PROFESSIONAL INFORMATION

SCHEDULING STATUS
S5

1. NAME OF THE MEDICINE NAME OF THE MMEDICINE

FLUANXOL Tablets 0,5 mg

FLUANXOL Tablets 1 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Each tablet contains flupentixol dihydrochloride equivalent to flupentixol 0,5 mg or 1 mg.

Contains sugar:

Each 0.5 mg tablet contains 20,00 mg Lactose monohydrate

Each 1 mg tablet contains 19,85 mg Lactose monohydrate

For full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet

0,5 mg: Round, slightly biconvex, yellow, film coated tablets marked FD

1 mg: Oval, slightly biconvex, yellow, film coated tablets marked FF

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term symptomatic treatment of depression of mild to moderate severity (with or without anxiety).

PROFESSIONAL INFORMATION

4.2 Posology and method of administration

Posology

Adults

Standard initial dosage is 1 mg as a single morning dose.

After one week the dose may be increased to 2 mg if there is inadequate clinical response. Daily dosage of more than 2 mg should be in divided doses up to a maximum 3 mg. In view of the activating properties of FLUANXOL, it is advisable to give the last dose of the day no later than 4.00 p.m.

Patients may respond to FLUANXOL within two or three days. If no effect has been observed within one week at maximum dosage FLUANXOL tablets should be withdrawn.

Elderly

Older patients should receive half the recommended dosages, i.e. 0.5-1.5 mg daily.

Patients often respond to flupentixol within two or three days. If no effect has been observed within one week of maximum dosage the drug should be withdrawn.

4.3 Contraindications

Hypersensitivity to flupenthixol or to any of the excipients (see section 6.1).

FLUANXOL is not recommended for the treatment of severe depression requiring ECT and/or hospitalisation.

In states of excitement or overactivity (including mania).

Pre-existing CNS depression or coma, bone marrow suppression or phaeochromocytoma.

Circulatory collapse, depressed level of consciousness due to any cause (e.g. severe alcohol, barbiturate and opiate intoxications), coma.

Pregnancy and lactation (see Section 4.6)

Not recommended for children.

4.4 Special warnings and precautions for use

Neuroleptic malignant syndrome may occur. The symptoms are: hyperthermia, muscle rigidity, fluctuating consciousness, instability of the autonomous nervous system.

PROFESSIONAL INFORMATION

Treatment:

- Discontinuation of the neuroleptic
- Symptomatic treatment and use of general supportive measures.
- Dantrolene and bromocriptine may be helpful.

Symptoms may persist for longer than a week after discontinuation of FLUANXOL tablets.
Increased mortality has been observed more often in patients with pre-existing organic brain syndrome, mental retardation, and opiate and alcohol abuse.

FLUANXOL may cause QT prolongation. Persistently prolonged QT intervals may increase the risk of cardiac dysrhythmias, resulting in an increased risk of death. Therefore, FLUANXOL should be used with caution in susceptible individuals (with hypokalaemia, hypomagnesaemia or genetic predisposition) and in patients with a history of cardiovascular disorders, e.g. QT prolongation, significant bradycardia (<50 beats per minute), a recent acute myocardial infarction, uncompensated heart failure, or cardiac dysrhythmia.

Concomitant treatment of FLUANXOL tablets with other antipsychotics should be avoided (see section 4.5).

Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant medicines such as FLAUNXOL tablets in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany medicine therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and

unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Cases of venous thromboembolism (VTE) have been reported. All possible risk factors for VTE should be identified before and during treatment with FLUANXOL tablets and preventive measures undertaken.

Elderly

Cerebrovascular - An approximately 3-fold increased risk of cerebrovascular accident (stroke) has been seen in randomised placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded. FLUANXOL should be used with caution in patients with risk factors for stroke.

Increased mortality in elderly people with dementia - Data from two large observational studies showed that elderly people with dementia who are treated with FLUANXOL tablets are at an increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Elderly and debilitated patients may be more prone to the adverse effects of FLUANXOL tablets. FLUANXOL is not indicated for the treatment of dementia-related behavioural disturbances.

Special precautions

Caution should be exercised in patients having: liver disease; cardiac disease or dysrhythmias; severe respiratory disease; renal failure; epilepsy (and conditions predisposing to epilepsy e.g. alcohol withdrawal or brain damage); Parkinson's disease; narrow angle glaucoma; prostatic hypertrophy; hypothyroidism; hyperthyroidism; myasthenia gravis; phaeochromocytoma, diabetes mellitus, and patients who have shown hypersensitivity to thioxanthenes or other antipsychotics.

FLUANXOL effects on the vomiting centre may mask the symptoms of overdosage of other agents and or disorders such as gastrointestinal obstructions.

PROFESSIONAL INFORMATION

Regular eye examinations are advisable for patients receiving long-term FLUANXOL therapy and avoidance of undue exposure to sunlight is recommended. Haematological parameters should be monitored periodically.

FLUANXOL should be used with caution in patients with organic brain syndrome, convulsions and advanced hepatic disease.

FLUANXOL may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients.

Excipients

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take FLUANXOL tablets.

4.5 Interaction with other medicines and other forms of interaction

Combinations requiring precaution for use

FLUANXOL may enhance the sedative effect alcohol and the effects of barbiturates and other CNS depressants.

FLUANXOL may increase or reduce the effect of antihypertensive medicines.

Concomitant use of FLUANXOL and lithium increases the risk of neurotoxicity.

Tricyclic antidepressants and FLUANXOL mutually inhibit the metabolism of one another.

FLUANXOL may reduce the effect of levodopa and the effect of adrenergic medicines.

Concomitant use of FLUANXOL tablets with metoclopramide and piperazine increases the risk of extrapyramidal disorder.

Increases in the QT interval related to antipsychotic treatment may be exacerbated by the co-administration of other medicines known to significantly increase the QT interval. Co-administration of such medicines should be avoided.

Relevant classes include:

- class Ia and III antidysrhythmics (e.g. quinidine, amiodarone, sotalol, dofetilide)
- some antipsychotics (e.g. thioridazine)
- some macrolides (e.g. erythromycin)
- some antihistamines (e.g. astemizole)
- some quinolone antibiotics (e.g. gatifloxacin, moxifloxacin)

The above list is not exhaustive and other individual medicines known to significantly increase QT interval (e.g. cisapride, lithium) should be avoided.

Medicines known to cause electrolyte disturbances such as thiazide diuretica (hypokalaemia) and medicines known to increase the plasma concentration of flupenthixol should also be used with caution as they may increase the risk of QT prolongation and cardiac dysrhythmias, resulting in an increased risk of death (see Section 4.4).

4.6 Fertility, pregnancy and lactation

FLUANXOL should not be used during pregnancy and lactation.

Pregnancy

The newborn babies of mothers treated with FLUANXOL in late pregnancy, or labour, may show signs of intoxication such as lethargy, tremor and hyperexcitability and have a low Apgar score.

Neonates exposed to FLUANXOL during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery.

There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder.

Consequently, newborns should be monitored carefully.

Breastfeeding

Flupenthixol is excreted into the breast milk. Mothers on treatment with FLUANXOL should not breastfeed their babies.

PROFESSIONAL INFORMATION

4.7 Effects on ability to drive and use machines

FLUANXOL is a non-sedating drug in the low-moderate dosage range however some sedation is anticipitated with increasing dose.

Based on the pharmacodynamic and pharmacokinetic profile, reported adverse reactions, FLUANXOL has a minor influence on the ability to drive and use machines.

4.8 Undesirable effects

Extrapyramidal reactions may occur.

Tardive dyskinesia may develop.

In the listing below a Frequent event is defined as either a very common or common event (>1/100); all other events are defined as Less frequent.

PROFESSIONAL INFORMATION

Organ Class	**Frequency**	**Preferred term**
Cardiac disorders	Frequent	Tachycardia, palpitations
	Less frequent	Electrocardiogram QT prolonged.
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, neutropenia, leukopenia, agranulocytosis.
Nervous system disorders	Frequent	Somnolence, akathisia, hyperkinesia, hypokinesia, tremor, dystonia, dizziness, headache
	Less frequent	Tardive dyskinesia, dyskinesia, parkinsonism, speech disorder, convulsions, neuroleptic malignant syndrome
Eye disorders	Frequent	Accommodation disorder, abnormal vision
	Less frequent	Oculogyration
Respiratory, thoracic and mediastinal disorders	Frequent	Dyspnoea
Gastrointestinal disorders	Frequent	Dry mouth, salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea.
	Less Frequent	Abdominal pain, nausea, flatulence
Renal and urinary disorders	Frequent	Micturition disorder, urinary retention
Pregnancy, puerperium and perinatal conditions	Less frequent	Neonatal withdrawal syndrome (see 4.6)
Skin and subcutaneous tissue disorders	Frequent	Hyperhidrosis, pruritus
	Less frequent	Rash, photosensitivity reaction, dermatitis
Musculoskeletal and connective tissue disorder	Frequent	Myalgia
	Less frequent	Muscle rigidity
Endocrine disorders	Less frequent	Hyperprolactinaemia.
Metabolism and nutrition disorders	Frequent	Increased appetite, increased weight
	Less frequent	Decreased appetite, hyperglycaemia, abnormal glucose tolerance
Vascular disorders	Less frequent	Hypotension, hot flushes, venous thromboembolism

PROFESSIONAL INFORMATION

General disorders and administration site conditions	Frequent	Asthenia, fatigue
Immune system disorders	Less frequent	Hypersensitivity, anaphylactic reaction
Hepatobiliary disorders	Less frequent	Abnormal liver function test, jaundice
Reproductive system and breast disorders	Less frequent	Ejaculation failure, erectile dysfunction, gynaecomastia, galactorrhoea, amenorrhoea
Psychiatric disorders	Frequent	Insomnia, depression, nervousness, agitation, decreased libido
	Less frequent	Confusional state, suicidal ideation, suicidal behaviour *

* Cases of suicidal ideation and suicidal behaviours have been reported during FLUANXOL therapy or early after treatment discontinuation (see section 4.4).

Cases of QT prolongation, ventricular dysrhythmias, ventricular fibrillation, ventricular tachycardia, Torsade de Pointes and sudden unexplained death have been reported for FLUANXOL (see section 4.4).

Abrupt discontinuation of FLUANXOL may be accompanied by withdrawal symptoms. The most common symptoms are nausea, vomiting, anorexia, diarrhoea, rhinorrhoea, sweating, myalgias, paraesthesias, insomnia, restlessness, anxiety, and agitation. Patients may also experience vertigo, alternate feelings of warmth and coldness, and tremor. Symptoms generally begin within 1 to 4 days of withdrawal and abate within 7 to 14 days.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

PROFESSIONAL INFORMATION

4.9 Overdose

Symptoms:

Somnolence, coma, movement disorders, convulsions, shock, hyperthermia/hypothermia.

ECG changes, QT prolongation, Torsades de Pointes, cardiac arrest and ventricular dysrrhythmias have been reported when administered in overdose or when administered together with medicines known to affect the heart.

Treatment

Treatment is symptomatic and supportive. Measures to support the respiratory and cardiovascular systems should be instituted. Epinephrine (adrenaline) should not be used as further lowering of blood pressure may result.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.6.5 Miscellaneous Structures (Thioxanthenes)

Flupenthixol is a neuroleptic of the thioxanthene group.

Flupenthixol has an anxiolytic, antidepressive mood stabilising effect and certain activating properties.

Flupenthixol is mainly effective through a blockade of central monoamine receptors, especially in the dopaminergic system.

5.2 Pharmacokinetic properties

Maximum serum concentration is reached about 4 hours after oral administration. The bioavailability of flupentixol is about 40 %. Protein binding is above 95 %.

The half-life is about 35 (19 - 39) hours. There are large individual variations in the therapeutic serum concentration. Flupentixol is metabolised mainly in the liver and is excreted mainly via the faeces and the urine.

PROFESSIONAL INFORMATION

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:

Betadex,

lactose monohydrate,

maize starch,

hydroxypropylcellulose,

microcrystalline cellulose,

croscarmellose sodium,

talc,

hydrogenated vegetable oil,

magnesium stearate.

Coating: Opadry II 85F38027 Yellow, macrogol/PEG 6000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 ºC.

Protect from light.

6.5 Nature and contents of container

FLUANXOL Tablets 0,5 mg:

PVC/PE/PVdC/ Aluminium foil blister strips of 10 tablets each, 30 tablets per carton or white HDPE containers with childproof closures and tamper-evident seals containing 30, 50 or 100 tablets.

PROFESSIONAL INFORMATION

FLUANXOL Tablets 1 mg:

PVC/PE/PVdC/ Aluminium foil blister strips of 10 tablets each, 30 tablets per carton or white HDPE containers with childproof closures and tamper-evident seals containing 30, 50, 60 or 100 tablets.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

H. Lundbeck (Pty) Ltd

Office A1002, 1st Floor, Knightsbridge

33 Sloane Street, Bryanston, 2190, South Africa

8. REGISTRATION NUMBER(s)

FLUANXOL Tablets 0,5 mg: B/2.6.5/1372

FLUANXOL Tablets 1 mg: B/2.6.5/1380

Namibia: NS3	FLUANXOL Tablets 0,5 mg	04/2.6.5/1541
Namibia: NS3	FLUANXOL Tablets 1 mg	04/2.6.5/1542
Botswana: BS2	FLUANXOL Tablets 0,5 mg	B9306165
Botswana: BS2	FLUANXOL Tablets 1 mg	B9306170

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

January 1994

10. DATE OF REVISION OF THE TEXT

23 December 2024