PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

MYPAID

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:	
Ibuprofen	200 mg
Paracetamol	250 mg

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules.

Hard empty gelatin capsules of size 'O' having opaque white body and opaque dark green cap, printed with 'R25' in black colour. Containing white granular powder

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

MYPAID is indicated for the relief of headache from musculoskeletal origin, fever, muscular, menstrual and dental pain.

4.2 Posology and method of administration

Adults and children over 12 years: Two capsules every four hours, but not more than six capsules in twenty-four hours.

Capsules are to be taken with food or after meals with sufficient water.

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

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

DO NOT EXCEED THE RECOMMENDED DOSE

Not recommended for use in children under twelve years of age.

Method of administration: Oral administration only.

4.3 Contraindications

- Hypersensitivity to ibuprofen, paracetamol or to any of the excipients listed in section 6.1
- patients with uncontrolled asthma or bronchospasm,
- bleeding disorders,
- cardiovascular disease,
- heart failure
- history of gastrointestinal

  perforation, ulceration, or bleeding (PUBs) related to previous NSAIDs, including MYPAID. The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of MYPAID in patients with a history of ulcers, and the elderly. When gastrointestinal bleeding or ulceration occurs in patients receiving MYPAID, treatment with MYPAID should be stopped.
- renal failure,
- severe liver function impairment
- patients receiving coumarin anticoagulants.
- pregnant or breastfeeding women: 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.
- Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory medicines.
- Nasal polyps associated with aspirin-induced bronchospasm

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 doctor, hospital or Poison Centre must be contacted immediately.

- Dosages in excess of those recommended may cause severe liver damage.
- Consult a doctor if no relief is obtained from the recommended dosage.
- Do not use for more than ten days without consulting a doctor.
- MYPAID should be given with care to the elderly
- Patients with congestive heart failure**,** cirrhosis, diuretic-induced volume depletion, or renal insufficiency require local synthesis of vasodilating prostaglandins to maintain renal perfusion and therefore these patients are at greater risk of developing renal dysfunction due to NSAID- induced inhibition of renal prostaglandin synthesis
- MYPAID should be discontinued in patients who experience blurred or diminished vision or changes in colour vision.
- Patients with collagen disease may be at increased risk of developing aseptic meningitis.
- Caution is required in patients with a history of hypertension as fluid retention and oedema have been reported in association with MYPAID therapy. In view of the MYPAID's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, selective serotonin-reuptake inhibitors or anti-platelet medicines such as aspirin (see section 4.5).
- MYPAID 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. MYPAID 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 MYPAID, between 20 to 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of MYPAID 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 NSAIDs treatment is necessary between 20 weeks and 30 weeks gestation, limit MYPAID use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if MYPAID treatment extends beyond 48 hours. Discontinue MYPAID if oligohydramnios occurs and follow up according to clinical practice.
- The antipyretic, analgesic and anti-inflammatory action of ibuprofen may mask symptoms of the occurrence or worsening of infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When MYPAID is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as MYPAID. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities,myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue MYPAID and evaluate the patient immediately.
- Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/ Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with MYPAID must immediately be discontinued and appropriate treatment instituted (see Section 4.8).

4.5 Interaction with other medicines and other forms of interaction

Interactions with other medicines

- *NSAIDs*: use of two or more NSAIDs concomitantly could result in an increase in side effects.
- *Anti-coagulants*: MYPAID may enhance the effects of anti-coagulants such as warfarin.
- *Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):* increased risk of gastrointestinal bleeding.
- *Aspirin*: Concomitant administration of MYPAID and aspirin is not generally recommended due to the increased adverse effects
- *Antihypertensives* or *diuretics*: MYPAID may reduce the antihypertensive effect of *ACE inhibitors*, *betablockers* and *diuretics*, and may cause natriuresis and hyperkalaemia. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
- *Alcohol, corticosteroids, clopidogrel, ticlopidine, bisphosphonates, oxpentifylline* may increase the risk of gastrointestinal perforation, bleeding and ulceration (PUBs) (see section 4.4).
- *Cardiac glycosides:* MYPAID may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
- *Lithium*: MYPAID may increase the steady-state concentration of lithium.
- *Methotrexate*: MYPAID may increase and prolong the methotrexate plasma concentration and increase risk of methotrexate toxicity.
- *Nephrotoxic medicines* e.g. *ciclosporin, tacrolimus* may increase the risk of nephrotoxicity further.
- *Quinolones antibiotics:* Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking MYPAID and quinolones may have an increased risk of developing convulsions.
- *Mifepristone*: MYPAID should not be used for 8 to 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone
- *Phenytoin*: MYPAID may enhance the effects of phenytoin
- *Sulphonylurea antidiabetics*: NSAID's may enhance the effects of sulphonylurea antidiabetics.
- *Bone marrow depressants:* The leucopenic and/or thrombocytopenic effects of these medicines may be increased.
- *Hepatotoxic medicines (zidovudine, co-trimoxazole,isoniazid, tuberculosis medicines)*: Hepatotoxic substances may increase the possibility of paracetamol accumulation and overdose. The risk of

hepatotoxicity of paracetamol may be increased by medicines which induce liver microsomal enzymes such as *anticonvulsants* and *alcohol*.

- *Metoclopramide* and *domperidone*: Absorption of paracetamolmay be accelerated.
- *Cholestyramine*: Absorption of paracetamol is reduced if given within one hour of cholestyramine.
- *Probenecid*: MYPAID excretion may be affected, and plasma concentrations altered
- *Medicines which decrease gastric emptying:* paracetamolabsorption is decreased by substances that decrease gastric emptying, e.g. *propantheline, antidepressants with anticholinergic properties, and narcotic analgesic*s
- *Chloramphenicol*: paracetamol may increase chloramphenicol plasma concentrations.
- *Moclobemide*: The effects of NSAID's might be enhanced by use with moclobemide.

Interactions with laboratory tests

- Diabetic patients may experience false results with blood glucose tests.

4.6 Fertility, pregnancy and lactation

MYPAID is not recommended for use by pregnant or breastfeeding women (see section 4.3). Use of NSAIDs, including MYPAID, 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 MYPAID duration between 20 and 30 weeks of gestation should be limited and avoided at dose and around 30 weeks of gestation and later in pregnancy. The use of MYPAID may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of MYPAID should be considered.

4.7 Effects on ability to drive and use machines

MYPAID may impair the ability to drive and use machinery. No studies on the effect of ability to drive or use machines have been performed. Undesirable effects such as dizziness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

System Organ Class	*Frequency*	*Undesirable effect*
Infections and infestations	Less frequent	Aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).
Blood and lymphatic system disorders	Less frequent	Blood disorders e.g., neutropenia, leucopenia, pancytopenia, agranulocytosis, thrombocytopenia, haematopoietic disorders (anaemia, haemolytic anaemia, aplastic anaemia), bleeding episodes (e.g. epistaxis, menorrhagia).
Immune system disorders	Less frequent	Hypersensitivity reactions including skin rashes, urticaria and pruritus as well as asthmatic attacks. Severe hypersensitivity reactions where symptoms can include facial, tongue and larynx swelling, dyspnoea, tachycardia, hypotension up to life-threatening shock, serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis, angioedema
	Unknown	Drug-induced hypersensitivity syndrome (DIHS) [Hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension] (see Section 4.4).
Metabolic and nutrition disorders	Less frequent	Gynaecomastia, hypoglycaemic reaction
	Unknown	Pyroglutamic aciduria (5-oxoprolinuria), high-anion gap metabolic acidosis
Psychiatric disorders	Frequent	Nervousness
	Less frequent	depression, confusion, emotional lability, hallucinations, dream abnormalities.

Nervous system disorders	Frequent	dizziness, headache
	Less frequent	paraesthesia, drowsiness, insomnia, somnolence, paradoxical stimulation, optic neuritis, psychomotor impairment, extrapyramidal effects, tremor, convulsions.
Eye disorders	Less frequent	Visual impairment, blurred vision, other ocular reactions.
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo.
Cardiac disorders	Less frequent	Oedema, cardiac failure, angina pectoris, cardiac dysrhythmias, palpitations.
Vascular disorders	Less frequent	hypertension.
Respiratory, thoracic and mediastinal disorder	Less frequent	Asthma, bronchospasm, dyspnoea, wheezing, thickened respiratory tract secretions.
Gastrointestinal ~~system~~ disorders	Frequent	Dyspepsia, nausea, vomiting, diarrhoea, abdominal cramps and pain, bloating, constipation, ulcerative stomatitis, exacerbation of colitis, Crohn's disease (see section 4.4), gastritis, peptic ulceration, gastrointestinal bleeding and perforation with symptoms of melaena haematemesis sometimes fatal, particularly in the elderly.
	Less frequent	pancreatitis, flatulence, decreased appetite.
Hepatobiliary disorders	Less frequent	Abnormalities of liver function tests, hepatic damage, particularly in long-term therapy, acute hepatitis, jaundice.
Skin and subcutaneous tissue disorders	Less frequent	Skin rash, pruritus, sensitivity reactions resulting in reversible skin rash usually erythematous or urticarial, but sometimes more serious and may be accompanied by fever and mucosal lesions), exfoliative dermatoses and bullous reaction including Stevens-Johnson syndrome and toxic epidermal necrolysis.
	Unknown	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome). Acute Generalised Exanthematous

		Pustulosis (AGEP), Fixed drug eruptions (FDE) (see Section 4.4)
Renal and urinary disorders	Less frequent	Impairment of renal function, nephrotic syndrome; interstitial nephritis that may be accompanied by acute renal insufficiency; renal tissue damage (papillary necrosis) with increased serum urea, haematuria, proteinuria, urinary retention, acute reversible renal failure, renal colic

Post-marketing experience:

The following side effects have been reported and frequencies are unknown: Fixed drug eruptions FDE) and drug-induced hypersensitivity syndrome (DIHS) (see Section 4.4).

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. Healthcare Providers are asked to report any suspected adverse reactions 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

Adverse Drug Reactions may also be reported to Adcock Ingram Limited using the following email: Adcock.AEReports@adcock.com

4.9 Overdose

The most likely symptoms of overdosage are nausea, vomiting and tinnitus. Treatment is symptomatic and supportive.

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. 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.

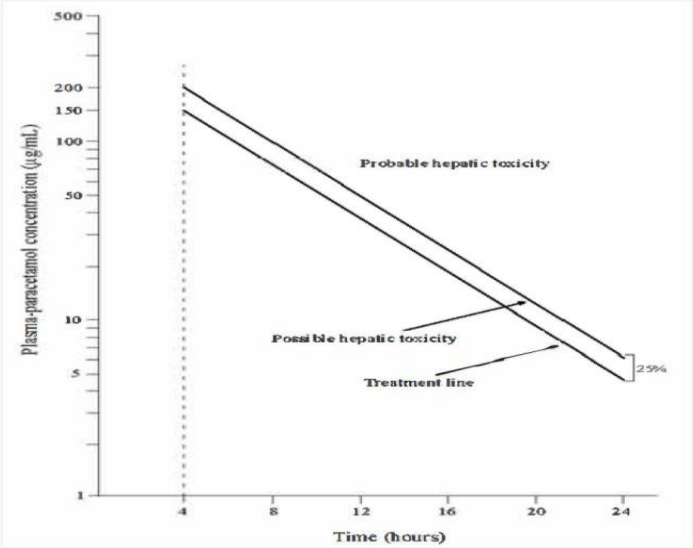
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml 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 1000 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, unless high, may be misleading. Patients at risk of liver

damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level.

The plasma paracetamol level can be plotted against time since ingestion in the nomogram below.



Reference: Martindale: The Complete Drug Reference

Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/ kg IV over 16 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

5. PHARMACOLOGICAL PROPERTIES

A 2.8 Analgesic combinations

WHO ATCC Code: M01AE51 ibuprofen, combinations

5.1 Pharmacodynamics properties

MYPAID capsules have an analgesic, anti-inflammatory and antipyretic action Paracetamol has analgesic and antipyretic effects. Ibuprofen has analgesic, antipyretic and anti-inflammatory activities. Ibuprofen inhibits platelet aggregation.

5.2 Pharmacokinetic properties

Paracetamol: Absorption following oral administration is well and almost complete. Paracetamol is metabolised in the liver primarily by conjugation. Paracetamol has a half-life of 1 to 4 hours, time to peak concentration of 0,5 to 2 hours, time to peak effect of 1 to 3 hours and the duration of action of 3 to 4 hours. Paracetamol is renally excreted primarily as metabolites and 3 % of a dose may be excreted unchanged.

Ibuprofen: Well absorbed after oral administration. Onset of action for pain relief is 30 minutes and the time for peak effect for fever is 2 to 4 hours. The half-life of ibuprofen is about 2 hours and the duration of action for fever is 6 to 8 hours or more and is 4 to 6 hours for pain. More than 90 % of an ingested dose is excreted in the urine as metabolites or their conjugates. Protein binding of ibuprofen is more than 95 %.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Microcrystalline cellulose (Avicel pH 101) [E460],
- Starch 1500,
- Sodium stearyl fumarate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 ºC.

6.5 Nature and contents of container

Plastic containers with 30 and 60 capsules.

Blister packs of 30 and 60 capsules

Not all pack sizes may be marketed at the same time.

6.6 Special precautions for disposal

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road,

Erand Gardens,

Midrand, 1685

Customer Care: 0860 ADCOCK (232625)

8. REGISTRATION NUMBER

27/2.8/0289

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07 May 1993

10. DATE OF REVISION OF THE TEXT

04 November 2024