SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

ADCO SALTERPYN TABLETS,150 mg/8 mg/320 mg/ 32 mg, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Meprobamate	150 mg
Codeine phosphate	8 mg
Paracetamol	320 mg
Caffeine anhydrous	32 mg

Preservative:

Paraben blend: 0,025 % *m/m*

Contains TARTRAZINE.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Green, round, bisected tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pain and pain associated with tension.

4.2 Posology and method of administration

Posology

Adults: Two tablets every 6 to 8 hours.

DO NOT EXCEED THE RECOMMENDED DOSE.

Paediatric population

Refer to section 4.3.

Method of administration

ADCO SALTERPYN TABLETS are to be taken orally

4.3 Contraindications

- Hypersensitivity to any of the active substances or to any of the other ingredients listed in section 6.1.
- Patients with acute intermittent porphyria.
- Patients with renal or hepatic insufficiency.

- Patients with asthma or respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion.
- Patients with head injuries and conditions in which intracranial pressure is raised.
- Patients with heart failure secondary to chronic lung disease.
- Patients with a history of cardiac disease.
- Patients with epilepsy and all convulsive states.
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.
- After operations on the biliary tract.
- Patients with acute alcoholism.
- Children under the age of 12 years.
- In women who are breastfeeding (see section 4.6).
- During the third trimester of pregnancy (see section 4.6).
- Children (0 - 18 years of age) who undergo tonsillectomy or adenoidectomy surgery for obstructive sleep apnoea syndrome due to an increased risk of developing serious and life-threatening adverse reactions (see section 4.4)

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.

Symptoms of porphyria may be exacerbated with the use of meprobamate, as contained in ADCO SALTERPYN TABLETS (see section 4.3).

The use of ADCO SALTERPYN TABLETS may lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressant medicines, with consequent impairment of judgement and co-ordination (see section 4.5).

Paracetamol administration in excess of the recommended dosage may cause severe liver damage. Patients should be warned to not use continuously for more than 10 days without consulting their doctor.

Caution is recommended in patients with moderate renal failure and patients on dialysis, as plasma concentrations of ADCO SALTERPYN TABLETS and its conjugates are increased.
Use with caution in renal impairment, chronic malnutrition, or dehydration.

Exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction. The prolonged use of high doses of codeine, as contained in ADCO SALTERPYN TABLETS, has produced

dependence of the morphine type, whereas prolonged use of the meprobamate component may lead to the development of dependence of the barbiturate-alcohol type.

Opioid use disorder (abuse and dependence)
Tolerance, physical and psychological dependence and opioid use disorder (OUD) may develop upon repeated administration of opioids such as codeine. Abuse or intentional misuse of ADCO SALTERPYN TABLETS may result in overdose and/or death.

Patients should be informed about the risks and signs of OUD as well as serious clinical outcomes. If these signs occur, patients should be advised to contact their doctor.

Withdrawal symptoms, such as restlessness and irritability may occur once the medicine is stopped.

Increased risk of addiction in patients with personal or family history of substance abuse or mental health disorders.

Opioid-induced Hyperalgesia (OIH) and Allodynia
Opioid pain medicines have been associated with opioid-induced hyperalgesia (OIH), a condition where opioids cause an increase in pain (called hyperalgesia) or an increased sensitivity to pain (called allodynia). Increases in pain typically occur following a dose increase and resolve quickly following proper diagnosis and management of the condition. Symptoms of OIH include (but may not be limited to) increased levels of pain upon opioid dosage increase, decreased levels of pain upon opioid dosage decrease, or pain from ordinarily non-painful stimuli (allodynia).

Hypersensitivity reactions such as skin rashes, urticaria and purpura may occur with meprobamate, as contained in ADCO SALTERPYN TABLETS. These reactions may be more severe with angioedema, bronchospasm or anuria. Paracetamol may also cause skin rashes and other allergic reactions: the rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by drug fever and mucosal lesions (see section 4.8).

Severe cutaneous adverse reactions (SCARs): Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Stevens-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 ADCO SALTERPYN TABLETS must immediately be discontinued and appropriate treatment instituted (see section 4.8).

Codeine, as contained in ADCO SALTERPYN TABLETS, should be given with caution to patients with hypothyroidism, adrenocortical insufficiency, impaired liver function, prostatic hypertrophy or shock. It should be used with caution in patients with

inflammatory or obstructive bowel disorders. The dosage should be reduced in elderly and debilitated patients.

Codeine, as contained in ADCO SALTERPYN TABLETS, is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of morphine toxicity.

Caffeine, as contained in ADCO SALTERPYN TABLETS, should be given with care to patients with a history of peptic ulceration (see section 4.8).

ADCO SALTERPYN TABLETS contain tartrazine which may cause allergic-type reactions (including bronchial asthma) in certain individuals. The overall incidence of tartrazine sensitivity is low; it is however, frequently seen in patients who also have aspirin sensitivity.

ADCO SALTERPYN TABLETS contains a paraben blend, which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicines and other forms of interaction

Monoamine oxidase inhibitors
ADCO SALTERPYN TABLETS is contraindicated in patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment (see section 4.3).

Alcohol
Simultaneous intake of alcohol or other central nervous system depressant medicines (such as anaesthetics, hypnotics, sedatives and phenothiazines) can aggravate the drowsiness and impaired concentration caused by ADCO SALTERPYN TABLETS (see sections 4.4 and 4.8), with consequent impairment of judgement and co-ordination.

Meprobamate may lower tolerance to alcohol and other central nervous system depressants. It may induce the hepatic microsomal enzymes involved in medicine metabolism.

Paracetamol as in ADCO SALTERPYN TABLETS

Hepatotoxic medicines:
Increased risk of hepatotoxicity.

Enzyme-inducing medicines:
Increased risk of hepatotoxicity and possible decrease in therapeutic effects of ADCO SALTERPYN TABLETS.

Metoclopramide:
Absorption of ADCO SALTERPYN TABLETS may be accelerated.

Domperidone: Absorption of ADCO SALTERPYN TABLETS may be accelerated.

Probenecid:
Pre-treatment with probenecid can decrease ADCO SALTERPYN TABLETS clearance and increase its half-life. Although urinary excretion of the sulphate and glucuronide conjugates of paracetamol are reduced, that of paracetamol is unchanged.

Cholestyramine:
Absorption of ADCO SALTERPYN TABLETS is reduced if given within one hour of cholestyramine.

Salicylates:
Prolonged concurrent use of ADCO SALTERPYN TABLETS with salicylates increases the risk of adverse renal effects.

Antibiotics:
Chronic use of isoniazid, an antibiotic medicine often prescribed for tuberculosis, may increase the risk of liver damage when combined with ADCO SALTERPYN TABLETS, even at recommended doses.

Warfarin and anticoagulants:
Concurrent, chronic, high-dose administration of ADCO SALTERPYN TABLETS may increase the anticoagulant effect.
Paracetamol is recommended as the general analgesic and antipyretic of choice in patients on oral anticoagulant therapy. However, caution is needed since, although it has no effect on the gastric mucosa or on platelet function, some studies (with warfarin, anisindione, dicoumarol, or phenprocoumon) and isolated reports have found an increased risk of bleeding in patients taking regular doses of paracetamol while on an oral anticoagulant. An increase in INR has also been reported in controlled studies of the use of paracetamol in patients stabilised on warfarin. Increased monitoring of anticoagulant therapy may be appropriate for those also taking paracetamol regularly.

Antiepileptics:
The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing medicines such as carbamazepine, phenobarbital, phenytoin, or primidone.

Antibacterials:
The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing medicines such as rifampicin.

Severe hepatotoxicity at therapeutic doses or moderate overdoses of paracetamol has been reported in patients receiving isoniazid, alone or with other medicines for tuberculosis.

Antivirals:
Severe hepatotoxicity has occurred after use of paracetamol in a patient taking zidovudine and co-trimoxazole. However, neither short-term nor long-term studies (the latter also in an individual patient) have shown any alteration of zidovudine elimination in patients taking zidovudine and paracetamol.
Paracetamol has also been found to enhance the antiviral effect of interferon alfa.

4.6 Fertility, pregnancy and lactation
Pregnancy
Use of ADCO SALTERPYN TABLETS during the third trimester of pregnancy is contraindicated (see section 4.3).
Use of ADCO SALTERPYN TABLETS during the first and second trimester of pregnancy should be avoided.

Breastfeeding
ADCO SALTERPYN TABLETS is contraindicated for use by breastfeeding women (see section 4.3).

Fertility
Data on the effect of ADCO SALTERPYN TABLETS on fertility is not available

4.7 Effects on ability to drive and use machines
ADCO SALTERPYN TABLETS may cause drowsiness (see section 4.8); therefore, it is dangerous to drive a vehicle or be in charge of machinery while on treatment with this medicine.

4.8 Undesirable effects
a) Summary of the safety profile
Sensitivity reactions resulting in reversible skin rash or blood disorders may occur.

b) Tabulated list of adverse reactions

SYSTEM ORGAN CLASS	**FREQUENCY**	**ADVERSE REACTIONS**
Codeine phosphate:		
Psychiatric disorders:	Frequency not known.	Changes of mood.
Nervous system disorders:	Frequency not known.	Dizziness, drowsiness, confusion, vertigo, restlessness, orthostatic hypotension, raised intracranial

		pressure.
Eye disorders:	Frequency not known.	Miosis.
Cardiac disorders:	Frequency not known.	Bradycardia, palpitations.
Gastrointestinal disorders:	Frequency not known.	Constipation, nausea, vomiting, dry mouth.
Skin and subcutaneous tissue disorders:	Frequency not known.	Skin rashes, sweating and facial flushing, reactions such as urticaria and pruritus.
Renal and urinary disorders:	Frequency not known.	Micturition difficulty, ureteric or biliary spasm.
General disorders and administration site conditions:	Frequency not known.	Hypothermia.
Caffeine		
Nervous system disorders:	Frequency not known.	Headaches, insomnia, restlessness and excitement.
Eye disorders:	Frequency not known.	Scintillating scotoma.
Ear and labyrinth disorders:	Frequency not known.	Tinnitus.
Cardiac disorders:	Frequency not known.	Tachycardia, extrasystoles.
Gastrointestinal disorders:	Frequency not known.	Nausea, increased gastric secretion, gastric ulceration.
Musculoskeletal and connective tissue disorders:	Frequency not known.	Muscle tremor.
Meprobamate:		
Blood and the lymphatic system disorders:	Frequency not known.	Blood disorders including agranulocytosis, eosinophilia, leukopenia, thrombocytopenia and aplastic anaemia.
Immune system disorders:	Frequency not known.	Hypersensitivity reactions including skin rashes, urticaria, purpura, angioedema, bronchospasm, anuria.
Nervous system disorders:	Frequency not known.	Drowsiness, paraesthesia, weakness, headaches, excitement, dizziness, and ataxia.
Eye disorders:	Frequency not	Disturbances of vision.

	known.	
Cardiac disorders:	Frequency not known.	Tachycardia and dysrhythmia.
Vascular disorders:	Frequency not known.	Hypotension.
Gastrointestinal disorders:	Frequency not known.	Nausea, vomiting and diarrhoea.
Skin and subcutaneous tissue disorders:	Frequency not known.	Erythema multiforme.
Paracetamol:		
Blood and the lymphatic system disorders:	Less frequent.	Agranulocytosis, thrombocytopenia, neutropenia, pancytopenia, leukopenia, anaemia
Immune system disorders:	Frequency not known.	Skin rashes (erythematous or urticarial) and other allergic reactions, including drug fever, mucosal lesions, fixed drug eruptions (FDE), drug-induced hypersensitivity syndrome (DIHS) (see sections 4.4 &. Hypersensitivity reactions are characterised by urticaria, dyspnoea and hypotension. Angioedema can also occur.
Metabolism and nutrition disorders	Less frequent	Pyroglutamic aciduria (5-oxoprolinuria) and high-anion gap metabolic acidosis
Ear and labyrinth disorders	Frequency not known	Hearing loss
Cardiac disorders	Frequency not known	Possible increase in the risk of hypertension
Gastrointestinal disorders	Less frequent	Pancreatitis
Hepato-biliary disorders	Less frequent	Hepatitis
Renal and urinary disorders	Less frequent	Renal colic, renal failure and sterile pyuria
	Frequency not known	Nephropathy
Skin and subcutaneous tissue disorders	Less frequent	Dermatitis, skin rashes, severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis

		(TEN), Stevens–Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)

Post-marketing experience:

Codeine Phosphate:		
Gastrointestinal Disorder:	Less frequent	Acute Pancreatitis*
Paracetamol:		
Immune system disorders:	Frequency not known.	Fixed drug eruptions (FDE), drug-induced hypersensitivity syndrome (DIHS) (see section 4.4).

*Increased risk of abdominal pain, including pancreatitis has been reported.

c) Description of selected adverse reactions

Caffeine:

Caffeine increases gastric secretion and may cause gastric ulceration.

Meprobamate:

Hypersensitivity reactions such as skin rashes, urticaria and purpura may occur or may be more severe with angioedema, bronchospasm or anuria (see section 4.4).
Symptoms of porphyria may be exacerbated (see section 4.3).

Paracetamol:

Paracetamol may cause skin rashes and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by drug fever and mucosal lesions (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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms of overdosage with codeine phosphate include the following: nausea, vomiting, restlessness, sensory disturbances, muscle tremor, diuresis, palpitations, stupor, shock, central stimulation with exhilaration, convulsions, drowsiness, respiratory depression, hypotension with circulatory failure, respiratory collapse, cyanosis and coma. Intensive supportive therapy may be necessary to correct respiratory failure and shock.

The specific antagonist naloxone may be used to counteract severe respiratory depression.

Paracetamol overdose: 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 medicines 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 dysrhythmias have been reported.

Treatment for paracetamol overdosage:
Although evidence is limited, it is recommended that for 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, a single dose of 50 g activated charcoal is given. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above).

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 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

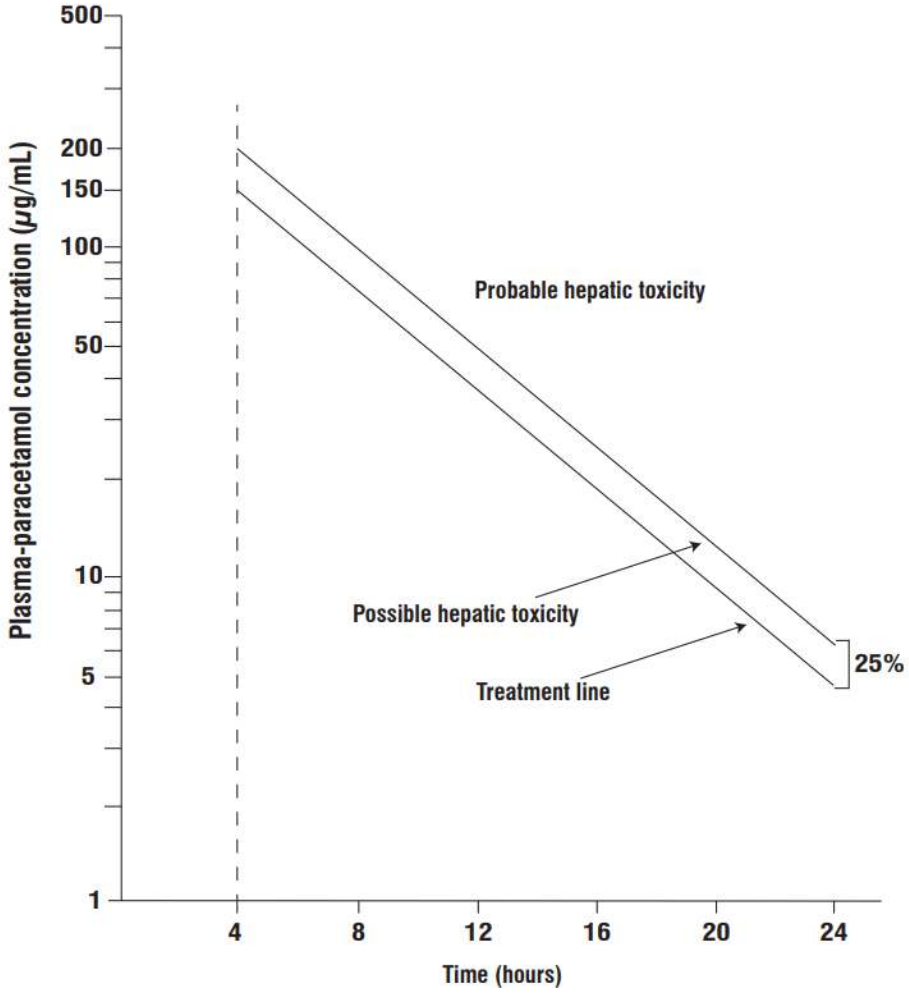
may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours 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 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.

A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion. Reference: Martindale, The Complete Drug Reference.



Symptoms of overdosage with meprobamate are mainly due to the depressant effect on the central nervous system. See also section 4.8.
Patients should be managed with intensive symptomatic and supportive therapy, with particular attention being paid to the maintenance of
cardiovascular, respiratory and renal functions, and the maintenance of
the electrolyte balance.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.8 Analgesic combinations.

ADCO SALTERPYN TABLETS have analgesic and skeletal muscle-relaxing properties.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicone dioxide.
Colour apple green deep/lake blend (LB510007).
Magnesium stearate.
Povidone.
Maize starch/pre-gelatinised starch.
Purified talc.
Powdered acacia.
Paraben blend.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C in a dry place. Protect from light. Do not remove the blister from the carton until required for use.

6.5 Nature and contents of container

ADCO SALTERPYN TABLETS are packed in:

- PVC film and aluminium foil blisters of 20 and 100 tablets.
- Amber PVC jars with white HDPE screw on caps, or amber HDPE bottles/jars with screw on closures and cotton wool in pack sizes of 500 and 1 000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused medicine or waste material should be disposed of in accordance with local

requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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

8. REGISTRATION NUMBER(S)

27/2.8/0574

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 December 1993

10. DATE OF REVISION OF THE TEXT

12 March 2025

Botswana (S1C): BOT1803390 Namibia (NS4): 04/2.8/1594