Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Serenace 2 mg/ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of solution contains 2 mg haloperidol.

Excipients: Methyl parahydroxybenzoate (E218) 0.5 mg/ml.
Propyl parahydroxybenzoate (E216) 0.05 mg/ml.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution
Clear, colourless, odourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Recommended use
For the management of cases of schizophrenia, hypomania, mania, agitation, psychotic illness, paranoid psychosis, childhood behaviour disorders especially associated with problems in mentally retarded, and severe motor tics and Gilles de la Tourette Syndrome, intractable hiccup, control of severe nausea and vomiting excluding that of hyperemesis gravidarum.

4.2 Posology and method of administration

Adults
The usual initial dose is 1.5 to 20mg daily depending on the individual patient's characteristics and the severity of the disorder, with increments until optimum response is obtained. Reduction of the dosage can then be made to the usual maintenance dose of 3 to 10mg daily.

Elderly
In the elderly, half the above doses are usually sufficient. Maximum and maintenance doses will usually be lower for geriatric and debilitated patients because of greater sensitivity.

Gilles de la Tourette Syndrome
The usual initial dose is 2mg daily with increments to the level of optimal control, generally 6 to 50mg followed by a gradual reduction to a maintenance level, which is generally around 4mg.

Children
An initial dosage of 0.025 to 0.05mg/kg body weight can be used with a maximum of 10mg daily, with a subsequent maintenance level of 0.05mg/kg body weight.
The higher dose levels generally should be combined with anti-Parkinsonian drugs especially in children and the elderly.

Adjustments of dosage should be on the basis of the individual patient's condition and response.

Route of administration
Oral Use.

4.3 Contraindications

Use in lactation in women breast-feeding infants.
Use in comatose states.
Use in-patients with Parkinson's disease.
Use in-patients hypersensitive to butyrophenones.

4.4 Special warnings and precautions for use

Haloperidol should only be used with great caution in patients with established or likely basal ganglial lesions or with thyrotoxicosis. It should be used only with care in patients with hepatic or renal dysfunction, or epilepsy.

Caution should be exercised in the case of patients with cardiovascular disease or family history of QT prolongation if considering introduction of haloperidol.

Addition of other antipsychotic medication to haloperidol should be avoided.

Haloperidol may cause drowsiness or affect mental concentration. The user should not drive or operate machinery unless the drug has shown not to interfere with his physical or mental ability.

Haloperidol may, particularly at high doses, induce side effects of the extrapyramidal type. It is therefore often necessary to administer anti-Parkinsonian drugs as a prophylactic measure. Prolonged use especially at high doses may result in tardive dyskinesia.

In common with other antipsychotics haloperidol has been associated with persistent dyskinesia. Tardive dyskinesia may develop in some patients on long term therapy, possibly in relation to total cumulative dose, or may develop after drug therapy has been discontinued. The risk is reported to be greater in elderly patients on high-dose therapy.

Characteristic symptoms are rhythmical involuntary movements of tongue, face, mouth or jaw sometimes accompanied by involuntary movements of the extremities. They may persist for many months or even years and, while they gradually disappear in some patients, they appear to be permanent in others.

At the first signs of tardive dyskinesia which may be orofacial dyskinesia the benefit of continued treatment should be carefully assessed against the risk of the development of persistent dyskinesia. Withdrawal of treatment with careful observation of the dyskinesia and psychotic condition has been suggested in order to assess the need for continued neuroleptic therapy and to reveal persisting dyskinesia. Should it be necessary to reinstate treatment, the antipsychotic agent may mask the syndrome. Antiparkinsonian agents have proved of little value in this syndrome.

Haloperidol should be used with caution in patients in which transient hypotension might be detrimental such as those with severe cardiovascular disease. The hypotension may not respond to adrenaline.

Haloperidol may block the vasopressor activity of adrenaline with a further lowering of blood pressure.

Relatively high dose may lead to impaired body temperature control, malignant neuroleptic syndrome and hyperthermia, autonomic dysfunction, rigidity and coma. The drug should be withdrawn, preferably in stages.

Rarely sudden death has been reported in psychotic patients usually on high dosage.

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 Serenace and preventative 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 is insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Serenace is not licenced for the treatment of dementia-related behavioural disturbances.

4.5 Interaction with other medicinal products and other forms of interaction

Haloperidol will potentiate the effects of central nervous system depressants including alcohol and analgesics.
There is a potential risk of prolongation of the QT interval in patients receiving both haloperidol and other drugs with known QT prolonging properties. This risk may also occur with other drugs causing electrolyte disturbances or metabolic inhibitors of haloperidol.

Concomitant use of lithium salts and haloperidol may result in severe neuromuscular syndrome with impaired consciousness and fever. In cases where the combination is used lithium levels should be maintained below 1 mmol/litre. If unexpected pyrexia occurs in the presence of extrapyramidal side effects both lithium and haloperidol should be stopped immediately.

Combination with methyldopa may lead to enhanced sedation and mental disturbances. Haloperidol may antagonise the effects of sympathomimetic agents.

4.6 Fertility, pregnancy and lactation

Haloperidol should not be used during pregnancy unless considered essential by the physician. Some teratgenesis has been demonstrated in mice, but not in other species. No evidence of teratogenesis has been shown in human beings to date. The drug is excreted in breast milk reaching levels comparable to maternal plasma.

4.7 Effects on ability to drive and use machines

Haloperidol may cause drowsiness or affect mental concentration. The user should not drive or operate machinery unless the drug has shown not to interfere with his physical or mental ability.

4.8 Undesirable effects

Side effects include dizziness, feeling drowsy and mentally dulled, headaches, anxiety, insomnia, hypotension, dystonia, gastrointestinal disturbances, anorexia, blurred vision, tachycardia, abnormal liver function, jaundice, urinary retention, photosensitisation and hypersensitivity reactions. Hyperprolactinaemia, gynaecomastia, galactorrhoea and oligo- or amenorrhoea may occur. Impairment of sexual function, including erection dysfunction, priapism and ejaculation have been reported. Arrhythmia and hypertension may also occur uncommonly. There is a potential risk of QT prolongation with haloperidol, which may rarely result in precipitation of ventricular arrhythmias such as ventricular tachycardia or fibrillation, torsades de pointes, cardiac arrest or sudden unexplained death. Leucopenia and hypothermia have also been reported.
Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs – Frequency unknown.

4.9 Overdose

Intensification of the known pharmacological and adverse effects may occur. The most prominent would be severe extrapyramidal symptoms, hypotension or sedation. The patient may appear comatose with respiratory depression and hypotension, which could be severe enough to produce a shock like state. Extrapyramidal reactions may include muscular weakness or rigidity and a generalised or localised tremor. With accidental overdosage, hypothermia, bradycardia, sinus arrhythmia and hypertension have been reported in young children.

No specific antidote has been identified.

In the event of overdosage the stomach should be emptied by aspiration and lavage. Emetics should not be used. Establishment of patient airway and artificial ventilation may be needed. Hypotension may be counteracted by placing the patient in the head-down position and by the use of plasma expander and careful use of a vasopressor agent such as noradrenaline. Adrenaline should not be used. Severe extrapyramidal reactions should be treated with parental antihistamines or antiparkinsonian drugs. The relatively long plasma elimination half-life of haloperidol should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Antipsychotic: N05A.

5.2 Pharmacokinetic properties

A butyrophenone is variably absorbed form the gastrointestinal tract but with extensive first pass metabolism in the liver with entero hepatic recycling. The drug is widely distributed in the body, is strongly protein bound and has a half-life of 12-40 hours.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E1520)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Lactic acid
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze. Store in the original package.

6.5 Nature and contents of container

Bottle: Amber glass bottles containing 100 ml or 500 ml of solution.

Closure: White plastic (polypropylene HDPE) screw cap,
or
HDPE, EPE wadded, tamper evident screw cap,
or
HDPE, EPE, tamper evident, child resistant closure.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Norton Healthcare Ltd
T/A IVAX Pharmaceuticals UK
Ridings Point
Whistler Drive
Castleford
West Yorkshire, WF10 5HX
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 282/63/4

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 17 December 2006

10 DATE OF REVISION OF THE TEXT

March 2011