Summary Product Characteristics for Pharmaceutical Product

1. Name of the medicinal product

Surepyn Tablets

2. Qualitative and quantitative composition

Each tablet contains Paracetamol 450mg, Doxylamine succinate 5mg, Caffeine 50mg, Codeine Phosphate 10mg

Excipients with known effect

Contains Lactose

For a full list of excipients, see section 6.1

3. Pharmaceutical form

A round yellow-coloured tablet scored on one side and plain on the other.

4. Clinical particulars

4.1 Therapeutic indications

The tablets are recommended for use as an analgesic in the relief of moderate pain such as is associated with rheumatism, neuralgia, musculoskeletal disorders, headache and discomfort associated with influenza, feverishness and feverish colds, toothache and dysmenorrhoea.

4.2 Posology and method of administration

Adults and children over 12 years:
1 or 2 tablets taken orally; every four hours as needed.
Not exceed 8 tablets per day.

4.3 Contraindications

- Hypersensitivity to any of the ingredients in Surepyn.
- The dosage in renal functional impairment must be reduced.
- Should be taken with caution by asthmatics.
- Respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, after an operation on the biliary tract, acute alcoholism, head injuries and conditions in which intracranial pressure is raised.
- Should not be given during an attack of bronchial asthma or in heart failure secondary to chronic lung disease.
- Surepyn is contraindicated in patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

4.4 Special warnings and precautions for use

Paracetamol:
Surepyn 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. A dosage in excess of those recommended may cause severe liver damage.

Codeine phosphate:
Exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction. This medicine may lead to drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents. Patients should be warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration may lead to accidents.
Codeine phosphate:
• should be used with caution in patients with obstructive bowel disorders, liver impairment, myasthenia gravis, prostatic hypertrophy, impaired renal function or shock.
• should be used with caution or in reduced doses in patients with adrenocortical insufficiency and hypothyroidism.
• dosages should be reduced in debilitated and elderly patients.
• may affect the activity of other medicines by delaying their absorption

Caffeine:
Caffeine should be given with care to patients with a history of peptic ulceration.

Doxylamine succinate:
Doxylamine succinate has anticholinergic properties and should be used with care in conditions such as glaucoma and prostatic hypertrophy.

4.5 Interaction with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with an increased risk of bleeding; occasional doses have no significant effect. Codeine may affect the activity of other medicines by delaying their absorption. The depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines. The effects of atropine and tricyclic antidepressants may be enhanced by the doxylamine succinate (an antihistamine). Doxylamine succinate may also mask the warning symptoms of damage caused by ototoxic medicines and may affect the metabolism of medicines in the liver. Doxylamine succinate may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillizers.

4.6 Pregnancy and lactation

The safety of Surepyn during pregnancy and lactation has not been established.

4.7 Effects on the ability to drive and use machines

This medicine may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

Frequency	**System organ class**	**Undesirable effects**
Frequent	Nervous system disorders	Insomnia, drowsiness, confusion, sedation, deep sleep, inability to concentrate, lassitude, incoordination, dizziness, headache, dry mouth, nervousness, tremors, convulsions.
	Vascular disorders	Headache, facial flushing, vertigo, orthostatic hypotension, hypotension**.**
Frequency Unknown	Blood and the lymphatic system disorders	Neutropenia, pancytopenia and leucopenia, agranulocytosis, anaemia, thrombocytopenia, haemolytic anaemia.
	Cardiac disorders	Tachycardia, extrasystoles, bradycardia, palpitation.
	Ear and labyrinth disorders	Tinnitus, vertigo.
	Eye disorders	Scintillating scotoma, miosis.
	Gastrointestinal disorders	Increases in gastric secretions and gastric ulceration, nausea, vomiting, constipation, dry mouth, gastrointestinal disturbances, diarrhoea.
	General disorders and administration site conditions	Hypothermia.
	Hepato-biliary disorders	Hepatitis, biliary spasm.
	Immune system disorders	Allergy, anaphylaxis.

	Musculoskeletal, connective tissue and bone disorders	Muscle tremor, muscular weakness.
	Psychiatric disorders	Irritability, anxiety, neurosis, restlessness, excitement, mood changes, raised intracranial pressure.
	Renal and urinary disorders	Renal colic, renal failure, sterile pyuria, difficulty in micturition, ureteric spasm.
	Skin and subcutaneous tissue disorders	Urticaria, pruritus and sweating. 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.

Reporting of suspected adverse reactions:
Healthcare professionals are asked to report any suspected adverse reactions via the pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Prompt treatment is essentia**l.** 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 the 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, HIV/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 twodays of acute poisoning, do not

reflect the potential seriousness of the overdosage.
Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage:
Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration.

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.
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”.

Codeine phosphate: Symptoms of overdosage with codeine include excitement and in children, convulsions may occur. Treatment is

symptomatic and supportive.

Doxylamine succinate: The most common symptom of overdosage is impaired consciousness and psychotic behaviour.

Caffeine: Overdose may cause diuresis, tachycardia, irritability, nervousness, restlessness, gastrointestinal disturbances and CNS stimulation such as agitation, excitement, insomnia and tremors. The management of caffeine toxicity is generally symptomatic and supportive (e.g., hydration). For acute ingestion gastric lavage is advised.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Analgesic combinations.

Surepyn tablets combine the analgesic and antipyretic action of paracetamol with the analgesic action of codeine phosphate. Doxylamine succinate has sedative and antihistamine properties and in combination with the above analgesics is of value, especially in tension states.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. The concentration of the drug in plasma reaches a peak in 30 - 60 minutes and the plasma half-life is 1 - 4 hours.
Paracetamol is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. Excretion is almost exclusively renal in the form of conjugated metabolites.
Doxylamine succinate is readily absorbed from the gastrointestinal tract. Following oral administration the effects start within 15 to 30 minutes and peak within one hour. In humans, 60 - 80% of doxylamine given has been recovered in urine at 24 hours post-dose.
The bioavailabilities of paracetamol and codeine phosphate when given as a combination are similar to those when they are given separately.
Codeine is mainly metabolized by glucuronidation to codeine-6-glucuronide. Minor routes of metabolism include O-demethylation leading to morphine, N-demethylation to norcodeine and both O- and N-demethylation to normorphine. Morphine and norcodeine are further transformed into glucuronide conjugates. Unchanged codeine and its metabolites are mainly excreted by the urinary route within 48h (84.4±15.9%). The O-demethylation of codeine to morphine is catalyzed by the cytochrome P450 isozyme 2D6 (CYP2D6) which shows genetic polymorphism that may affect the efficacy and toxicity of codeine. Genetic polymorphism in CYP2D6 leads to ultra-rapid, extensive and poor metabolizer phenotypes.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. Pharmaceutical particulars

6.1 List of excipients

Dibasic Calcium Phosphate
Microcrystalline cellulose
Lactose
Maize Starch
Povidone K-30
Sodium Methyl Paraben
Sodium Propyl Paraben
Aerosil
Sodium Starch Glycolate
Talc
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C

6.5 Nature and contents of the container

Alu-PVC blister pack
Pack size: 2x10 tablets

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder and manufacturing site addresses

National Pharmacy Limited
P.O BOX 17843-00500
Nairobi, Kenya.

Manufacturing site address:

Zain Pharma limited
Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice And Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing authorisation number(s)

CTD9511- Surepyn tablets

9. Date of first authorisation/renewal of the authorisation

Date of first authorization: 29-May-2023

10. Date of revision of the text

15-Sep-2023

11. Dosimetry:

Not Applicable

12. Instructions for preparation of radiopharmaceuticals:

Not Applicable