Legals & References

References: 1. Compral pain powder dissolution evaluation. Document no. 23/AD/063 (on file) 2. Diener HC, Pfaffenrath V, Pageler L, et al. The fixed combination of acetylsalicylic acid, paracetamol and caffeine is more effective than single substances and dual combination for the treatment of headache: a multicentre, randomized, double[1]blind, single-dose, placebo-controlled parallel group study. Cephalalgia 2005;25:776–787. doi:10.1111/j.1468- 2982.2005.00948. 3. Weiser T, Weigmann H. Effect of Caffeine on the Bioavailability and Pharmacokinetics of an Acetylsalicylic Acid-Paracetamol Combination: Results of a Phase I Study. Adv Ther 2019;36:597-607. https://doi.org/10.1007/s12325-019-0891-5. 4. Circana data April MAT 2024

Product Legal details:
S0 Compral® Pain Tablets. Each tablet contains paracetamol 100 mg; aspirin 400 mg; caffeine anhydrous 30 mg. Reg. No. B/2.8/1147. (Approved PI, November 2021).
Pack size < 38 sachets) S0 Pack sizes ≥ 38 sachets) S1 Compral® Pain Powders. Each powder contains aspirin 453,6 mg; caffeine anhydrous 64,8 mg; paracetamol 324,0 mg. Reg. No. 36/2.8/0009. (Approved PI, October 2021)
Company Legal details:
For full prescribing information refer to the Professional Information approved by SAHPRA. Adcock Ingram Limited. Co. Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021, South Africa. Customer Care: 0860 ADCOCK/232625. www.adcock.com

AIPPL

PC.NO.:8559

For the professional information for COMPRAL PAIN POWDERS scan the QR Code.
Vir die professionele inligting vir COMPRAL PAIN POWDERS skandeer die QR-kode.

The same information is available at www.adcock.com/Products/ProductInfo
Dieselfde inligting is beskikbaar by www.adcock.com/Products/ProductInfo

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS [S0] - Pack sizes of 38 or smaller [S1] - Pack sizes larger than 38

PRODUCT NAME, STRENGTH AND PHARMACEUTICAL FORM
COMPRAL® PAIN POWDERS
Aspirin 453,6 mg; Caffeine 64,8 mg and Paracetamol 324 mg per sachet
Sugar free

[illegible]
COMPRAL PAIN POWDERS is available without a doctor's prescription, for you to treat a mild illness. Nevertheless, you still need to use COMPRAL PAIN POWDERS carefully to get the best results from it.
- **[illegible]**
- Do not share COMPRAL PAIN POWDERS with any other person.
- Ask your health care provider or pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve after 10 days.

[illegible]
1. What COMPRAL PAIN POWDERS is and what it is used for
2. What you need to know before you take COMPRAL PAIN POWDERS
3. How to take COMPRAL PAIN POWDERS
4. Possible side effects
5. How to store COMPRAL PAIN POWDERS
6. Contents of the pack and other information

1. What COMPRAL PAIN POWDERS is and what it is used for
COMPRAL PAIN POWDERS belongs to a group of medicines called analgesic combinations.
COMPRAL PAIN POWDERS is used for the symptomatic relief of mild to moderate pain such as headaches, **[illegible]**

2. What you need to know before you take COMPRAL PAIN POWDERS
Do not take COMPRAL PAIN POWDERS:
- If you have or ever had a problem of your blood not clotting properly, have severe liver function problems or if you are taking medicines to reduce blood clotting.
- If you are hypersensitive (allergic) to aspirin or other NSAIDs, paracetamol, caffeine or to any of the ingredients of COMPRAL PAIN POWDERS. (listed in section 6)
- If you have a history of asthma, bronchospasm (sudden constrictions of the muscles of the passage ways by which air passes through the nose to the air sacs of the lungs), angioedema (painless swelling of the tissue layer under the **[illegible]**
- If you have or ever had a stomach ulcer, damage or bleeding of the stomach related to previous use of aspirin and other NSAID's (class of medicines which aspirin belongs to) including COMPRAL PAIN POWDERS.
- If you have kidney failure, liver failure or heart failure.
- If you have or ever had gout.
- If you are pregnant, do not use NSAIDs at 30 weeks or later in your pregnancy because these medicines may cause problems in your unborn baby.

Warning and precautions

COMPRAL PAIN POWDERS contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose even if the person may not be showing or experiencing any symptoms, the nearest doctor, hospital or Poison Centre must be contacted immediately.

Take special care with COMPRAL PAIN POWDERS:
- To not exceed the recommended daily dose as it may cause serious harm to your liver.
- To not give it to children and adolescents under the age of 18 years of age.
- If your symptoms do not improve within 10 days of continuous use, please consult your doctor.
- Consult your doctor if no relief is obtained with the recommended dosage.
- Excessive and prolonged use of this medicine may be dangerous.
- Seek medical advice if cough persists, or if it is accompanied by high fever, skin rash or persistent headache.

Aspirin may cause Reye's syndrome. Reye's syndrome is a rare but serious illness, in children and teenagers [illegible] give COMPRAL PAIN POWDERS to children under 18 years of age unless prescribed by a doctor. If the child changes in behaviour with nausea and vomiting, consult your doctor because these symptoms could be an early sign of Reye's syndrome.

Check with your doctor before taking COMPRAL PAIN POWDERS if you:
- Have a history of high blood pressure or heart disease, as you may experience water retention and swelling. Heart failure may suddenly occur.
- For elderly, as you may experience an increased frequency of side effects especially having an ulcer, stomach and intestinal bleeding, which may cause death. Your risk of experiencing these side effects is higher with increasing doses of COMPRAL PAIN POWDERS.
- Have a history of ulcers, because your risk of having an ulcer, stomach and intestinal bleeding is higher, with increasing doses of COMPRAL PAIN POWDERS.
- Have a history of:
  [illegible] which affects the lower gut sphincter), angiodysplasia (vascular malformation of the gut).

These conditions may worsen.

Check with your doctor before taking COMPRAL PAIN POWDERS if you have:
Uncontrolled hypertension, liver or kidney problems, heart problems, dyspepsia (a persistent or recurrent pain or **[illegible]** glucose in the blood).

You may need to avoid using COMPRAL PAIN POWDERS altogether or limit the amount you take as prolonged use of high doses may lead to anaemia, blood disorders, stomach and intestinal bleeding, peptic ulceration and renal papillary necrosis (death of kidney papillae, that is, areas where the openings of the collecting ducts enter the kidney and where **[illegible]**

If you experience serious skin reactions, some of which can cause death, such as:
- Exfoliative dermatitis (widespread reddening and scaling of the skin)
- **[illegible]**
- Toxic epidermal necrolysis (characterised by widespread reddening of the skin, death of body tissue due to too little **[illegible]** of lining that covers the surface of organs inside the body, beneath the skin), or any other sign of hypersensitivity (allergic reaction).

- Tell your doctor or health care provider if you are pregnant or plan to become pregnant. Taking NSAIDs at around 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you **[illegible]** in your womb around your baby. You should not take NSAIDs around 30 weeks of pregnancy or later.
- Do not use NSAIDs such as COMPRAL PAIN POWDERS regularly during the third trimester of pregnancy. This may result in premature closure of the foetal ductus arteriosus in utero (closure before desirable time, of the unborn baby's blood vessel which is part of the vessels connecting the lungs and heart), and possibly, in persistent pulmonary hypertension (high blood pressure in blood vessels of the lungs) of the new-born. The onset of labour may be delayed and its duration increased.
- **[illegible]** class to which aspirin belongs) including cyclooxygenase-2 (COX-2) selective inhibitors (NSAIDs that target COX-2, an **[illegible]** reactions can occur and bronchospasm (sudden constrictions of the muscles of the passage ways by which air passes through the nose to the air sacs of the lungs) may suddenly occur in patients suffering from or with previous **[illegible]**
- Aspirin decreases platelet aggregation and increases bleeding time. Blood related disorders can occur and may be severe. You should report any unusual bleeding symptoms to your doctor.
- High doses of Aspirin, more than 1g daily, may worsen acute haemolytic anaemia (increased red blood cell **[illegible]** enzyme G6PD, which protects red blood cells).
- Contains paracetamol. Do not use this medicine if you are taking any other prescription or non-prescription medicines containing paracetamol. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.
- If you suffer from liver or kidney disease, you should take COMPRAL PAIN POWDERS under medical supervision.
- **[illegible]** considered in patients diagnosed with liver or kidney impairment before use.

Cases of liver failure have been reported in patients with depleted glutathione (a protein) levels, such as those: **[illegible]** underweight, are chronic heavy users of alcohol, have sepsis (severe infection).

In patients with glutathione (a protein) depleted states, the use of COMPRAL PAIN POWDERS may increase the risk of metabolic acidosis. Signs of metabolic acidosis include:
[illegible]

Excess intake of caffeine (e.g. tea, coffee and some canned drinks) should be avoided while taking COMPRAL PAIN POWDERS.
Contact a doctor immediately if you get a combination of these symptoms.

Other medicines and COMPRAL PAIN POWDERS
Always tell your health care provider if you are taking any other medicine (This includes complementary or traditional medicines).
The following medicines may cause an interaction when used in combination with COMPRAL PAIN POWDERS:
- *Other NSAIDS* **[illegible]** together with COMPRAL PAIN POWDERS: Increased risk of side effects.
- *Sulphonamides* (group of antibiotics): Possible enhanced activity of sulphonamides.
- *Sulphonylureas* (medicines used to lower blood sugar levels), e.g. glibenclamide. Aspirin may enhance the effects of anti-diabetic medicines.
- *Uricosurics* (medicine used to treat gout such as probenecid and sulphinpyrazone): Aspirin can reduce the effect of uricosurics while probenecid can increase the amount of aspirin circulating in the body.
- *Barbiturates and other sedatives*: may mask the respiratory symptoms (associated with the body's breathing system) of aspirin overdosage and have been reported to enhance its toxicity.
- *Antiepileptics* (for seizures) such as carbamazepine, phenobarbital, phenytoin or primidone: Possible decrease in desirable effects of paracetamol.
- *Lamotrigine* (mainly used to treat seizures) Paracetamol affects the metabolic disposition (fate of the medicine after it is taken into the body) of lamotrigine. The percentage of lamotrigine recovered in the urine increases and is reduced in the blood thus making it less effective.
- *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* (medicines used to thin blood e.g. warfarin): aspirin 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 **[illegible]** therefore not recommended.
- *Anticoagulants* (medicines used to thin blood e.g. warfarin): Increased risk of bleeding in patients taking regular doses of paracetamol. Increased monitoring of anticoagulant therapy is recommended.
- *Loop Diuretics (medicines that result in high water loss e.g. furosemide)*: Aspirin may reduce their activity. NSAIDs can cause acute kidney failure, especially in dehydrated patients. If your take a diuretic with aspirin, it is necessary to ensure you take enough water and to have your kidney function and blood pressure monitored by the doctor, particularly when starting diuretic treatment.
- *Phenytoin*: Aspirin increases serum levels of phenytoin (amount of phenytoin present in your blood at the time of testing); serum phenytoin should be well monitored by your doctor.
- *Valproate*: Aspirin interferes with the breakdown of valproate and hence could increase valproate's toxicity; valproate levels should be well monitored by your doctor.
- *Methotrexate (≤15 mg/ week)*: The toxicity of methotrexate may be enhanced by use together with aspirin. In case of use together with aspirin, kidney function should be monitored.
- *Alcohol*: use together with aspirin increases the risk of stomach and intestinal bleeding.
- *Diuretics and antihypertensive agents* (medicines used to reduce water levels in your body and blood pressure e.g. *beta blockers, angiotensin converting enzyme (ACE) inhibitors*): Antihypertensive effect may be decreased. Therefore, take caution when using them together with COMPRAL PAIN POWDERS. Patients, especially the elderly, should have their blood pressure periodically monitored. You should take adequate water and check with your doctor for consideration of monitoring kidney function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors, due to the increased risk of nephrotoxicity.
- *Potassium-sparing medicines*: treatment together with aspirin may be associated with increased serum potassium levels (amount of potassium in the blood at the time of testing). Serum potassium levels should be monitored frequently.
- *Antacids*: may increase excretion of aspirin by alkalinisation of urine.
- *Metoclopramide* (medicine used for nausea and vomiting): Increased absorption of paracetamol.
- *Cholestyramine* (medicine used to reduce high cholesterol and to treat itching caused by partial blockage of the bile): Absorption of paracetamol is reduced if given within one hour of cholestyramine.
- *Antibacterials* such as:
- (I) *Isoniazid or Rifampicin* (medicine for treatment of an infectious disease mainly of the lungs called tuberculosis): chronic use may increase the risk of liver damage when combined with paracetamol at recommended doses.
- (II) *Flucloxacillin* (medicine used to treat skin, wound, chest and bone infections) caution is advised when taken together with paracetamol as this may result in:
  - pyroglutamic aciduria (a condition that prevents production of glutathione, a chemical involved in important processes in the body e.g. processing medication)
  - high anion gap metabolic acidosis (condition that occurs when there is too much acid in the body, characterised by a high difference between the negatively charged and positively charged electrolytes in the blood)
- *Antivirals* such as *Zidovudine* (used to treat infection caused by HIV): Paracetamol may delay the metabolism of zidovudine and cause severe toxic damage to the liver.
- *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 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 **[illegible]** inhibitory effect on the clearance.
- *Antidepressants*: **[illegible]** 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*: **[illegible]** 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

COMPRAL PAIN POWDERS with food, drink and alcohol
Avoid excessive intake of caffeine (e.g. coffee, tea and some canned drinks) while taking COMPRAL PAIN POWDERS.
If you take aspirin with alcohol, it could increase the risk of stomach and intestinal bleeding.

Pregnancy, breastfeeding and fertility
[illegible] has not been established.
If you are pregnant, or breast-feeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking the medicine.
[illegible] doctor.
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 **[illegible]** 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.
Not recommended for use during breastfeeding. Aspirin is secreted into breastmilk in low concentrations. There is **[illegible]** lactation because of the possible risk of Reye's syndrome and the potential impairment of platelet function in the infant. **[illegible]**

Driving and using machines
[illegible]
It is not always possible to predict to what extent COMPRAL PAIN POWDERS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which COMPRAL PAIN POWDERS affects them.

3. How to take COMPRAL PAIN POWDERS
[illegible] told you. Check with your doctor or pharmacist or nurse if you are not sure. DO NOT EXCEED THE RECOMMENDED DOSE. Not for use in children and adolescents under 18 years of age. Use the lowest effective dose for the shortest possible duration of treatment. 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.

If you take more COMPRAL PAIN POWDERS than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Paracetamol
You will require specialised treatment as soon as possible. A delay in starting treatment may mean that antidote **[illegible]** the time for effective treatment has passed.
You may be prone to paracetamol poisoning if you take repeated high doses (greater than 5 - 10 g/day) of COMPRAL PAIN POWDERS for several days, if you suffer from chronic alcoholism, chronic liver disease, AIDS, malnutrition, and if you use medicines such as barbiturates (for anxiety, insomnia and seizures), isoniazid (for tuberculosis), rifampicin (for tuberculosis), phenytoin (for seizures) and carbamazepine (for seizures).
[illegible]
• Pale skin • Nausea • Vomiting • Loss of appetite • Abdominal pain
[illegible]
Other symptoms are:
• Liver damage or injury 12 to 48 hours after taking COMPRAL PAIN POWDERS but sometimes delayed. • Abnormalities of glucose breakdown. • Excess quantity of acid in the blood. • Liver damage which may progress to disease of the **[illegible]**

N-acetylcysteine should be given to all cases of suspected overdose as soon as possible, preferably within 8 hours of **[illegible]** of paracetamol was taken.
IV (via the vein): An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection, given intravenously (IV) over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml of dextrose injection over the next 4 hours and then 100 mg/kg in 1 000 ml over the next 16 hours. **[illegible]**
Orally (by mouth) not the treatment of choice: 140 mg/kg dissolved in water may be taken initially, followed by 70 mg/kg solution every four (4) hours for seventeen (17) doses.

Aspirin: Symptoms of aspirin overdosage include:
• Dizziness • Tinnitus (ringing in the ears) or deafness • Vertigo (loss of balance) • Deafness • Sweating • Nausea or vomiting • Mental confusion • Increased respiratory rate (number of breaths per minute) • Hyperventilation (fast breathing) • Warm hands and feet with rapid pulses • Increased acid in the blood • Increase in ketones in the blood • Reduced functioning of the central nervous system.

In children serious signs of overdosage may develop rapidly.
Uncommon features include vomiting of blood, high body temperature, low blood sugar, low potassium blood level, low **[illegible]** in the lungs. Central nervous system features including confusion, disorientation, coma and involuntary contraction of muscles are less common in adults than in children.
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.

Caffeine: Symptoms of caffeine overdosage include:
• Epigastric pain (pain in the upper region of the abdomen) • Vomiting • Diuresis (increased urination) • Cardiac arrhythmia • Restlessness • Excitement • Agitation • Anxiety • Convulsions (seizures) • Muscle tremor • Tinnitus (ringing in the ears) • Visual spot disturbances • Increased rate or rhythm of heartbeat • Abnormal heartbeats.
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.

If you forget to take a dose of COMPRAL PAIN POWDERS
Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects
COMPRAL PAIN POWDERS can have side effects.
[illegible] worsen or if you experience untoward effects while taking COMPRAL PAIN POWDERS, please consult your health care provider for advice.
If any of the following happen, stop taking COMPRAL PAIN POWDERS and tell your doctor immediately or go to the casualty department at your nearest hospital:
• **[illegible]** of the lips, tongue and face. The rash may be red or itchy with swelling but sometimes may be more serious and accompanied by fever and ulcers or abscesses. • You experienced any bleeding from your stomach (symptoms can include blood in your stools or vomit) • You experienced an increase in the number of nosebleeds or bruising • You experienced ringing in your ears or temporary hearing loss • You experienced any swelling or water retention. • When used in children, changes in behaviour, nausea and vomiting occur (it could be early signs of Reye's syndrome).
These are very serious side effects. If you have them, you may have had a serious reaction to COMPRAL PAIN POWDERS. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:
Very rare:
Paracetamol: Blood related reactions including low blood platelet count, lack of white blood cells, and a type of anaemia in which the red blood cells, white blood cells and platelets are all reduced in number.

Less frequent:
Paracetamol: • Pyroglutamic aciduria (an inherited disorder of amino acid metabolism) • Hearing loss • Skin rashes **[illegible]** and face. The rash may be red or itchy with swelling but sometimes may be more serious and accompanied by fever and ulcers or abscesses.

Frequency unknown:
Paracetamol: **[illegible]**

Aspirin
• Cardiovascular: Swelling, high blood pressure, heart failure • Gastrointestinal: Ulcers in stomach or duodenum, **[illegible]** indigestion, abdominal pain, faeces containing digested blood, vomiting blood, mouth ulcers and cold sores, worsening **[illegible]** disorder) and severe skin reaction. • Kidney and Urinary Disorders: Kidney problems, increased uric acid in urine. • Dizziness may occur in some cases. • Hepatobiliary: Elevation in transaminase levels. • Blood and lymphatic system disorders • Immune system disorders • Temporary hearing loss • Sodium and Fluid retention

Caffeine
- Gastrointestinal disorders: Nausea, increased stomach secretions and stomach ulcers.
- Cardiac disorders: Palpitations
- **[illegible]**
- Nervous system disorders: Dizziness and headache

[illegible]

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist, or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form" found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of COMPRAL PAIN POWDERS.

5. How to Store COMPRAL PAIN POWDERS
Store all medicines out of reach of children. Store in airtight containers, protected from light at or below 25 °C. Do not store in a bathroom. Do not use after the expiry date stated on the polypaper or carton. Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What COMPRAL PAIN POWDERS contains
The active substances are: Aspirin 453,6 mg, Caffeine anhydrous 64,8 mg, Paracetamol 324 mg
The other ingredient: Colloidal Anhydrous Silica

What COMPRAL PAIN POWDERS looks like and contents of the pack
[illegible]
846 mg of powder is packed in polypaper sachets in packs of 2, 10, 24, 38, 48 and in single doses.
Not all pack sizes may be marketed.

[illegible]
Adcock Ingram Limited
1 New Road, Erand Gardens, Midrand, 1685
Customer Care: 0860 ADCOCK / 232625

[illegible]
15 October 2021

Registration Number
32/2.8/0009

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

Botswana: BOT0801428 S4

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Ticket#2023110310322068 Compral digital December 2023
Ticket#2023110310322069 Compral digital January 2024
Ticket#2023112410326344 Compral pain relief landing page

SCHEDULING STATUS: S2

PROPRIETARY NAME AND DOSAGE FORM: COMPRAL® PAIN TABLETS

COMPOSITION:

Each tablet contains:

Paracetamol	100 mg
Aspirin	400 mg
Caffeine anhydrous	30 mg

List of excipients: Acacia, starch corn, purified talc, hydrogenated cottonseed oil, sodium lauryl sulphate, colloidal silicon dioxide, microcrystalline cellulose, purified water

Sugar free

PHARMACOLOGICAL CLASSIFICATION:

A 2.8 Analgesic combinations

PHARMACOLOGICAL ACTION:

COMPRAL PAIN TABLETS have analgesic, anti-inflammatory and antipyretic actions. They inhibit the biosynthesis of prostaglandins.

INDICATIONS:

COMPRAL PAIN TABLETS are effective for the relief of pain of mild to moderate intensity and is also indicated in a wide variety of febrile conditions.

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 TABLETS.**

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 TABLETS.**

Not for use in children and adolescents under 18 years of age.

WARNINGS AND SPECIAL PRECAUTIONS:

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.

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.

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

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 TABLETS** therapy. In view of the **COMPRAL PAIN TABLETS** 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 TABLETS**, 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 TABLETS**, in patients with a history of ulcers, and the elderly.

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

COMPRAL PAIN TABLETS 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 TABLETS** should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Regular use of NSAIDs such as **COMPRAL PAIN TABLETS** 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.

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

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.

Store in a safe place out of reach of children.

INTERACTIONS

Aspirin

Aspirin may enhance the activity of oral antidiabetic preparations and sulphonamides. Aspirin diminishes the effects of antigout 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: **COMPRAL PAIN TABLETS** may enhance the effects of anti - coagulants such as warfarin.

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

PREGNANCY AND LACTATION

Safety and efficacy in pregnancy and lactation have not been established.

Pregnancy

Not to be taken during the first and third trimesters of pregnancy except under the advice and supervision of a medical doctor.

DOSAGE AND DIRECTIONS FOR USE:

DO NOT EXCEED THE RECOMMENDED DOSE

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

Adults: 1 to 2 tablets, 4 hourly.

Not more than 4 doses in 24 hours.

Not for use in children and adolescents under 18 years of age.

SIDE EFFECTS

Paracetamol:

Skin rashes and other allergic reactions may occur. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by fever and mucosal lesions. The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leucopenia.

Aspirin:

Dizziness or irritation of the gastric mucosa and resultant dyspepsia, haematemesis, and melaena may occur in some cases. Some persons, especially asthmatics exhibit notable sensitivity to aspirin which may include skin eruptions, paroxysmal bronchospasm and dyspnoea.

Prolonged use of high doses may lead to anaemia, blood dyscrasias, gastrointestinal haemorrhage, peptic ulceration and renal papillary necrosis.

Cardiac disorders:

Oedema, hypertension and cardiac failure.

Gastrointestinal system disorders:

The most commonly observed adverse events are gastrointestinal in nature. 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.

Skin and subcutaneous tissue disorders:

Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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.

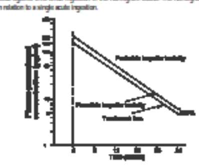
Treatment for paracetamol overdosage:

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 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 - 37th Edition.

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 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, 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.

IDENTIFICATION:

White, scored, bevel-edged tablets with the word "COMPRAL" imprinted on one side.

PRESENTATION:

Polypaper strips of 2 tablets packed in a display carton or a display board of 48 x 2's .

ALU/PVC/PVDC blister packs containing 12, 24, 36 or 72 tablets .

ALU/ALU blister packs of 2 tablets, packed into a display carton of 50 x 2's.

ALU/ALU blister packs of 6 tablets per strip packed into a cardboard cartons of 12, 24, 48 and 96 tablets.

PP/HDPE tracer of 50 and 100 tablets.

Not all packs and pack sizes are necessarily marketed .

STORAGE INSTRUCTIONS:

Store at or below 25 °C in a well-closed container. Exposure to air should be kept to a minimum.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

B/2.8/1147

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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