

## PROFESSIONAL INFORMATION

### SCHEDULING STATUS

**S0** – Pack sizes of 38 or smaller

**S1** – Pack sizes larger than 38

### 1. NAME OF THE MEDICINE

#### COMPRAL® PAIN POWDERS

**Aspirin 453,6 mg; Caffeine 64,8 mg and Paracetamol 324 mg per sachet**

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of powder contains:

Aspirin 453,6 mg

Caffeine anhydrous 64,8 mg

Paracetamol 324 mg

Sugar free

For full list of excipients, see section 6.1

### 3. PHARMACEUTICAL FORM

Powders

A fine, white, crystalline powder with a slight acidic odour and very bitter taste

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

For the symptomatic relief of mild to moderate pain such as headaches, dysmenorrhoea (painful menstrual period), pain in muscles and joints, dental pain and inflammation, pain associated with colds or flu and fever.

#### 4.2 Posology and method of administration

##### **DO NOT EXCEED THE RECOMMENDED DOSE.**

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

Not recommended for children and adolescents under the age of 18 years.

Adults: One powder to be taken after a meal with water. May be repeated every four hours, if necessary. Do not exceed six powders per day.

## Method of administration

Dose to be taken orally.

### 4.3 Contraindications

- Patients with haemophilia, severe renal impairment, or patients receiving oral anticoagulant therapy
- Intolerance or hypersensitivity to aspirin or other NSAIDs, paracetamol, caffeine or to any of the ingredients of COMPRAL PAIN POWDERS.
- Patients in whom asthma, bronchospasm, angioedema, urticaria, or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory drugs (NSAID's).
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Heart failure
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including COMPRAL PAIN POWDERS.
- Renal Failure
- Hepatic Failure
- A history of gout
- Third trimester of pregnancy (see section 4.6)
- 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.

### 4.4 Special warnings and precautions for use

**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 asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.**

Dosages in excess of those recommended may cause severe liver damage.

**COMPRAL PAIN POWDERS should not be used in children and adolescents under 18 years of age.**

Do not use continuously for more than 10 days without consulting a doctor.

Consult a doctor if no relief is obtained from the recommended dosage.

Excessive and prolonged use of this medicine may be dangerous.

Medical advice should be sought if cough persists, or if it is accompanied by high fever, skin rash or persistent headache.

### **Aspirin**

**Aspirin has been implicated in Reye's Syndrome, a rare but serious illness, in children and teenagers with chickenpox or influenza. A doctor should be consulted before aspirin is used in such patients.**

There is an association between aspirin and Reye's syndrome when given to children during or immediately after a viral illness. Reye's Syndrome is a rare but serious illness, which affects the brain and liver. For this reason, children and teenagers (under 18 years of age) who have or are recovering from chicken pox or flu-like symptoms should not use this product, unless prescribed by a physician. When using this product, if changes in behaviour with nausea and vomiting occur, the patient should consult a doctor because these symptoms could be an early sign of Reye's syndrome.

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 COMPRAL PAIN POWDER therapy. In view of the COMPRAL PAIN POWDERS inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including COMPRAL PAIN 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 COMPRAL PAIN POWDERS, in patients with a history of ulcers, and the elderly.

When gastrointestinal bleeding or ulceration occurs in patients receiving COMPRAL PAIN POWDERS, treatment with COMPRAL PAIN POWDERS should be stopped.

COMPRAL PAIN POWDERS should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal 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. COMPRAL PAIN POWDERS should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Foetal Toxicity: Limit use of NSAIDs, including COMPRAL PAIN POWDERS, between 20 and 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. 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.

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

Regular use of NSAIDs such as COMPRAL PAIN POWDERS during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in utero*, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.

Aspirin should be administered with caution to patients with uncontrolled hypertension, impaired renal or hepatic function, dyspepsia, anaemia and when the patient is dehydrated, or suffering from diabetes mellitus. Prolonged use of high doses may lead to anaemia, blood dyscrasias, gastrointestinal haemorrhage, peptic ulceration and renal papillary necrosis.

Concomitant use of aspirin with other systemic NSAID's including cyclooxygenase-2-selective inhibitors, should be avoided due to the potential for additive undesirable

effects. Serious hypersensitivity reactions or anaphylaxis can occur, bronchospasm may be precipitated in patients suffering from or with previous history of asthma, allergic disease or nasal polyps.

Aspirin decreases platelet adhesiveness and increases bleeding time. Therefore aspirin therapy should be stopped several days before surgical procedures. Haematological and haemorrhagic effects can occur and may be severe. Patients should report any unusual bleeding symptoms to their physician.

Doses of more than 1 g aspirin daily may precipitate acute haemolytic anaemia in patients with G6PDH deficiency.

### **Paracetamol**

COMPRAL PAIN POWDERS contains paracetamol. Do not use with any other paracetamol containing products. Concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.

Paracetamol should be given with care to patients with impaired kidney and liver function and patients with alcohol dependence.

Patients suffering from liver or kidney disease should take COMPRAL PAIN POWDERS under medical supervision.

Underlying liver disease increases the risk of paracetamol related liver damage. The overall benefit-risk should be considered in patients diagnosed with liver or kidney impairment before use.

Cases of hepatic failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol or have sepsis. In patients with glutathione depleted states, the use of paracetamol may increase the risk of metabolic acidosis.

### **Caffeine**

Excess intake of caffeine (e.g. tea, coffee and some canned drinks) should be avoided while taking COMPRAL PAIN POWDERS.

#### **4.5 Interactions with other medicines and other forms of interaction:**

Aspirin, paracetamol and caffeine combination medicines should not be used together with other non-steroidal anti-inflammatory medicines (NSAIDs) including acetylsalicylic acid and cyclo-oxygenase-2-specific inhibitors as these may increase the risk of adverse effects. Aspirin, paracetamol and caffeine combination medicines should be used with caution when taken in combination with the following medicines as interactions have been reported.

##### ***Aspirin***

*Sulphonylureas*: Possible enhanced activity of oral antidiabetic preparations and sulphonamides. Some downward readjustment of the dosage of the antidiabetic may be appropriate if large doses of salicylates are used. Increased blood glucose controls are recommended.

*Uricosurics*: Diminished effect of antigout preparations such as probenecid and sulphinyprazone, due to inhibition of tubular resorption, leading to high plasma levels of aspirin.

*Barbiturates and other sedatives*: may mask the respiratory symptoms of aspirin overdose and have been reported to enhance its toxicity.

*Other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)*: Use of two or more NSAIDs concomitantly could result in an increase in side effects.

*Corticosteroids*: increased risk of gastrointestinal ulceration or bleeding (PUBs).

*Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs)*: increased risk of gastrointestinal bleeding.

*Anticoagulants and Platelet Aggregation Inhibitors*: COMPRAL PAIN POWDERS may enhance the effects of anticoagulants such as coumarins (e.g. warfarin) and heparin, and of platelet aggregation inhibitors such as ticlopidine, clopidogrel and cilostazol as

there is an increased risk of bleeding. Clinical and laboratory monitoring of the bleeding time and prothrombin time should be performed.

*Thrombolytics:* There is an increased risk of bleeding. Particularly treatment with COMPRAL PAIN POWDERS should not be initiated within the first 24 hours after treatment with alteplase in acute stroke patients. Concomitant use is therefore not recommended.

*Loop Diuretics (e.g. furosemide):* Aspirin may reduce their activity due to competition and inhibition of urinary prostaglandins. NSAIDs can cause acute kidney failure, especially in dehydrated patients. If a diuretic is administered simultaneously with aspirin, it is necessary to ensure adequate hydration of the patient to monitor the kidney function and blood pressure, particularly when starting diuretic treatment.

*Phenytoin:* Aspirin increases serum levels of phenytoin; serum phenytoin should be well monitored.

*Valproate:* Aspirin inhibits its metabolism and hence could increase its toxicity; valproate levels should be well monitored.

*Methotrexate ( $\leq 15$  mg/ week):* The toxicity of methotrexate may be enhanced by concomitant use of aspirin. In case of concomitant use with aspirin as contained in COMPRAL PAIN POWDERS, renal function should be monitored.

*Alcohol:* Co-administration with aspirin increases the risk of gastrointestinal haemorrhage.

*Diuretics and antihypertensive agents (e.g. beta blockers, angiotensin converting enzyme (ACE) inhibitors):* Antihypertensive effect may be decreased. Therefore, take caution when co-administering with COMPRAL PAIN POWDERS. Patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors, due to the increased risk of nephrotoxicity.

*Potassium-sparing drugs:* Concomitant treatment may be associated with increased serum potassium levels. Serum potassium levels should be monitored frequently.

*Antacids:* may increase excretion of aspirin by alkalinisation of urine.

## **Paracetamol**

*Metoclopramide:* Absorption of paracetamol may be accelerated

*Cholestyramine:* Cholestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

*Antibacterials:* Chronic use of isoniazid or rifampicin may increase the risk of liver damage when combined with COMPRAL PAIN POWDERS, even at recommended doses

*Flucloxacillin:* Caution is advised when COMPRAL PAIN POWDERS is used concurrently with flucloxacillin due to accumulation of pyroglutamic acid, resulting in pyroglutamic aciduria and high anion gap metabolic acidosis.

*Anticoagulants:* The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding.

*Antiepileptics:* Possible decrease in therapeutic effects of COMPRAL PAIN POWDERS with concomitant use with enzyme-inducing medicines such as carbamazepine, phenobarbital, phenytoin or primidone.

*Lamotrigine:* COMPRAL PAIN POWDERS affects the metabolic disposition of lamotrigine. Lamotrigine's area under the plasma concentration-time curve and half-life are reduced and increase the percentage of lamotrigine recovered in the urine.

*Antivirals:* COMPRAL PAIN POWDERS may delay the metabolism of zidovudine which can result in severe hepatotoxicity.

*Probenecid:* Pre-treatment with probenecid can decrease COMPRAL PAIN POWDERS clearance and increase its plasma half-life.



*NSAIDs:* Prolonged concurrent use of COMPRAL PAIN POWDERS with NSAIDs increases the risk of adverse renal effects.

### **Caffeine**

Caffeine undergoes extensive metabolism by hepatic microsomal cytochrome P450 isoenzyme CYP1A2 and is subject to many interactions with other medicines and substances that enhance or reduce its metabolic clearance.

*Antibacterials:* elimination half-life of caffeine as contained in COMPRAL PAIN POWDERS increases and clearance decreases when co-administered with ciprofloxacin, enoxacin and piperidic acid. Enoxacin had the greatest inhibitory effect on the clearance.

*Antidepressants:* Fluvoxamine has been reported to significantly reduce the clearance and prolong the elimination half-life of caffeine.

*Antiepileptics:* The mean clearance of caffeine was increased and its half-life decreased in epileptic patients taking phenytoin. Treatment with carbamazepine or valproic acid had no effect on the pharmacokinetics of caffeine.

*Methoxsalen:* Single oral doses of 1.2 mg/kg methoxsalen have reduced the clearance of caffeine in patients with psoriasis.

*Sex hormones:* The clearance of caffeine has been reported to be reduced and its elimination half-life increased in women taking oral contraceptives.

*Sympathomimetics:* Giving caffeine with ephedrine has been reported to produce significant cardiovascular, metabolic and hormonal responses, including increased systolic blood pressure and heart rate, and raised fasting glucose and insulin.

*Lithium:* Caffeine can increase the elimination of lithium from the body. Therefore concomitant use is not recommended

## **4.6 Fertility, pregnancy and lactation**

### **Fertility**

No data available

### **Pregnancy**

Not to be taken during the first and third trimesters of pregnancy (See section 4.3 and section 4.4), except under the advice and supervision of a medical doctor.

Use of NSAIDs, including COMPRAL PAIN 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 COMPRAL PAIN 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.

Regular use of NSAIDs such as COMPRAL PAIN POWDERS during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus in utero, and possibly, in persistent pulmonary hypertension of the new-born.

The onset of labour may be delayed and its duration increased, with increased risk of bleeding tendency in both the mother and child. If the expected benefit to the mother is greater than the possible risk to the foetus, the lowest effective dose and the shortest duration of treatment should be considered.

Caffeine is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

### **Lactation**

Not recommended for use during breastfeeding.

Aspirin is secreted into breastmilk in low concentrations. There is insufficient information on the effects of aspirin at low concentration in infants. Treatment should be avoided during lactation because of the possible risk of Reye's syndrome and the potential impairment of platelet function in the infant. Paracetamol is excreted in breastmilk but not in a significant amount at recommended dosages. Caffeine in breastmilk may potentially have a stimulating effect on breast fed infants but significant toxicity has not been observed.

#### 4.7 Effects on ability to drive and use machines

**COMPRAL PAIN POWDERS** has no or negligible influence on the ability to drive or the use of machinery.

#### 4.8 Undesirable effects

##### a) Summary of the safety profile

Adverse events are more likely to occur with increasing dose and duration of use.

##### b) Tabulated list of adverse reactions

Adverse reactions are tabulated below by System Organ Class (SOC) and frequency. The following convention has been utilized for the classification of undesirable effects: Very common ( $\geq 1/10$ ), common ( $\geq 1/100$ ,  $< 1/10$ ), uncommon ( $\geq 1/1000$ ,  $< 1/100$ ), rare ( $\geq 1/10\ 000$ ,  $< 1/1000$ ), very rare ( $< 1/10\ 000$ ), not known (cannot be estimated from available data).

#### Aspirin

Body System	Undesirable Effect	Frequency
Blood and lymphatic system disorders	Prolonged bleeding time, thrombocytopenia, ecchymosis, anaemia and blood dyscrasias.	Frequency Unknown
Immune system disorders	Hypersensitivity reactions (e.g. anaphylaxis, angioedema, paroxysmal bronchospasm, dyspnoea, urticaria, skin reactions and rhinitis).	Frequency Unknown
Metabolism and nutrition disorders	Sodium and Fluid retention	Frequency Unknown
Ear and labyrinth disorders	Temporary hearing loss, tinnitus	Frequency Unknown

Cardiac Disorders	Oedema, hypertension and cardiac failure.	Frequency Unknown
Gastrointestinal Disorders	The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, irritation of the gastric mucosa, 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.	Frequency Unknown
Hepatobiliary	Reye's Syndrome (see section 4.4), Elevation in transaminase levels.	Frequency Unknown
Skin and subcutaneous tissue disorders	Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.	Frequency Unknown
Renal and urinary disorders:	Renal dysfunction, increased blood uric acid levels, Prolonged use of high doses may lead to renal papillary necrosis.	Frequency Unknown
Nervous system disorders	Dizziness	Frequency Unknown

## Paracetamol

Body System	Undesirable Effect	Frequency
Blood and lymphatic system disorders	Thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis	Very rare
Immune system disorders	Anaphylaxis, cutaneous hypersensitivity reactions including among others, skin rashes (erythematous or urticarial, may be more serious and may be accompanied by fever and mucosal lesions) angioedema, Steven-Johnson syndrome and Toxic Epidermal necrolysis	Very rare
Metabolism and nutrition disorders	Accumulation of pyroglutamic acid, resulting in pyroglutamic aciduria and high anion gap metabolic acidosis	Less frequent
Ear and labyrinth disorders	Hearing loss	Less frequent
Renal and urinary disorders:	Nephropathy	Frequency unknown
Cardiac disorders	Hypertension	Frequency unknown
Other	Pancreatitis	Frequency unknown

## Caffeine

Body System	Undesirable Effect	Frequency
Psychiatric Disorders	Insomnia, restlessness, anxiety and irritability, nervousness	Frequency unknown
Cardiac disorders	Palpitations	Frequency unknown
Gastrointestinal Disorders	Nausea, increased gastric secretions, may cause gastric ulceration. Gastrointestinal disturbances	Frequency unknown
Nervous system disorders	Dizziness, headache	Frequency unknown

### 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>

### 4.9 Overdose

**Prompt treatment is essential.** In the event of an overdose, 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.

Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present. If overdose is confirmed or suspected, seek immediate advice from your Poison Centre (contact details: Phone: 0861-555-777; Website: <http://www.paediatrics.uct.ac.za/poisons-information-centre>; Email: [poisonsinformation@uct.ac.za](mailto:poisonsinformation@uct.ac.za)) and refer patient to nearest Emergency Medical Centre for management and expert treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage.

**Paracetamol:**

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. Nausea, vomiting, anorexia and abdominal pain may persist for a week or more. Cerebral oedema and nonspecific myocardial depression have also occurred.

In the event of overdosage consult a doctor or take the patient to the nearest hospital immediately. Specialised treatment is essential as soon as possible

**Treatment for paracetamol overdosage:**

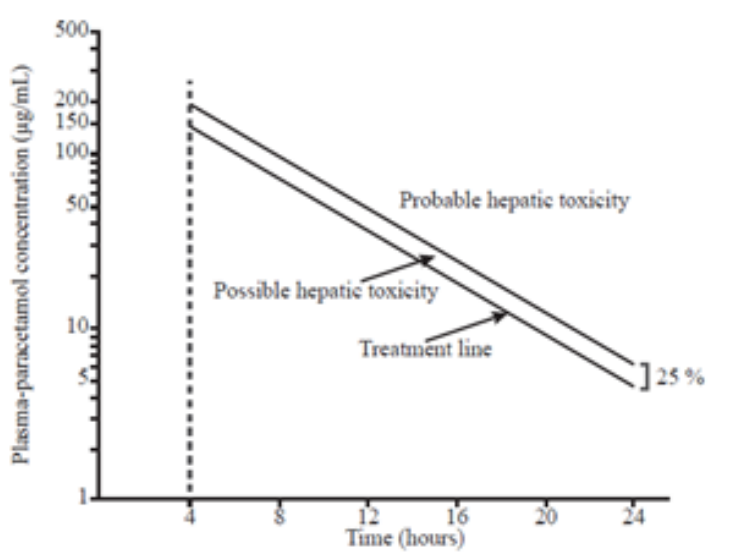
Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 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 stuporose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration.

**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 **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.



Source: Martindale: The Complete Drug Reference – 37<sup>th</sup> Edition.



Those whose plasma paracetamol levels are on or 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 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.

### **Aspirin**

Symptoms include dizziness, tinnitus, vertigo, deafness, sweating, nausea, vomiting, mental confusion, increased respiratory rate hyperventilation, warm extremities with bounding pulses, respiratory alkalosis, metabolic acidosis, ketosis and depression of the central nervous system. In children serious signs of overdose may develop rapidly.

Uncommon features include haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopenia, increased PT/INR, intravascular coagulation, renal failure and noncardiac, pulmonary oedema. Central nervous system features including confusion, disorientation, coma and convulsions are less common in adults than in children.

### **Caffeine**

Large doses may cause epigastric pain, vomiting, diuresis, cardiac arrhythmia, restlessness, excitement, agitation, anxiety, convulsions, muscle tremor, tinnitus, scintillating scotoma, tachycardia and extrasystoles.

In the event of overdose consult a doctor or take the patient to the nearest hospital immediately. Specialised treatment is essential as soon as possible.

The latest information regarding the treatment of overdose can be obtained from the nearest Poison Centre.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Category and class: A 2.8 Analgesic combinations

COMPRAL PAIN POWDERS has analgesic, antipyretic and anti-inflammatory properties.

## **5.2 Pharmacokinetic properties**

No data available

## **5.3 Preclinical safety data**

No data available

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Colloidal Anhydrous Silica

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf life**

24 months

## **6.4 Special precautions for storage**

Store in airtight containers, protected from light at or below 25 °C.

## **6.5 Nature and contents of container**

846 mg of powder packed in polypaper sachets in packs of 2, 10, 24, 38, 48 and in single doses.

Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal**

No special requirements

# **7. HOLDER OF CERTIFICATE OF REGISTRATION**

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

**8. REGISTRATION NUMBERS**

36/2.8/0009

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

20 September 2002

**10. DATE OF REVISION OF THE TEXT**

15 October 2021

Namibia: NS0 05/2.8/0146  
NS1 05/2.8/0146

Botswana: BOT0801428 S4