning.

There have been one postmarketing reports describing patients with weakness, hyperreflexing, and incoordination following the use of a selective sentoning. There have been rare postmarketing reports describing patients with weakness, hyperreflecia, and incoadantion following the use of a selective serotonin reuptate inhibitor (SSR) and summitipion. It concernitant heatment with summitipata and an SSR (e.g., fluoretine, fluoretinie, patronitie, patrolinie, distribution, and appropriate observation of the political is ordived. Preferrital interactions with drugs that inhibitor are Metabolized by Cytochrame P450 Isazymess: Bosed on a finding of substantial interactions of fluorecomine with certain drugs and limited in with data for the IIII.44 iscenzyme, it appears that fluorecomine inhibits iscenzymes that are known to be involved in the metabolism of drugs such as wardom, theophylline and proparadol. A Chincially significant fluorecomine interaction is possible with drugs having a narrow therapeutic ratio such as terferodine, estemizable assignation, the polyviline, certain herozodizepines and phenytoin. If UNOX* Tabeles are to be administrated together with a drug that is eliminated via axidation would be under the substantial and the proparadol and the proparadol and other between the proparadol and other between the complete prescribing information for recommendations regarding (NS drugs such as monoratine acadase inhibitors, planzalam, duargeom, forazeom, planzalam, fluorecom, and other between the proparadol and other between the Marbabolisms.

Smokers had a 25% increase in the metabolism of fluorecomine congrared to norsmokers. Electroconvulsive Therapy (ECT): There are no clinical studies establishing the benefits or its sket of combined use of CCT. In fluorecomine melecte.

studies establishing the benefits or risks of combined use of ECT and fluvoxomine molecte.

Cardinogenesis, Murtagenesis, Impairment of Fertility

Cardinogenesis; There is no evidence of cardinogenesis; multigenicity or impairment of fertility with fluvoxomine molecte. There was no evidence of cardinogenesis; There is no evidence of cardinogenesis; There is no evidence of cardinogenicity in tast heeted orably with fluvoxomine molecte for 30 months or harmstess treated orably with fluvoxomine molecte for 30 flemales) or 2.6 males) months. The doily doses in the flight dose groups in these studies were increased over the course of the study from a minimum of many flowing or maximum of 240 mg/kg in the maximum human doily dose on a mg/m² basis. Mutagenesis; No evidence of mutagenic potential was observed in a mouse microaucleus test, on in with or homosome aberation test, or the Ames microbial mutagen test with or without metabolic activation. Impairment of Fertility: In tertility studies of male and female inits, up to 80 mg/kg/doy analy of fluvoxomine molecte. (approximately 2 times the maximum human doily dose on a mg/m² basis) had no effect on mating performance, duration of gestation, or pregnancy rate.

daily dose on a mg/m² basis) had no effect on maning periorinance, wavenum or government, or programmy.

Pragnancy

Tearlagenic Effects - Pregnancy Category C: In teratology studies in rats and robbits, daily and doses of fluvoxamine malente of up to 80 and 40 mg/kg, respectively (approximately 2 fines the maximum human daily dose on a mg/m² basis) caused as fetal malformations. However, in form reproduction studies in which spengion that was well as microsen in any martinity at this fiscent at 9 mg/kg and above but not at 20 mg/kg), and (2) decreases in page postinity at this fiscent at 90 mg/kg and above but not at 20 mg/kg). (Oose of 5, 20, 80, and 160 mg/kg are apportantely 0.1, 0.5, 2, and 4 times the maximum human daily dose on a mg/m² be dose that the second state of t

Nursing Mothers

As for many other drugs, flyvoxamine is secreted in human breast milk. The decision of whether to discontinue musing or to discontinue the drug should take into account the potential for serious adverse effects from exposure to fluvoxamine in the rursing 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 treatment 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

Operating USA potients porhopoling in controlled premarkating studies with LUVOX Tablets were 65 years of age or over. No overall differences in safety were absenced between these potients and younger potients. Other reported chiral temperatures not identified differences in response between the elderly and younger potients. However, the cleanance of ituroxominie is decreased by about 50% in elderly compared to younger potients. Govern elder individuals also cannot be ruled out. Consequently, LUVOX (ablest should be slowly intended during initiation.

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 adv

Adverse events in OCD Pediatric Population
In pediatric patients (N=57) treated with LUYOX** Toblets, 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 from in the placebe group (N=63) were: charamed frinking, cough increase, drysmorthiae, actlymosis, remoterable positions, higheriness, indection, many; reaction, and, singuisty, and weigh these. Events for, which the incidence in fluvoxamine malerate was equal to or less than the incidence in placebo (N=63) and involved two or more of the pediatric

The study pointed were addominate joint abnormal decents, level, headach, noneso, nervousness, pain, pharyngiffs and rhinks.

Incidence in Controlled Trials - Commonly Observed Adverse Events in Controlled Clinical Trials: LIVOX 100ths have been studied in controlled that of the discussion of the controlled that of the discussion of the controlled that of the discussion from Table 2 were: somnolence, insomnia, nervousness, tremor, nousea, dyspepsia, anorexia, vorniting, 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 libida, Through Property, principating, inhibition of rate pervession. Adverse Events Occurring at an Incidence of 196; Table 2 removes observed 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 thials (6 week) in which patients were dosed in a range of generally 100 to 300 mg/day. This table shows the percentings of patients in each goary who had all less to ne occurrence of an even of some time during their teamers. Reported adverse events were classified using a standard GOSIARFbosed Dictionary reminalogy. The prescriber should be aware that these figures comor be used to predict in incidence of side effects in the course of usual medical practice where potent characteristics and other foctors may differ from those that prevailed in the clinical mids. Similarly, the cited frequencies comor 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-dual totats in the indeedlect incidence rate in the population studied. Adverse Events in OCO Placabo Contribled Studies Whitch Markadly Different (defined as at least a two-fold difference) in Rate from the Pooled Event Rates in OCO and Depression Placebo Controlled Studies: The events in OCO studies with a two-fold decrease in tale compared to event rates in OCO and depression studies were dysphagia and analytopia (mostly blurned vision). Additionally, there was an approximate 25% decrease in nousea. The events in OCO studies with a tworegularity and unusury more incomposed to event rates in COD and depression studies were confereing, charantel ejaculation (mostly delayed acidation), awaity, infection, thinks, amangasmia (in males), depression, libida decreased, pharyngins, agitation, impotence, myaclanus/huitch, thirst, weight loss, leg camps, myadgia and urinary retention. These events are listed in order of decreasing rates in the COD trials.

Integrated to dearly remain, in the electric or a local at value of accessing late. In the Countries, Virtial Sign Changes

Comparisons of fluvoxamine indeper on placebo groups in separate pools of short-term DCD and depression trials on (1) median change from baseline on various virtid signs variobles and on (2) incidence of patients meeting criteria for potentially important changes from baseline on various virtid signs variobles revieded no important differences between fluvoxamine malletale 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 winalysis variables and on (2) incidence of patients meeting criterio for potentially important changes from baseline on various serum chemistry, hematology, and winalysis variables revealed no important differences between fluvoxamine malerate and placebo.

Comparisors of flavoxomine moleate and placebo groups in separate pools of short-term OCO and depression trials on (1) mean change from baseline on various ECG variables and on (2) incidence of patients meeting criteria for patentially important changes from baseline on various ECG variables revealed

Table 2: TREATMENT-EMERGENT ADVERSE EVENT INCIDENCE RATES BY BODY SYSTEM IN OCD AND DEPRESSION POPULATIONS COMBINED (fluvoxamine [n=892] vs. placebo [n=778] by potients—percentage): BODY AS WHOLE: Headade (22 vs. 20). Asthenia (14 vs. 6); Flu Syndrome (3 vs. 2); Chills (2 vs. 1). CARDIOVASCULAR: Polpitations (3 vs. 2). DIGESTIVE SYSTEM: Nausea (40 vs. 14); Astherio (14 vs. 6); Fib Symdrome (3 vs. 2); Cultis (2 vs. 1); CARDIOVASCULAR: Peliptrions (3 vs. 2); DiffeSTIVE \$15 YEAR: Mouse (40 vs. 1); Districts (10 vs. 1); Contention (10 vs. 8); Dyspend (10 vs. 5); Districts (6 vs. 2); Ventrion (5 vs. 2); Politics (4 vs. 3); Districts (3 vs. 1); Dysplagi (2 vs. 1); MERVOUS \$75 YEAR: Somoleire (22 vs. 1); Inscrint (21 vs. 10); Dys Mouth (14 vs. 10); Nervourses (12 vs. 5); Districts (12 vs. 1); Analytic (2 vs. 1); Analytic (2 vs. 1); Depression (2 vs. 1); Politics (12 vs. 1); Depression (2 vs. 1); Depress

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poin, abnormed dreams, oppetite increase, bock poin, chest poin, cortusion, dysmenorthea, fever, infaction, ley comps, migration, mydipa, pain, paresthesis, pharyngilis, postult hippotension, points, sorth, initials, this and minimals. "Riculdess" Toothords—" thought entrotion and obsess," and "criniss." Worstly felling worm, hot, or flushed. "Mostly" blurned vision." "Mostly "delayed ejaculation." (incidence based on number of male primals." Which is the property of the pr

Non-US Postmarketing Reports

Voluntury reports of odverse events in patients taking LUYOX Tablets that have been received since market introduction and are of unknown causal rectionship to LUYOX Tablets use include: toxic epidermal necrolysis, Stevens-holmson syndrome, Henoch-Schoenlein purpura, bullous enuption, pringism, agranulocytosis, neuropathy, autosis anemia, anaphylactic reaction, hyponothemia, oculta renal failure, hepathis, and severe akinesia with fever when fluvosomine was co-administered with antipoychota medication.

CAUTION: Federal law prohibits dispensing without prescription.

8F1252 Rev 3/97

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

Pharmacia&Upjohn

Solvay **Pharmaceuticals**

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Effective first-line SSRI therapy for OCD...



Emerging from the profound anxiety of OCD

Low incidence of agitation

• 2% vs 1% for placebo¹

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 profile

- Relatively low incidence of anticholinergic side effects in controlled trials of OCD and depression. LUVOX® Tablets vs placebo¹: dizziness 11% vs 6%; constipation 10% vs 8%; dry mouth 14% vs 10%
- 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%¹
- Concomitant use of LUVOX® Tablets and monoamine oxidase inhibitors is not recommended¹



AVAILABLE IN 25-mg TABLETS



*Parameters occurring ≥ 1% with fluvoxamine maleate.

Please see brief summary of prescribing information on adjacent page.

First-line SSRI therapy for obsessions and compulsions