SUMMARY OF PRODUCT CHARACTERISTICS

Physician Prescribing Information

1. NAME OF THE MEDICINAL PRODUCT

Clopixol Depot 200
Clopixol Depot 500

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Zuclopenthixol decanoate 200 mg/ml.
Zuclopenthixol decanoate 500 mg/ml.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oily Solution for injection, IM.

200 mg/ml: Clear, yellowish oil, practically free from particles.
500 mg/ml: Clear, yellow oily fluid, practically free from particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clopixol Depot Injection is a depot neuroleptic preparation designed for the maintenance treatment of acute and chronic schizophrenia and other paranoid psychoses, especially where compliance with oral medication is a problem.

4.2 Posology and method of administration

Adults:
Dosage and interval between injections should be individually adjusted according to the condition of the patient. This in order to achieve a maximum suppression of psychotic symptoms with a minimum of side effects.

Zuclopenthixol decanoate 200 mg/ml
In the maintenance treatment the dosage range would normally be 200-400 mg (1-2 ml) every second to fourth week.
A few patients may need higher doses or shorter intervals between doses.
Injection volumes exceeding 2ml (400 mg) should be distributed between two injection sites.
If volumes larger than 2-3 ml of the 200 mg/ml solution are required the more concentrated solution (zuclopenthixol decanoate 500 mg/ml) should be preferred.

Treatment is usually started with 100 mg. One week later, or when symptoms recur (but not more than 4 weeks later) a second injection of 100-200 mg or more is given.

**Zuclopenthixol decanoate 500 mg/ml**

250-500 mg (½ml - 1 ml) every one to four weeks, depending on the response. When changing the medication from oral zuclopenthixol or zuclopenthixol acetate i.m. to maintenance treatment with zuclopenthixol decanoate the following guidelines should be used:

1) **Change from oral zuclopenthixol to zuclopenthixol decanoate**
   
x mg p.o. daily corresponds to 8x mg decanoate every 2 weeks.
x mg p.o. daily corresponds to 16x mg decanoate every 4 weeks.

   Oral zuclopenthixol should be continued during the first week after the first injection but in diminishing dosage.

2) **Change from zuclopenthixol acetate to zuclopenthixol decanoate**

   Concomitantly with the (last) injection of zuclopenthixol acetate (100 mg), 200-400 mg (1-2 ml) of zuclopenthixol decanoate 200 mg/ml should be given intramuscularly and repeated every 2nd week. Higher doses or shorter intervals may be needed.

Zuclopenthixol acetate and zuclopenthixol decanoate can be mixed in a syringe and given as one injection (co-injection).

Patients being transferred from other depot preparations should receive a dose in the ratio of 200 mg zuclopenthixol decanoate equivalent to 25 mg fluphenazine decanoate, to 40 mg cis(Z)-flupentixol decanoate, or to 50 mg haloperidol decanoate.

Subsequent doses of zuclopenthixol decanoate and interval between injections should be adjusted to the response of the patient.

**Elderly:**
Elderly patients should receive dosages in the lower end of the dosage range.

**Children**
Clopixol Depot is not recommended for use in children due to lack of clinical experience.

**Reduced renal function**
Clopixol Depot can be given in usual doses to patients with reduced renal function.

**Reduced liver function**
Careful dosing and, if possible, a serum level determination is advisable.

**Method of administration**
Clopixol Depot is administered by intramuscular injection into the upper outer quadrant of the gluteal region. Injection volumes exceeding 2 ml should be distributed between 2 injection sites. Local tolerability is good.

**Note:**
As with all oily injections it is important to ensure by aspiration before injection, that inadvertent intravascular entry does not occur.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients, (see section 6.1).

Circulatory collapse, depressed level of consciousness due to any cause (e.g. intoxication with alcohol, barbiturates or opiates), coma.

4.4 Special warnings and precautions for use

The possibility of development of neuroleptic malignant syndrome (hyperthermia, muscle rigidity, fluctuating consciousness, instability of the autonomous nervous system) exists with any neuroleptic. The risk is possibly greater with the more potent agents. Patients with pre-existing organic brain syndrome, mental retardation and opiate and alcohol abuse are over-represented among fatal cases.

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

Symptoms may persist for more than a week after oral neuroleptics are discontinued and somewhat longer when associated with the depot forms of the drugs.

Like other neuroleptics zuclopenthixol decanoate should be used with caution in patients with organic brain syndrome, convulsion and advanced hepatic disease.

As described for other psychotropics zuclopenthixol decanoate may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients.

Patients on long-term therapy, particularly on high doses, should be monitored carefully and evaluated periodically to decide whether the maintenance dosage can be lowered.

As with other drugs belonging to the therapeutic class of antipsychotics, zuclopenthixol decanoate may cause QT prolongation. Persistently prolonged QT intervals may increase the risk of malignant arrhythmias. Therefore, zuclopenthixol decanoate should be used with caution in susceptible individuals (with hypokalemia, hypomagnesia 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 arrhythmia. Concomitant treatment with other antipsychotics should be avoided (see section 4.5).

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with zuclopenthixol decanoate and preventive measures undertaken.

Elderly

Cerebrovascular
An approximately 3-fold increased risk of cerebrovascular adverse events have 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 for other antipsychotics or other patient populations. Zuclopenthixol decanoate 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 antipsychotics are at a small 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.

Zuclopenthixol decanoate is not licensed for the treatment of dementia-related behavioural disturbances.

4.5 Interaction with other medicinal products and other forms of interaction

Zuclopenthixol may potentiate the effects of anticoagulants
Antipsychotics may enhance the absorption of corticosteroids and digoxin.

Combinations requiring precautions for use
Zuclopenthixol decanoate may enhance the sedative effect of alcohol and the effects of barbiturates and other CNS depressants.

Neuroleptics may increase or reduce the effect of antihypertensive drugs; the antihypertensive effect of guanethidine and similar acting compounds is reduced.

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

Tricyclic antidepressants and neuroleptics mutually inhibit the metabolism of each other.

Zuclopenthixol decanoate may reduce the effect of levodopa and the effect of adrenergic drugs.

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

Since zuclopenthixol is partly metabolised by CYP2D6 concomitant use of drugs known to inhibit this enzyme may lead to decreased clearance of zuclopenthixol.

Increases in the QT interval related to antipsychotic treatment may be exacerbated by the co-administration of other drugs known to significantly increase the QT interval. Co-administration of such drugs should be avoided. Relevant classes include:
- class la and III antiarrhythmics (e.g. quinidine, amiodarone, sotalol, dofetilide)
- some antipsychotics (e.g. thioridazine)
- some macrolides (e.g. erythromycin)
- some antihistamines (e.g. terfenadine, astemizole)
- some quinolone antibiotics (e.g. gatifloxacin, moxifloxacin)

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

Drugs known to cause electrolyte disturbances such as thiazidediuretica (hypokalemia) and drugs known to increase the plasma concentration of zuclopenthixol decanoate should also
be used with caution as they may increase the risk of QT prolongation and malignant arrhythmias (see section 4.4).

4.6 Pregnancy and lactation

Pregnancy

Zuclopenthixol decanoate should not be administered during pregnancy unless the expected benefit to the patient outweighs the theoretical risk to the foetus.

The newborns of mothers treated with neuroleptics in late pregnancy, or labour, may show signs of intoxication such as lethargy, tremor and hyperexcitability and have a low apgar score.

Animal-reproduction studies on zuclopenthixol have not given evidence of an increased incidence of foetal damage or other deleterious effects on the reproduction process.

Lactation

As zuclopenthixol is found in breast milk in low concentrations it is not likely to affect the infant when therapeutic doses are used. The dose ingested by the infant is less than 1% of the weight related maternal dose (in mg/kg). Breast-feeding can be continued during zuclopenthixol decanoate therapy if considered of clinical importance but observation of the infant is recommended, particularly in the first 4 weeks after giving birth.

4.7 Effects on ability to drive and use machines

Clopixol Depot is a sedative drug. Patients who are prescribed psychotropic medication may be expected to have some impairment in general attention and concentration and should be cautioned about their ability to drive or operate machinery.

4.8 Undesirable effects

Undesirable effects are for the majority dose dependent. The frequency and severity are most pronounced in the early phase of treatment and decline during continued treatment.

Extrapyramidal reactions may occur, especially during the first few days after an injection and in the early phase of treatment. In most cases these side effects can be satisfactorily controlled by reduction of dosage and/or use of antiparkinsonian drugs. The routine prophylactic use of antiparkinsonian drugs is not recommended. Antiparkinsonian drugs do not alleviate tardive dyskinesia and may aggravate them. Reduction in dosage or, if possible, discontinuation of zuclopenthixol therapy is recommended. In persistent akathisia a benzodiazepine or propranolol may be useful.

Frequencies are taken from the literature and spontaneous reporting. Frequencies are defined as:

- very common (≥1/10),
- common (≥1/100 to <1/10),
- uncommon (≥1/1000 to <1/100),
- rare (≥1/10000 to <1/1000),
- very rare (<1/10000),
- or not known (can not be estimated from the available data).

<table>
<thead>
<tr>
<th>Cardiac disorders</th>
<th>Common</th>
<th>Tachycardia, palpitations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare</td>
<td>Electrocardiogram QT prolonged.</td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system</td>
<td>Rare</td>
<td>Thrombocytopenia, neutropenia,</td>
</tr>
<tr>
<td>disorders</td>
<td>Leukopenia, agranulocytosis.</td>
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<tr>
<td><strong>Nervous system disorders</strong></td>
<td></td>
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<tr>
<td>Very common</td>
<td>Somnolence, akathisia,</td>
<td></td>
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<tr>
<td></td>
<td>hyperkinesia, hypokinesia.</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>Tremor, dystonia, hypertonia,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dizziness, headache, paraesthesia,</td>
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<tr>
<td></td>
<td>disturbance in attention, amnesia,</td>
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<tr>
<td></td>
<td>gait abnormal.</td>
<td></td>
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<tr>
<td>Uncommon</td>
<td>Tardive dyskinesia, hyperreflexia,</td>
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<tr>
<td></td>
<td>dyskinesia, parkinsonism, syncope,</td>
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<td></td>
<td>ataxia, speech disorder, hypotonia,</td>
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<td></td>
<td>convulsion, migraine.</td>
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<tr>
<td>Very rare</td>
<td>Neuroleptic malignant syndrome.</td>
<td></td>
</tr>
<tr>
<td><strong>Eye disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>Accommodation disorder, vision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>abnormal.</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Oculogyration, mydriasis.</td>
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<tr>
<td><strong>Ear and labyrinth disorders</strong></td>
<td></td>
<td></td>
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<tr>
<td>Common</td>
<td>Vertigo.</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Hyperacusis, tinnitus.</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and medistinal disorders</strong></td>
<td>Nasal congestion, dyspnoea.</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very common</td>
<td>Dry mouth.</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>Salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea.</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Abdominal pain, nausea, flatulence.</td>
<td></td>
</tr>
<tr>
<td><strong>Renal and urinary disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>Micturition disorder, urinary retention, polyuria.</td>
<td></td>
</tr>
<tr>
<td><strong>Skin and subcutaneous tissue disorders</strong></td>
<td>Hyperhidrosis, pruritus.</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Rash, photosensitivity reaction, pigmentation disorder, seborrhoea, dermatitis, purpura.</td>
<td></td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorder</strong></td>
<td>Myalgia.</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Muscle rigidity, trismus, torticollis.</td>
<td></td>
</tr>
<tr>
<td><strong>Endocrine disorders</strong></td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperprolactinaemia.</td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Common</td>
<td>Increased appetite, weight increased.</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Decreased appetite, weight decreased.</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
<td>Hyperglycaemia, glucose tolerance impaired, hyperlipidaemia.</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Uncommon</td>
<td>Hypotension, hot flush.</td>
</tr>
<tr>
<td></td>
<td>Very rare</td>
<td>Venous thromboembolism</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Common</td>
<td>Asthenia, fatigue, malaise, pain.</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Thirst, injection site reaction, hypothermia, pyrexia.</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Rare</td>
<td>Hypersensitivity, anaphylactic reaction.</td>
</tr>
<tr>
<td>Hepato-biliary disorders</td>
<td>Uncommon</td>
<td>Liver function test abnormal.</td>
</tr>
<tr>
<td></td>
<td>Very rare</td>
<td>Cholestatic hepatitis, jaundice.</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Uncommon</td>
<td>Ejaculation failure, erectile dysfunction, female orgasmic disorder, vulvovaginal dryness.</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
<td>Gynaecomastia, galactorrhoea, amenorrhoea, priapism.</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Common</td>
<td>Insomnia, depression, anxiety, nervousness, abnormal dreams, agitation, libido decreased.</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Apathy, nightmare, libido increased, confusional state.</td>
</tr>
</tbody>
</table>

As with other drugs belonging to the therapeutic class of antipsychotics, rare cases of QT prolongation, ventricular arrhythmias - ventricular fibrillation, ventricular tachycardia, Torsade de Pointes and sudden unexplained death have been reported for zuclopenthixol decanoate (see section 4.4).

Abrupt discontinuation of zuclopenthixol decanoate 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.
4.9 Overdose

Due to the administration form overdose symptoms are unlikely to occur.

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

ECG changes, QT prolongation, Torsade de Pointes, cardiac arrest and ventricular arrhythmias have been reported when administered in overdose together with drugs 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. Convulsions may be treated with diazepam and movement disorders with biperiden.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Neuroleptics (antipsychotics)
ATC-code: N 05 AF 05

Mechanism of action
Zuclopenthixol is a neuroleptic of the thioxanthene group.

The antipsychotic effect of neuroleptics is related to their dopamine receptor blocking effect but possibly also 5-HT (5-hydroxytryptamine) receptor blockade contributes. In vitro zuclopenthixol has high affinity for both dopamine D₁ and D₂ receptors, for α₁-adrenoceptors and 5-HT₂ receptors but no affinity for cholinergic muscarine receptors. It has weak histamine (H₁) receptor affinity and no α₂-adrenoceptor blocking activity.

In vivo the affinity for D₂ binding sites dominates over the affinity for D₁ receptors. Zuclopenthixol has proven to be a potent neuroleptic in all the behavioural studies for neuroleptic (dopamine receptor blocking) activity. Correlation is found in the in vivo test models, the affinity for dopamine D₂ binding sites in vitro and the average, daily oral antipsychotic doses.

Like most other neuroleptics zuclopenthixol increases the serum prolactin level.

Pharmacological studies have clearly demonstrated that zuclopenthicol decanoate in oil has a prolonged neuroleptic effect and that the amount of drug necessary to maintain a certain effect over a long period is considerably smaller with the depot preparation than with daily oral administration of zuclopenthicol. In terms of clinical use the findings in pharmacological studies may indicate that a prolonged neuroleptic effect without overt sedation may be
obtained with the depot preparation. Moreover, the risk of interference with anaesthetics may be expected to be low.

Clinical efficacy
In clinical use zuclopenthixol decanoate is intended for the maintenance treatment of chronic psychotic patients. Positive results also have been obtained in the management of hyperactive and aggressive mentally handicapped patients.

Zuclopenthixol decanoate induces a transient dose-dependent sedation. However, if the patient is switched to maintenance treatment with zuclopenthixol decanoate from oral zuclopenthixol or from i.m. zuclopenthixol acetate the sedation will be no problem. Tolerance to the unspecific sedative effect develops rapidly.

Zuclopenthixol decanoate is particularly useful in the treatment of patients, who are agitated, restless, hostile, or aggressive.

Zuclopenthixol decanoate permits continuous treatment especially of those patients who are unreliable in taking the oral medication prescribed for them. Zuclopenthixol decanoate thus prevents the frequent relapses due to noncompliance in patients on oral medication.

5.2 Pharmacokinetic properties

Absorption
By esterification of zuclopenthixol with decanoic acid zuclopenthixol has been converted to a highly lipophilic substance, zuclopenthixol decanoate. When dissolved in oil and injected intramuscularly the ester diffuses rather slowly from the oil to the body water phase where it is rapidly hydrolysed releasing the active zuclopenthixol.

Following intramuscular injection maximum serum concentration is reached over a period of 3-7 days. With an estimated half-life of 3 weeks (reflecting the release from the depot) steady state conditions will be attained after about 3 months' repeated administration.

Distribution
The apparent volume of distribution (\(V_d\)) is about 20 l/kg. The plasma protein binding is about 98-99%.

Biotransformation
The metabolism of zuclopenthixol proceeds along three main routes - sulphoxidation, side chain N-dealkylation and glucuronic acid conjugation. The metabolites are devoid of psychopharmacological activity. Zuclopenthixol dominates over metabolites in brain and other tissues.

Elimination
The elimination half-life (\(T_{1/2}\)) of zuclopenthixol is about 20 hours and the mean systemic clearance (\(Cl_s\)) is about 0.86 l/min.

Zuclopenthixol is excreted mainly with faeces, but also to some degree (about 10%) with the urine. Only about 0.1% of the dose is excreted unchanged with the urine, meaning that the drug load on the kidneys is negligible.

In nursing mothers zuclopenthixol is excreted in small amounts with the breast milk. In steady state the pre-dose mean ratio milk conc./serum conc. in women treated orally or with the decanoate was about 0.29.

Linearity
The kinetics is linear. The mean steady state pre-injection serum level of zuclopenthixol corresponding to a 200 mg dose of zuclopenthixol decanoate every 2 weeks is about 10 ng/ml (25 nmol/l).

**Elderly patients**
The pharmacokinetic parameters are widely independent of the age of the patients.

**Reduced renal function**
Based on the above characteristics for elimination it is reasonable to assume that reduced kidney function is likely not to have much influence on the serum levels of parent drug.

**Reduced hepatic function**
No data available.

**Polymorphism**
An in vivo investigation has shown that some part of the metabolic pathways is subject to genetic polymorphism of the sparteine/debrisoquine oxidation (CYP2D6).

**Pharmacokinetic / Pharmacodynamic relationship**
A pre-injection serum (plasma) concentration of 2.8-12 ng/ml (7-30 nmol/l) and a max./min. fluctuation < 2.5 is suggested as a guideline for maintenance treatment of schizophrenic patients with a low-moderate degree of illness. Pharmacokinetically a dose of 200 mg/2 weeks or 400 mg/4 weeks of zuclopenthixol decanoate is equivalent to a daily oral dose of 25 mg zuclopenthixol.

### 5.3 Preclinical safety data

**Acute toxicity**
Zuclopenthixol has low acute toxicity.

**Chronic toxicity**
In chronic toxicity studies there were no findings of concern for the therapeutic use of zuclopenthixol.

**Reproduction toxicity**
Based on data from reproduction toxicity studies there is no reason to have special concern for the use of zuclopenthixol in women of child bearing potential. However, in a peri/postnatal study in rats, dosages of 5 and 15 mg/kg/day resulted in an increase of stillbirths, reduced pup survival and delayed development of pups. The clinical significance of these findings is unclear and it is possible that the effect on pups was due to neglect from the dams that were exposed to doses of zuclopenthixol producing maternal toxicity.

**Mutagenicity and carcinogenicity**
Zuclopenthixol has no mutagenic or carcinogenic potential. In a rat oncogenecity study 30 mg/kg/day for two years (top dosage) resulted in slight non-statistical increases in the incidence of mammary adenocarcinomas, pancreatic islet cell adenomas, carcinomas in females and thyroid parafollicular carcinomas. The slight increase in the incidence of these tumors is a common finding for D₂ antagonists, which increase prolactin secretion when administered to rats. The physiological differences between rats and humans with regard to prolactin make the clinical significance of these findings unclear, but it is accepted as not predicting an oncogenic risk in patients.

**Local toxicity**
Local muscle damage is seen after injection of aqueous solutions of neuroleptics, including zuclopenthixol. The muscle damage shows a much higher degree after the aqueous solution
of neuroleptics than after the oily solutions of zuclopenthixol acetate and zuclopenthixol decanoate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Triglycerides, medium-chain.

6.2 Incompatibilities

Zuclopenthixol decanoate should only be mixed with zuclopenthixol acetate, which also is dissolved in Triglycerides, medium-chain (Ph. Eur.).

Zuclopenthixol decanoate should not be mixed with depot formulations with sesame oil as the vehicle because this would result in definite changes in the pharmacokinetic properties of the involved preparations.

6.3 Shelf life

200 mg/ml: 3 years.

500 mg/ml: 4 years.

6.4 Special precautions for storage

Do not store above 25°C, protected from light.

In accordance with normal practice partially used vials should be discarded at the end of each session.

6.5 Nature and contents of container

Boxes of 5 × 500 mg (1 ml ampoule) 1 × 500 mg (1 ml ampoule)

Boxes of 10 × 200 mg (1 ml ampoule)

Boxes of 1 × 10 ml vials.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

H. Lundbeck A/S
Ottiliavej 9
DK-2500 Valby, Copenhagen, Denmark

8. LICENSE HOLDER

Lundbeck Israel Ltd.,
4 Derech HaShalom st, Tel-Aviv

9. MARKETING AUTHORISATION NUMBER(S)

CLOPIXOL DEPOT 200 - 069 70 25491
10. DATE OF REVISION OF TEXT

December 2011