SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. NAME OF THE MEDICINALPRODUCT

Afrab Haloperidol tablet

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each tablet contains Haloperidol 5mg

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICAL FORM

Tablet

A light pink round tablet with AFRAB inscribed on one side and a marked line on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Haloperidol is indicated for the treatment of the manifestations of several psychotic disorders including schizophrenia, acute psychosis, Tourette syndrome, and other severe behavioural states.

4.2 Posology and method of administration

Posology

Haloperidol in psychosis: In this instance, the oral forms can be used. For moderate symptomology: 0.5 to 2 mg 2 to 3 times a day orally. In some resistant cases, up to 30 mg/day may be necessary.

Haloperidol in schizophrenia: In moderately severe patients, dosing is 0.5 to 2 mg haloperidol orally 2 to 3 times a day. It should not exceed 30 mg daily in case of severe cases. To control acute agitation in a schizophrenic patient, dosing is 2 to 5 mg haloperidol intramuscularly every 4 to 8 hours.

Haloperidol in Tourette syndrome: Dosing is 0.5 to 2 mg orally 2 to 3 times a day in the moderately symptomatic cases, and for severe cases, it can be higher: 3 to 5 mg, 2 to 3 times a day.

Geriatric Use: the prevalence of tardive dyskinesia is the highest among older patients, especially older women.

Adult Dosage: Individualize. Initially: Moderate symptoms: 0.5mg–2mg 2–3 times daily. Severe, chronic, or resistant symptoms: 3mg–5mg 2–3 times daily. Debilitated: 0.5mg–2mg 2–3 times daily. Max: 100mg/day.

Children Dosage:
< 3 yrs：Not recommended. Total dose may be divided, to be given 2–3 times daily.
≥3yrs: initially 0.5mg daily may increase at increments of 0.5mg at 5–7 day intervals.

Psychosis: 0.05mg/kg/day–0.15mg/kg/day. Nonpsychotic behavior and Tourette's: 0.05mg/kg/day–0.075mg/kg/day. Max 6mg/day.

Method of administration

For oral administration.

4.3 Contraindications

Haloperidol is contraindicated if there is documented hypersensitivity to this drug, in Parkinson disease, dementia with Lewy body, comatose patient, in any condition with the depressed central nervous system (CNS). Since many drugs (barbiturates, benzodiazepines, and opioids) can cause depression to CNS, concurrent use of haloperidol should be avoided or used with great caution.

4.4 Special warnings and precautions for use

Haloperidol prolongs the hypnotic action of barbiturates and may potentiate the effects of alcohol and other central nervous system depressant drugs, such as anesthetics and narcotics; caution should therefore be exercised when it is used with agents of this type and adjustments in its dosage may be required. Haloperidol may lower the convulsive threshold and has been reported to trigger seizures in previously controlled known epileptics. When instituting haloperidol therapy in these patients, adequate anticonvulsant medication should be maintained concomitantly. Elderly or debilitated patients receiving the drug should be carefully observed for any evidence of over sedation which might lead to dehydration and reduced pulmonary ventilation and could result in complications, such as terminal bronchopneumonia. Although haloperidol is a relatively non-sedating neuroleptic, sedation may occur in some patients. Therefore, physicians should be aware of this possibility and caution patients about the danger of participating in activities requiring complete mental alertness, judgment and physical coordination, such as driving and operating dangerous machinery. Haloperidol has been reported to interfere with the anticoagulant properties of phenindione in an isolated case and the possibility should be kept in mind of a similar effect occurring when haloperidol is used with other anticoagulants. Administration to patients with severe cardiac involvement should be guarded, despite the fact that haloperidol is well tolerated by patients with cardiac insufficiency and that it has been used with favorable results to maintain the cardiovascular function of patients with excitive crises. In very rare instances, it has been felt that haloperidol was contributory to the precipitation of attacks in angina-prone patients. Moderate hypotension may occur with parenteral administration or excessive oral doses of haloperidol; however, vertigo and syncope occur only rarely. Haloperidol has lowered the level of cholesterol in the serum and liver of monkeys. An accumulation of desmosterol has been observed in the serum of rats given repeated high doses (10 mg/kg) of haloperidol. In man, mild transient decreases in serum cholesterol were reported in preliminary studies. However, in a study involving a group of schizophrenic patients on extended medication, significant lowering of serum cholesterol was not observed with haloperidol and there was no accumulation of desmosterol or 7-dehydrocholesterol. A significant lowering of cholesterol together with an accumulation of another sterol (possibly 7-dehydrocholesterol) has been reported in patients receiving a chemically related drug (trifluperidol) and skin and eye changes (ichthyosis and cataracts) have occurred clinically with another butyrophenone derivative. Skin and eye changes have not been observed in patients receiving haloperidol. However, it is advisable that all patients receiving haloperidol for a prolonged period of time be carefully observed for any changes in the skin and eyes. If such changes are seen, the drug should be discontinued promptly.

4.5 Interaction with other medicinal products and other forms of interaction

Neurological: Neuromuscular (extrapyramidal) effects such as Parkinson-like symptoms, akathisia, dyskinesia, dystonia, hyper-reflexia, rigidity, opisthotonas, and occasionally, oculogyric crisis are the most frequently reported side effects associated with the administration of haloperidol. Headache, vertigo and cerebral seizures have also been reported. The extra pyramidal reactions are usually dose-related in occurrence and severity and as a rule, tend to subside when the dose is reduced or the drug is temporarily discontinued. However, considerable inter-patient variability exists and although some individuals may tolerate higher than average doses of haloperidol, severe extra pyramidal reactions necessitating discontinuation of the drug, may occur at relatively low doses. Administration of an anti-Parkinson agent is usually but not always effective in preventing or reversing neuromuscular reactions associated with haloperidol. Tardive Dyskinesias: As with all antipsychotic agents, tardive dyskinesia may appear on some patients on long-term therapy or may appear after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes they may be accompanied by involuntary movements of extremities. There is no known effective treatment for tardive dyskinesia; anti-Parkinsonism agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment or increase the dosage of the agent or switch to a different antipsychotic agent, the syndrome may be masked. The physician may be able to reduce the risk of this syndrome by minimizing the unnecessary use of neuroleptic drugs and reducing the dose or discontinuing the drug if possible, when manifestations of this syndrome are recognized particularly in patients over the age of 50. It has been reported that fine vermicular movements of the tongue may be an early sign of the syndrome and if the medication is stopped at that time the syndrome may not develop. Behavioural: Insomnia, depressive reactions and toxic confusional states are the more common effects encountered. Drowsiness, lethargy, stupor and catalepsy, confusion, restlessness, agitation, anxiety, euphoria and exacerbation of psychotic symptoms, including hallucinations have also been reported. Cardiovascular: Tachycardia and hypotension have occurred but severe orthostatic hypotension has not been reported. However, should it occur, supportive measures, including intravenous vasopressors such as norepinephrine may be required. Autonomic: Dry mouth, blurred vision, urinary retention and incontinence have been reported. Allergic and Toxic: The overall incidence of significant hematologic changes in patients on haloperidol has been low.

4.6 Pregnancy and Lactation

Pregnancy

There are no well-controlled studies for the haloperidol use in pregnant women. But there are several reports, however, of cases of limb malformations in the newborn whose mother used haloperidol, but causal relationships were not appropriately established in these cases. Since these experiences do not exclude the possibility of a fetal anomaly due to haloperidol, this drug should be used only if the benefit outweighs the potential risk to the fetus.

4.7 Effects on ability to drive and use machines

None reported

4.8 Undesirable effects

• Acute Dystonia - (Develops within hours to days of initiation. Maybe presented as muscle spasm, stiffness, oculogyric crisis)

• Akathisia - (Develops within days to months of use of haloperidol - characterized by restlessness.)

• Neuroleptic malignant syndrome - (NMS; infrequent but severe condition. May present as High fever, muscle rigidity)

• Parkinsonism - (Develops after days to month use of haloperidol)

• Tardive dyskinesia - (Develops after years. Presents as chore especially orofacial region) • Anticholinergic effects - (Elevated temperature, dry mouth, drowsiness or sedation, constipation, urinary retention).

• Sedation

• Weight gain

• Erectile dysfunction in male

• Oligomenorrhea or amenorrhea in female

4.9 Overdose

Toxicities are the exaggerated symptoms of known pharmacologic effects and known adverse reactions. The most prominent toxicities of haloperidol are 1) severe extrapyramidal symptoms, hypotension, sedation. The patient may appear comatose with severe respiratory depression or shock from hypotension.
The extrapyramidal symptoms are muscular weakness or rigidity, a generalized or localized tremor that may be characterized by the akinetic or agitations types of movements, respectively. Haloperidol overdose is also associated with ECG changes known as torsade de pointes, which may cause arrhythmia or cardiac arrest.

Since there is no specific antidote, supportive treatment is the mainstay of haloperidol toxicity. If a patient develops sign symptoms of toxicities, the clinician should consider gastric lavage or induction of emesis as soon as possible, followed by the administration of activated charcoal. Maintenance of Airway, Breathing, and circulation are the most important factors for survival. A patent airway must be ensured by the use of an oropharyngeal airway or endotracheal tube or by tracheostomy if the patient is in a coma. Respiratory depression can be managed by artificial respiration or by mechanical respirators in severe cases or a comma.

Hypotension and circulatory collapse are manageable by using intravenous fluids, concentrated albumin, and vasopressor agents (phenylephrine or norepinephrine).

Epinephrine should not be used as it can decrease blood pressure. If the patient develops severe extrapyramidal reactions, antiparkinson medication should be considered. ECG and vital signs require monitored at regular intervals. Especially for signs of torsades de Pointes or Q-T prolongation or dysrhythmias, cardiac monitoring should be in place until the ECG becomes normal. If the patient develops arrhythmias, which could be life-threatening, prompt management should commence with

appropriate anti-arrhythmic measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Haloperidol exerts its antipsychotic effect through its strong antagonism of the dopamine receptor (mainly D2), particularly within the mesolimbic and mesocortical systems of the brain.

Pharmacotherapeutic group: Antipsychotic, ATC Code N05AD01

Mechanism of action

Haloperidol, a first-generation typical antipsychotic, exerts its antipsychotic effects by blocking dopamine D2 receptors in the brain. This drug reaches its maximum effectiveness when 72% of dopamine receptors are blocked. Haloperidol's effects are not limited to the D2 receptor, as it also exerts blocking action on noradrenergic, cholinergic, and histaminergic receptors. The blocking of these receptors is associated with various adverse drug reactions.

5.2 Pharmacokinetic properties

Absorption: Haloperidol, a highly lipophilic drug, undergoes extensive metabolism, leading to substantial interindividual variability in its pharmacokinetics. The oral formulation of haloperidol exhibits a bioavailability ranging from 60% to 70%. The time to reach peak plasma concentration is around 2 to 6 hours after oral administration, 20 minutes after intramuscular (IM) administration, and 6 days following depot IM administration.

Distribution: Approximately 89% to 93% of the drug binds to plasma proteins. The concentration of haloperidol in the brain is significantly higher than the serum concentrations.

Metabolism: Haloperidol is metabolized in the liver via sulfoxidation and oxidation pathways, with involvement from CYP3A4, CYP2D6, and minor CYP1A2 enzymes.

Elimination: Approximately 30% of haloperidol is primarily excreted in the urine, and the genetic polymorphism of CYP2D6 can significantly influence the plasma concentrations of the drug.

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Corn starch

Magnesium stearate

Povidone PVP-30

Sodium starch glycollate

Pregel starch

Lactose

Talc powder

Stearic acid

Aerosil 200

Tartrazine yellow colour

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store between 30°C and away from the reach of children.

6.5 Nature and contents of container

Jar pack of 1000 tablets

6.6 Special precautions for disposal

No special requirements

7 APPLICANT/MANUFACTURER

Afrab-Chem Limited,

22, Abimbola Street,

Isolo Ind. Estate,

Isolo, Lagos.

Nigeria**.**