4.5  Interaction with other medicinal products and other forms of interaction

4.5.1  Interactions with other medicinal products

Zuclopenthixol acetate can have an additive effect with anticholinergic agents. The risk of anticholinergic side effects may be increased by concomitant use of other anticholinergics. Patients on antiparkinsonian drugs may also experience an increase in extrapyramidal symptoms when treated with zuclopenthixol acetate.

4.5.2  Interactions with other forms of interaction

4.5.2.1  Drugs with a QT-interval prolonging effect

Zuclopenthixol acetate may cause QT-interval prolongation. Therefore, careful monitoring is recommended in patients with a history of cardiovascular disorders or in patients taking drugs with a potential to prolong the QT-interval (see section 4.4).

4.6  Pregnancy and lactation

4.6.1  Pregnancy

Zuclopenthixol acetate should not be administered during pregnancy unless the expected benefit to the patient outweighs the known risks to the fetus.

4.6.2  Lactation

The use of zuclopenthixol acetate is not recommended during breastfeeding.

4.7  Effects on ability to drive and use machines

Zuclopenthixol acetate may cause drowsiness and dizziness. In rare cases, these effects can persist for several days after treatment has stopped. Patients should be advised to avoid driving or operating machines until these symptoms have subsided.

4.8  Undesirable effects

4.8.1  Undesirable effects of major importance

4.8.2  Undesirable effects which may require withdrawal of the drug

4.8.3  Other undesirable effects

4.9  Overdosage

4.9.1  A single overdose of zuclopenthixol acetate

4.9.2  Acute or chronic overdosage

4.9.3  Overdosage in children

5. PHARMACEUTICAL FORM

5.1  Packaging and storage

5.2  Shelf life

5.3  Special precautions for storage

5.4  Disposal of containers and packaging

6. MARKETING AUTHORISATION HOLDER

7. COMPENDIAL REFERENCES
The apparent volume of distribution (V_d) of zuclopenthixol is about 20 to 30 times the mean systemic clearance (CL) is about 0.86 ml/min.

Zuclopenthixol is excreted mainly with feces, 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 is or the kidney is negligible.

In nursing mothers zuclopenthixol is excreted in small amounts with the breast milk. In usual state the free dose mean values 0.010% zuclopenthixol is recovered from breast milk of nursing mothers.

Lactation

The breast is linear. Average maximum serum level of zuclopenthixol corresponding to 300 mg dose of zuclopenthixol acetate is 102 ng/l (3.3 ng/ml). Three days after the injection the serum level is about one third of the maximum i.e. 35 ng/l (24 ng/ml).

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 to have no much influence on the serum level of parent drug.

Reduced hepatic function

No data available.

Premorbid

An in vivo investigation has shown that some part of the metabolic pathways is subject to genetic polymorphisms of the quinine/desmopressin oxidation (CYP2D6).

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.

Drug interaction

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 perinatal/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 but it is possible that the effect on pups was due to height from the dams that were exposed to doses of zuclopenthixol producing maternal toxicity.

Maternity and uncontrolled pregnancy

Zuclopenthixol has no mutagenic or clastogenic potential. In a rat intraperitoneal study a dose of 30 mg/kg/day for 4 days (one injection) resulted in slight non-statistical increase in the incidence of mammary adenocarcinoma, pancreatic islets adenoma, adenocarcinomas in females, and hyperplastic centrocarcinomas. The slight non statistical increase in mammary adenocarcinoma is not considered a positive finding as zuclopenthixol has not been shown to cause mammary tumors in rats. This increase is thought to be a reflection of a background incidence, which increase in spontaneous abortions when administered to rats. The physiological differences between rats and humans with regard to proliferation may make the clinical significance of these findings unclear, but it is accepted as not predicting an oncogenic risk in patients.

Lactation

Local muscle damage is seen after injection of aqueous solutions of neuroleptics, including zuclopenthixol. The muscle damage shown a musc higher degree after the aqueous solutions of neuroleptics than after the oily solutions of zuclopenthixol at state and zuclopenthixol decanoate.

6. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Neuroleptics (antineurotics) ATC code: N 05 AF 05

Mechanism of action

The antipsychotic effect of neuroleptics is related to their dopamine receptor blocking properties.

The antipsychotic effect of neuroleptics is related to their dopamine receptor blocking properties. It has weak histamine (H2) and 5-HT2 receptors but no affinity for cholinergic muscarine 1-adrenoceptors and 5 HT2 receptors but no affinity for cholinergic muscarine receptors.

5HT receptors.

The antipsychotic effect of neuroleptics is related to their dopamine receptor blocking properties.