PROPOSED PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS: S0

1.NAME OF MEDICINE

ADCO-DOL PAIN RELIEF POWDERS

Strength

Each sachet of powder contains:

Aspirin 500 mg

Paracetamol 325 mg

Caffeine 32.5 mg

Pharmaceutical form

Powder

2.QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each sachet of powder contains:

Aspirin 500 mg

Paracetamol 325 mg

Caffeine 32.5 mg

Sugar free

3.PHARMACEUTICAL FORM

Fine, homogenous, orange powder.

4.CLINICAL PARTICULARS

Therapeutic indications:

ADCO-DOL PAIN RELIEF POWDERS is indicated for the relief of mild to moderate pain and fever.

4.2 Posology and method of administration

Adults and children over 16 years old: One sachet of powder to be taken with water every six hours as needed. For best results take the powder dry on the tongue followed by a glass of water.

Do not exceed four (4) doses per 24 hours.

Not to be taken by children under 16 years.

Use the lowest effective dose for the shortest possible duration of treatment.

DO NOT EXCEED THE RECOMMENDED DOSE.

4.3 Contraindications:

Hypersensitivity (allergy) to the medicine (paracetamol and aspirin).

ADCO-DOL PAIN RELIEF POWDER should not be taken by patients suffering from:

- Renal disease, chronic gastritis, peptic ulcers, dyspepsia, hemophilia or on an oral anticoagulant
- Heart failure
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including ADCO-DOL PAIN RELIEF POWDERS.
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/ foetal renal dysfunction and premature closure of the foetal ductus arteriosus.
- Not to be taken by children under 16 years.

4.4 Special warnings and precautions for use:

Do not use continuously for more than ten days without consulting your doctor.

Consult your doctor if no relief is obtained with the recommended dosage.

Aspirin:

Aspirin has been implicated in Reye's Syndrome, a rare but serious illness in children and teenagers, with chicken pox and influenza. A doctor should be consulted before aspirin is used in such patients. It should be administered with caution to patients with impaired renal function, dyspepsia, anaemia and when the patient is dehydrated.

- Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with ADCO-DOL PAIN RELIEF POWDERS therapy. In view of the ADCO-DOL PAIN RELIEF POWDERS inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Caution is required in patients with significant risk factors for cardiovascular events (e.g., hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including ADCO-DOL PAIN RELIEF POWDERS, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
- The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of ADCO-DOL PAIN RELIEF POWDERS, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving ADCO-DOL PAIN RELIEF POWDERS, treatment with ADCO-DOL PAIN RELIEF POWDERS should be stopped.
- ADCO-DOL PAIN RELIEF POWDERS should be given with caution to patients with a history of gastrointestinal disease (e.g., ulcerative colitis, Crohn's disease, hiatus hernia, gastro-esophageal reflux disease, angiodysplasia) as the condition may be exacerbated.
- Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. ADCO-DOL PAIN RELIEF POWDER should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Paracetamol:

This product contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be doctor, hospital or Poison Centre must be contacted immediately.

Dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol under medical supervision.
Do not use continuously for more than ten days without consulting your doctor.
Consult your doctor if no relief is obtained with the recommended dosage.

Foetal Toxicity: Limit use of NSAIDs, including ADCO-DOL PAIN RELIEF POWDERS, between 20 to 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAID's in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.

If NSAID's treatment is necessary between 20 weeks and 30 weeks gestation, limit ADCO-DOL PAIN RELIEF POWDERS use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if ADCO-DOL PAIN RELIEF POWDERS treatment extends beyond 48 hours. Discontinue ADCO-DOL PAIN RELIEF POWDERS if oligohydramnios occurs and follow up according to clinical practice.

4.5 Interaction with other medicines and other forms of interaction

- Aspirin may enhance the activities of oral anti-diabetic preparations and sulphonamides. Aspirin diminishes the effects of anti-gout preparations such as probenecid and sulphinpyrazone.

- Barbiturates and other sedatives may mask the respiratory symptoms of aspirin overdosage and have been reported to enhance its toxicity.
- NSAIDs: use of two or more NSAIDs concomitantly could result in an increase in side effects
- Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs)
- Anti-coagulants: ADCO-DOL PAIN RELIEF POWDERS may enhance the effects of anti-coagulants such as warfarin
- Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

4.6 Fertility, pregnancy and lactation

Use of NSAIDs, including ADCO-DOL PAIN RELIEF POWDERS, can cause premature closure of the foetal ductus arteriosus and foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of ADCO-DOL PAIN RELIEF POWDERS dose and duration between 20 and 30 weeks of gestation should be limited and avoided at around 30 weeks of gestation and later in pregnancy.

4.7 Effects on ability to drive and use machines

The effects on ability to drive and use machines has not been established.

4.8Undesirable effects

System organ class	**Undesirable effects**
Blood disorders	Blood disorders Anaemia, blood dyscrasias
Cardiac disorders	Oedema, hypertension and cardiac failure

Gastrointestinal disorders	Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis
Hepato-biliary disorders	Liver disease
Immune system disorders	Hypersensitivity reactions which may include skin eruptions, paroxysmal bronchospasm and dyspnoea
Nervous system disorders	Dizziness, headache
Psychiatric disorders	Insomnia
Skin and subcutaneous tissue disorders	Sensitivity reactions resulting in reversible skin rash Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis
Renal and urinary disorders	Kidney disease Renal papillary necrosis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8**.**

May also report to Adcock Ingram Limited using the following email:

Adcock.AEReports@adcock.com

4.9 Overdose

Aspirin:

These include dizziness, tinnitus, sweating, nausea, vomiting, mental confusion, hyperventilation, respiratory alkalosis, metabolic acidosis, ketosis and depression of the central nervous system. In children serious signs of overdosage may develop rapidly.

PARACETAMOL:

Symptoms of overdosage include nausea and vomiting. Liver damage which may be fatal, may only appear after few days. Kidney damage has been described following acute intoxication.

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 -10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop

even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage: Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration. intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. The volume of intravenous fluid should be modified for children. Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses. A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below.

The nomogram should be used only in relation to a single acute ingestion. Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given are above the "high risk treatment line". Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety-six hours.

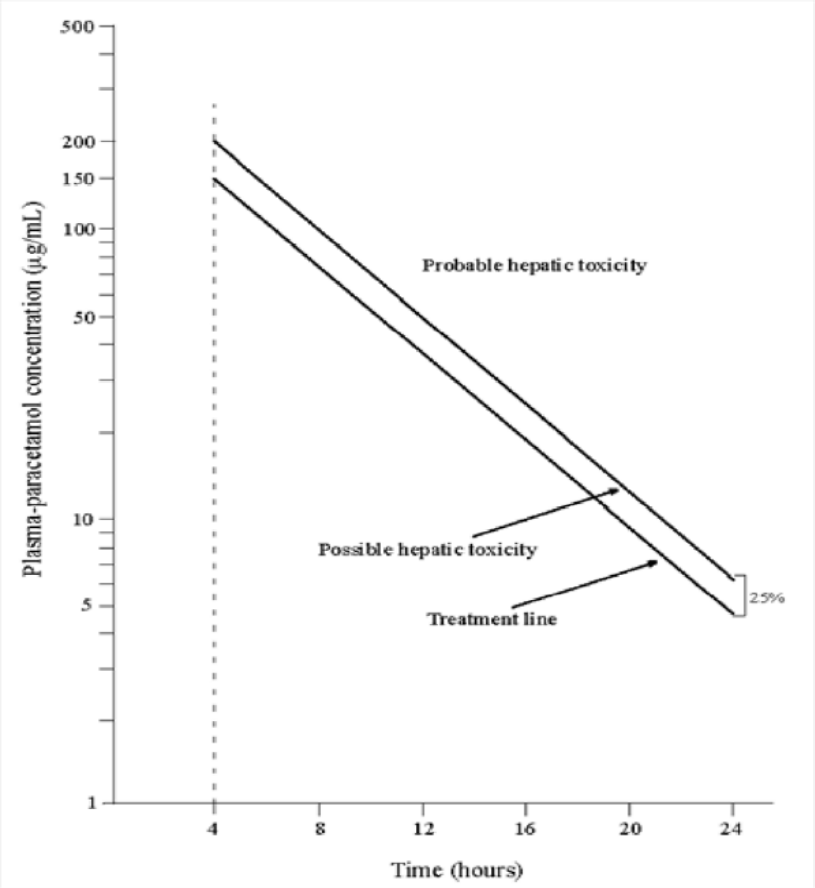

Figure 1. A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.

Caffeine:

Overdosage symptoms include restlessness, excitement, muscle tremor, tinnitus, scintillating scotoma, tachycardia and extrasystoles.

Treatment:

Treatment is supportive and symptomatic. Specialised treatment is essential as soon as possible. The latest information regarding the treatment of overdosage can be obtained from the nearest poison center.

In the event of overdosage consult a doctor or take the patient to the nearest hospital immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

A 2.9 Analgesic combinations

Mechanism of action

ADCO-DOL RELIEF POWDERS combine the analgesic and antipyretic action of aspirin and paracetamol together with the anti-inflammatory action of aspirin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Silicon Dioxide, Hexacol Red 2 G Lake, Sodium Cyclamate, Sodium Lauryl Sulphate, Sunset Yellow FCF Supra, Sunset Yellow FCF Lake.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 ºC in a safe place.

Protect from moisture.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Cartons of 10, 25 and 50 powders.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

R/2.9/238

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

August 1990

10. DATE OF REVISION OF THE TEXT

30 November 2021