SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINALPRODUCT

Afrab Risperidone 4 caplet

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each caplet contains 4mg of Risperidone.

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

3. PHARMACEUTICALFORM

Caplet.
Lemon green coated caplet with a broken line on one side

4. Clinical particulars

4.1 Therapeutic indications

Risperidone belongs to a group of medicines called „anti-psychotics".

Afrab Risperidone is used to treat the following:

- Schizophrenia, where you may see, hear or feel things that are not there, believe things that are not true or feel unusually suspicious, or confused.
- Mania, where you may feel very excited, elated, agitated, enthusiastic or hyperactive. Mania occurs in an illness called "bipolar disorder".
- Short-term treatment (up to 6 weeks) of long-term aggression in people with Alzheimer"s dementia, who harm themselves or others. Alternative (non-drug) treatments should have been used previously.
- Short-term treatment (up to 6 weeks) of long-term, aggression in intellectually disabled children (at least 5 years of age) and adolescents with conduct disorder. Afrab Risperidone can help alleviate the symptoms of your disease and stop your symptoms from coming back.

4.2 Posology and method ofadministration

<u>For the treatment of schizophrenia</u>
Adults :
• The usual starting dose is 2 mg per day; this may be increased to 4 mg per day on the second day
• Your dose may then be adjusted by your doctor depending on how you respond to the treatment
• Most people feel better with daily doses of 4 to 6 mg
• This total daily dose can be divided into either one or two doses a day. Your doctor will tell you which the best is for you.

Elderly people :
• Your starting dose will normally be 0.5 mg twice a day
• Your dose may then be gradually increased by your doctor to 1 mg to 2 mg twice a day
• Your doctor will tell you which the best is for you.

Children and adolescents :
• Children and adolescents under 18 years old should not be treated with Risperidone for schizophrenia.

For the treatment of mania
Adults :
• Your starting dose will usually be 2 mg once a day
• Your dose may then be gradually adjusted by your doctor depending on how you respond to the treatment
• Most people feel better with doses of 1 to 6 mg once a day.
Elderly people :
• Your starting dose will usually be 0.5 mg twice a day
• Your dose may then be gradually adjusted by your doctor to 1 mg to 2 mg twice a day depending on how much you respond to the treatment.
Children and adolescents :
• Children and adolescents under 18 years old should not be treated with Risperidone for mania.

For the treatment of long-standing aggression in people with Alzheimer"s dementia
Adults (including elderly people):
• Your starting dose will normally be 0.25 mg twice a day

• Your dose may then be gradually adjusted by your doctor depending on how you respond to the
treatment
• Most people feel better with 0.5 mg twice a day. Some patients may need 1 mg twice a day
• Treatment duration in patients with Alzheimer"s dementia should be not more than 6 weeks.

For the treatment of conduct disorder in children and adolescents
The dose will depend on your child"s weight:
For children who weigh less than 50 kg
• The starting dose will normally be 0.25 mg once a day
• The dose may be increased every other day in steps of 0.25 mg per day.
• The usual maintenance dose is 0.25 mg to 0.75 mg once a day.
For children who weigh 50 kg or more
• The starting dose will normally be 0.5 mg once a day
• The dose may be increased every other day in steps of 0.5 mg per day.
• The usual maintenance dose is 0.5 mg to 1.5 mg once a day.
Treatment duration in patients with conduct disorder should be not more than 6 weeks. Children under 5 years old should not be treated with Risperidone for conduct disorder.

People with kidney or liver problems
Regardless of the disease to be treated, all starting doses and following doses of risperidone should be halved. Dose increases should be slower in these patients. Risperidone should be used with caution in this patient group.

How to take Risperidone
Risperidone caplet should be swallowed with drinking of water.

4.3 Contraindications

Hypersensitivity to Risperidone

4.4 Special warnings and precautions for use

Caution should be taken in patients with heart problem, example include an irregular heart rythm or if you are prone to low blood pressure or if you are using medicine for your blood pressure.

4.5Interaction with other medicinal products and other forms of interaction

The following medicine may increase the effect of Risperidone:
Quinidine
Antidepressant such as paroxetine,fluxetine
Beta blockers
Phenothiazine
Cimetidin

4.6 Pregnancy and Lactation

Caution should be taken in pregnancy and breastfeeding.
The following symptoms may occur in newborn, of mother that have used Risperidon in the last trimester : shaking,muscle stiffness weakness, sleepiness,agitation.

4.7 Effects on ability to drive and use machines

Dizziness,tiredness,and vision problems may occur during treatment with Risperidon. Do not drive or use any tools or machines without talking to your doctor first

4.8 Undesirable effects

Blood clots in the veins, especially in the legs (symptoms include swelling, pain, and redness in the leg.

Dementia
Fever, muscle stiffness, sweating or a lowered level of consciousness (a disorder called "Neuroleptic Malignant Syndrome"). Immediate medical treatment may be needed

Involuntary rhythmic movements of the tongue, mouth and face. Withdrawal of risperidone may be needed.

The following side effects may happen:

<u>Very Common (affects more than 1 user in 10):</u>

Parkinsonism. This is a medical term that includes many symptoms. Each individual symptom may occur less frequently than in 1 in 10 people. Parkinsonism includes: increase in saliva secretion or watery mouth, musculoskeletal stiffness, drooling, jerks when bending the limbs, slow, reduced or impaired body movements, no expression on the face, muscle tightness, stiff neck, muscle stiffness, small, shuffling, hurried steps and lack of normal arm movements when walking, persistent blinking in response to tapping of the forehead (an abnormal reflex)

Headache, difficulty falling or staying asleep.

Common (affects 1 to 10 users in 100):

• Drowsiness, fatigue, restlessness, inability to sit still, irritability, anxiety, sleepiness, dizziness,
poor attention, feeling exhausted, sleep disorder

• Vomiting, diarrhoea, constipation, nausea, increased appetite, abdominal pain or , sore throat, dry mouth

• Weight increased, increase in body temperature, decreased appetite

• Difficulty breathing, lung infection (pneumonia), flu, infection of the breathing passages,
blurred vision, nose congestion, nose bleeding, cough

• Urinary tract infection, bed wetting

• Tremor, muscle spasm, involuntary movements of face or arms and legs, joint pain, back pain, swelling of arms and legs, pain in arms and legs
Rash, skin redness

• Fast beating heart, chest pain

• Blood prolactin hormone level increased.

4.9 Overdose

In case of overdoseage,consult your doctor.
Symptoms of overdosage include ;drowsiness or tiredness, or abnormal body movements, difficulty in standing or walking, dizziness due to low blood pressure, or have abnormal heartbeats or fits.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

The mechanism of action of RISPERDAL (risperidone), as with other drugs used to treat schizophrenia, is unknown. However, it has been proposed that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine Type 2 (D2) and serotonin Type 2 (5HT2) receptor antagonism. Antagonism at receptors other than D2 and 5HT2 may explain
some of the other effects of RISPERDAL . RISPERDALis a selective monoaminergic antagonist with high affinity (Ki of 0.12 to 7.3 nM) for the serotonin Type 2 (5HT2), dopamine Type 2 (D2), α1 and α2 adrenergic, and H1 histaminergic receptors. RISPERDALacts as an antagonist at other receptors, but with lower potency. RISPERDALhas low to moderate affinity (Ki of 47 to 253 nM) for the serotonin 5HT1C, 5HT1D, and 5HT1A receptors, weak affinity (Ki of 620 to 800 nM) for the dopamine D1 and haloperidol-sensitive sigma site, and no affinity (when tested at concentrations >10-5 M) for cholinergic muscarinic or β1 and β2 adrenergic receptors.

5.2 Pharmacokinetic properties

Risperidone is well absorbed. The absolute oral bioavailability of risperidone is 70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is 94% (CV=10%) when compared to a solution. Pharmacokinetic studies showed that RISPERDALM-TABOrally Disintegrating Tablets and RISPERDAL Oral Solution are bioequivalent to RISPERDAL Tablets. Plasma concentrations of risperidone, its major metabolite, 9-hydroxyrisperidone, and risperidone plus 9-hydroxyrisperidone are dose proportional over the dosing range of 1 to 16 mg daily (0.5 to 8 mg BID). Following oral administration of solution or tablet, mean peak plasma concentrations of risperidone occurred at about 1 hour. Peak concentrations of 9- hydroxyrisperidone occurred at about 3 hours in extensive metabolizers, and 17 hours in poor metabolizers. Steady-state concentrations of risperidone are reached in 1 day in extensive metabolizers and would be expected to reach steady-state in about 5 days in poor metabolizers. Steady-state concentrations of 9-hydroxyrisperidone are reached in 5-6 days (measured in extensive metabolizers). Food Effect Food does not affect either the rate or extent of absorption of risperidone. Thus, risperidone can be given with or without meals. Distribution Risperidone is rapidly distributed. The volume of distribution is 1-2 L/kg. In plasma, risperidone is bound to albumin and a1-acid glycoprotein. The plasma protein binding of risperidone is 90%, and that of its major metabolite, 9-hydroxyrisperidone, is 77%. Neither risperidone nor 9- hydroxyrisperidone displaces each other from plasma binding sites. High therapeutic
concentrations of sulfamethazine (100 mcg/mL), warfarin (10 mcg/mL), and carbamazepine (10mcg/mL) caused only a slight increase in the free fraction of risperidone at 10 ng/mL and 9- hydroxyrisperidone at 50 ng/mL, changes of unknown clinical significance. Metabolism Risperidone is extensively metabolized in the liver. The main metabolic pathway is through hydroxylation of risperidone to 9-hydroxyrisperidone by the enzyme, CYP 2D6. A minor metabolic pathway is through N-dealkylation. The main metabolite, 9-hydroxyrisperidone, has similar pharmacological activity as risperidone. Consequently, the clinical effect of the drug (e.g., the active moiety) results from the combined concentrations of risperidone plus 9- hydroxyrisperidone.
Excretion Risperidone and its metabolites are eliminated via the urine and, to a much lesser extent, via the feces. As illustrated by a mass balance study of a single 1 mg oral dose of 14C- risperidone administered as solution to three healthy male volunteers, total recovery of radioactivity at 1 week was 84%, including 70% in the urine and 14% in the feces. The apparent half-life of risperidone was 3 hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers and 30 hours (CV=25%) in poor metabolizers. The pharmacokinetics of the active moiety, after single and multiple doses, were similar in extensive and poor metabolizers, with an overall mean elimination half-life of about 20 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Lactose Monohydrate
Sodium Lauryl
Sulphate Maize Starch
FD & C Blue Dye
Magnesium Stearate
Colloidal Silicone Dioxide (Aerosil
200) Microcrystalline Cellulose
Titanium Dioxide
Luster Clear
Quiniline Yellow

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3years.

6.4 Special precautions for storage

Store below 30 ° C.

6.5 Nature and contents of container

Alu PVC blister pack of 2 x 10 caplets

6.6 Special precautions for disposal

No special requirements for disposal

7. APPLICANT/MANUFACTURER

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