SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Anquil 0.25 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0.25 mg benperidol.

Excipient with known effect
79.75 mg lactose per tablet

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White tablets, marked with “025” on one side and a breakline line on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the control of deviant anti-social sexual behaviour.

4.2 Posology and method of administration

Posology

Adults
0.25-1.5 mg/day in divided doses. Dosage is best initiated and adjusted under close clinical supervision as individual response to neuroleptic drugs is variable.

In determining dosage, consideration should be given to the patient’s age, severity of symptoms and previous response to other neuroleptic drugs.

Patients who are debilitated, or those with previously reported adverse reactions to neuroleptic drugs, may require less Anquil, and half the normal starting dose may be sufficient for therapeutic response.

In adolescents, a lower dose may be advisable.

Elderly
Half the normal starting dose may be sufficient for therapeutic response.

Paediatric population
Not recommended.

As with all medications the lowest effective dose should be used.

Method of administration
Oral.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypersensitivity to other butyrophenones.
Comatose states.
Patients with extrapyramidal symptoms, CNS depression, depressive disorders or Parkinson's disease.

4.4 Special warnings and precautions for use

Rare cases of sudden and unexplained death have been reported in psychiatric patients receiving antipsychotic drugs. However, Anquil has not been clearly implicated in any case.

Acute withdrawal symptoms, including nausea, vomiting and insomnia, have very rarely been described after abrupt cessation of high doses of antipsychotic drugs. Relapse may also occur and gradual withdrawal is advisable.

Where prolonged treatment with Anquil is envisaged, it would be a reasonable precaution to carry out regular blood counts and tests of liver function.

Caution is advised in patients with liver disease, renal failure, cardiovascular disease, epilepsy, and conditions predisposing to epilepsy and convulsions.

As with other neuroleptics, cases of QT interval prolongation may occur. Consequently, and if the clinical situation permits, absence of the following risk factors for onset of this type of arrhythmia should be verified prior to administration:

- Cardiac disease.
- A family history of sudden death and/or QT prolongation.
- Uncorrected electrolyte disturbances.
- A history of QT interval prolongation, ventricular arrhythmias or Torsades de Pointes.

Prior to initiation of treatment with Anquil, it may be appropriate to consider an ECG with measurement of serum calcium, magnesium and potassium levels. This is especially important in the elderly and patients with a positive personal or family history of cardiac disease or abnormal findings on cardiac clinical examination. During therapy, periodic serum electrolyte levels may be monitored and corrected if necessary, especially during long-term usage; if concomitant diuretics are taken; or during inter-current illness. Concomitant neuroleptics should be avoided.

An ECG may be appropriate to assess the QT interval whenever dose escalation is proposed and when the maximum therapeutic dose is reached. The dose of Anquil should be reduced if the QT interval is prolonged and discontinued if the QTc interval is greater than 500ms.

An approximately 3-fold increased risk of cerebrovascular adverse events 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 for other antipsychotics or other patient populations. Benperidol should be used with caution in patients with risk factors for stroke.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine as it contains lactose.

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 Anquil and preventive measures undertaken.

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.

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

4.5 Interaction with other medicinal products and other forms of interaction

In common with all neuroleptics, Anquil can increase the CNS depression produced by other CNS-depressant drugs, including alcohol, hypnotics, sedatives, strong analgesics or sedating antihistamines and may antagonise the action of adrenaline (epinephrine) and other sympathomimetic agents.

Certain agents (e.g. phenobarbital, carbamazepine, phenytoin, rifampicin, primidone), as well as smoking and alcohol consumption, which stimulate metabolising enzymes in the liver, may theoretically enhance the metabolic breakdown of neuroleptics, necessitating an increased dose. Fluoxetine, buspirone and ritonavir may cause an increase in the plasma concentration of Anquil necessitating a dose modification.

The effect of Anquil may be reduced by concomitant antimuscarinic medications.

Anquil may impair the anti-Parkinson effects of levodopa and other dopamine agonists. The dosage of anti-convulsants may need to be increased to take account of the lowered seizure threshold.

The use of Anquil with anticonvulsants such as barbiturates, carbamazepine, ethosuximide oxcarbazepine, phenytoin, primidone and valproate may lower the seizure threshold, thereby necessitating a review of the anticonvulsant dose requirement.

The risk of hypotension with antihypertensive drugs, anaesthetics and opioid analgesics may be increased when Anquil is given concomitantly.

Enhanced CNS effects when combined with methyldopa have been reported for some butyrophenones.

Medicines that can prolong the QT interval should be avoided, as should any medicines that can cause electrolyte imbalance. In particular amiodarone and moxifloxacin should be avoided.

It is advised that Anquil should be avoided if artemether/lumeffantrine is administered. Concomitant use of pramipexole or ropinirole with Anquil should be avoided as there may be antagonism of their effect.

The risk of extrapyramidal side-effects is increased if amantadine, metoclopramide or tetrabenazine are used concomitantly with Anquil.

Concomitant treatment with lithium increases the risk of extrapyramidal side-effects, and may cause neurotoxicity.

The effects of antipsychotics may be reduced by concomitant treatment with memantine.

The effect of sodium benzoate or sodium phenylbutyrate may be reduced by concomitant butyrophenones.

4.6 Fertility, Pregnancy and lactation

The safety of Anquil in pregnancy has not been established, although studies in animals have not demonstrated teratogenic effects. As with other drugs, it is not advisable to administer Anquil in pregnancy.

Butyrophenones are excreted in breast milk and are not recommended during lactation. If the use of Anquil is considered essential, breast feeding should be discontinued.

Neonates exposed to antipsychotics (including Anquil) 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.

4.7 Effects on ability to drive and use machines

Anquil may interfere with activities requiring mental alertness. Therefore, patients should be advised not to drive or operate machinery until their individual susceptibility is known.

4.8 Undesirable effects

The undesirable effects reported with Anquil during clinical trials and post-marketing surveillance are shown in the table below. They are listed by System-Organ Class (SOC) and in order of frequency, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Table 1 Frequency of adverse events

SOC	Frequency	Event
Blood and lymphatic system disorders	Not known	Blood disorder[1], granulocytopenia
[1] Blood dyscrasias, including granulocytopenia.		
Immune system disorders	Not known	Hypersensitivity[2]
[2] Reported effects have included oedema, skin rashes or hypersensitivity reactions such as exanthema and pruritus.		
Endocrine disorders	Not known	Hyperprolactinaemia[3], galactorrhoea, gynaecomastia, oligomenorrhoea
[3] Hormonal effects of antipsychotic neuroleptic drugs include hyperprolactinaemia, which may cause galactorrhoea, gynaecomastia and oligo-or amenorrhoea.		
Metabolism and nutrition disorders	Not known	Weight fluctuation
Nervous system disorders[4]	Rare	Neuroleptic malignant syndrome, depression, seizures, confusional state, agitation
	Not known	Sweating, dizziness, headache, extrapyramidal disorder, tremor, muscle rigidity, bradykinesia, akathisia, dystonia, oculogyric crysis, spasmodic dystonia, tardive dyskinesia, autonomic nervous system imbalance, altered state of consciousness, coma, mental impairment, insomnia

[4] In common with all neuroleptics, extrapyramidal symptoms may occur, e.g. tremor, muscle rigidity, hypersalivation, bradykinesia, akathisia, acute dystonia, oculogyric crisis and laryngeal dystonia.

Anti-Parkinson agents should only be given as required; they should not be prescribed routinely as a preventive measure.

As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or after drug discontinuation. The syndrome is mainly characterised by rhythmical involuntary movements of the tongue, face, mouth or jaw. The manifestations may be permanent in some patients. Anquil should be given in the minimal effective dose for the minimum possible time.

The syndrome may be masked when the treatment is reinstituted, when the dosage is increased or when a switch is made to a different antipsychotic drug. Treatment should be discontinued as soon as possible.

The potential seriousness and unpredictability of tardive dyskinesia and the fact that it has occasionally been reported to occur when neuroleptic antipsychotic drugs have been prescribed for relatively short periods in low dosage means that the prescribing of such agents requires especially careful assessment of risks versus benefit. Tardive dyskinesia can be precipitated or aggravated by anti-Parkinson drugs. Tardive dyskinesia may occur after abrupt drug withdrawal.

It has been reported that fine vermicular movements of the tongue may be an early sign of

SOC	Frequency	Event
tardive dyskinesia and that the full syndrome may not develop if the medication is stopped at that time. If signs and symptoms of tardive dyskinesia appear, the discontinuation of all neuroleptic drugs should be considered. As with other neuroleptics, rare cases of neuroleptic malignant syndrome, an idiosyncratic response characterised by hyperthermia, generalised muscle rigidity, autonomic instability, altered consciousness, coma and elevated CPK levels, have been reported. Signs of autonomic dysfunction such as tachycardia, labile arterial pressure and sweating may precede the onset of hyperthermia, acting as early warning signs. Antipsychotic treatment should be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted. Anquil, even in low dosage in susceptible (especially non-psychotic) individuals, may cause unpleasant subjective feelings of being mentally dulled or slowed down, dizziness, headache, or paradoxical effects of excitement, agitation or insomnia. Depression and seizures have been reported rarely. A causal relationship with Anquil has not been unequivocally established.		
Cardiac disorders[5]	Uncommon	Hypotension
	Rare	Ventricular tachycardia
	Not known	Tachycardia, Electrocardiogram QT prolonged, ventricular arrhythmias, ventricular fibrillation, Torsades de Pointes and cardiac arrest
[5] Dose-related hypotension can occur, particularly in the elderly who are more susceptible to the sedative and hypotensive effects. Benign tachycardia has occasionally been reported. As with other neuroleptics Electrocardiogram QT prolonged, ventricular arrhythmias (including ventricular fibrillation and rarely ventricular tachycardia), Torsades de Pointes and cardiac arrest may occur. In rare cases this may lead to sudden "unexplained" death. Treatment of undesirable cardiac effects includes withdrawal of the causal agent, and correction of hypoxia, electrolyte abnormalities and acid base disturbances.		
Vascular disorders[6]	Not known	Embolism venous, pulmonary embolism, deep vein thrombosis
[6] Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs.		
Gastrointestinal disorders	Not known	Nausea, vomiting, decreased appetite, constipation, dyspepsia, salivary hypersecretion
Hepatobiliary disorders	Not known	Jaundice, hepatic function abnormal[7]
[7] Transient abnormalities of liver function in the absence of jaundice have been reported.		
Skin and subcutaneous disorders	Not known	Pruritus
Pregnancy, puerperium and perinatal conditions	Not known	Drug withdrawal syndrome neonatal (see section 4.6)
General disorders and administration site conditions	Rare	Oedema, hyperthermia
Investigations	Not known	Body temperature fluctuation, blood creatine phosphokinase increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

In general, the manifestations of Anquil overdosage are an extension of its pharmacological action. In patients who have received daily doses of 160 mg, the most prominent side effects were extrapyramidal symptoms such as oculogyric crisis, salivation, muscle rigidity, akinesia and akathisia. Drowsiness or paradoxical excitement may occur.

Treatment

There is no specific antidote to Anquil. Treatment consists of supportive and symptomatic measures combined with standard measures to remove any unabsorbed drug. Extrapyramidal symptoms should be treated with anti-Parkinson drugs as required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antipsychotics, butyrophenone derivatives, ATC code: N05AD07

Benperidol is a potent neuroleptic of the butyrophenone series with general properties similar to those of haloperidol.

5.2 Pharmacokinetic properties

After administration of benperidol (2 mg tablets PO) to volunteers, the following values have been reported:
C_{max} 4.1 ± 1.7 µg/l , T_{max} 2.9 ± 1.8 h, $AUC_{(0-24)}$ 39.8 ± 9.4 µg.h/l.

After repeated administration of 3 and 12 mg benperidol to patients, plasma levels of 10 and 30 µg/l respectively have been reported.

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Starch
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Protect from light.

6.5 Nature and contents of container

The tablets are supplied in PVC/PVdC/Aluminium blister packs, containing 100 or 112 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 45043/0031

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

19/03/2025