Summary Product Characteristics for Pharmaceutical Product

1. Name of the medicinal product

Histamol

2. Qualitative and quantitative composition

Each tablet contains Paracetamol 325mg and Cetirizine 5mg

Excipients with known effect

Contains Sodium Benzoate

For a full list of excipients, see section 6.1

3. Pharmaceutical form

Tablet

White round flat uncoated tablets having one side break line and the other side plain.

4. Clinical particulars

4.1 Therapeutic indications

It is indicated for the symptomatic treatment of allergic rhinitis, fever and nasal congestion. Cetirizine + Paracetamol is a combination of two medicines: which relieve common cold symptoms. Cetirizine is an antihistamine which relieves symptoms like runny nose, watery eyes and sneezing. Paracetamol is an analgesic (pain reliever) and antipyretic (fever reducer).

4.2 Posology and method of administration

Adults and children (12 years and above)
One tablet 12 hourly or as recommended by the physician

Method of administration:
For oral use.

4.3 Contraindications

Hypersensitivity to paracetamol, cetirizine its parent compound hydrazine or any of the other constituents.

4.4 Special warnings and precautions for use

The occurrence of somnolence has been reported in some patients taking cetirizine; due caution should therefore be exercised when driving a car or operating potentially dangerous machinery.
Concurrent use of cetirizine with alcohol or other CNS depressants should be avoided because additional reductions in alertness and additional impairment of CNS performance may occur.
Increased risk of urinary retention Caution should be taken in patients with predisposition factors of urinary retention (e.g., spinal cord lesion, prostatic hyperplasia) as cetirizine may increase the risk of urinary retention.
Caution in epileptic patients and patients at risk of convulsions is recommended.
Patients should be advised not to take other Paracetamol-containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver. Prolonged use except under medical supervision may be harmful. Caution is advised in the administration of Paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatocellular insufficiency (including Gilbert's syndrome), severe hepatic insufficiency *(**Child-Pugh* **>9**), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6- phosphate dehydrogenase deficiency, hemolytic anaemia, dehydration. alcohol abuse and chronic malnutrition.

4.5 Interaction with other medicinal products and other forms of interaction

Due to the pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with this antihistamine. Neither pharmacodynamic nor significant pharmacokinetic interaction was reported in drug-drug interaction studies performed, notably with pseudoephedrine or theophylline (400 mg/day). However, Cetirizine hydrochloride may potentiate the effects of alcohol. Therefore caution is recommended at concomitant use of alcohol. Caution is recommended during concomitant use of CNS depressants.
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.

4.6 Pregnancy and lactation

Caution should be exercised when prescribing to pregnant women. For cetirizine very rare clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Caution should be exercised when prescribing cetirizine to lactating women. Cetirizine is excreted in human milk at concentrations representing 25% to

90% of those measured in plasma, depending on sampling time after administration.
Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy if clinically needed, however, as with any medicine it should be used at the lowest effective dose for the shortest possible time.
Paracetamol is excreted in breast milk but not in a clinically significant amount in recommended dosages. Available published data do not contraindicate breastfeeding.

4.7 Effects on the ability to drive and use machines

Patients intending to drive, engaging in potentially hazardous activities or operating machinery should not exceed the recommended dose and should take their response to the medicinal product into account. In sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

4.8 Undesirable effects

CETIRIZINE

Clinical studies have shown that cetirizine at the recommended dosage has minor undesirable effects on the CNS, including somnolence, fatigue, dizziness and headache. In some cases, paradoxical CNS stimulation has been reported.

Although cetirizine is a selective antagonist of peripheral H1-receptors and is relatively free of anticholinergic activity, isolated cases of micturition difficulty, eye accommodation disorders and dry mouth have been reported.

Instances of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported. Mostly these resolves upon discontinuation of the treatment with cetirizine hydrochloride.

PARACETAMOL

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class and frequency.

The following convention has been utilised for the classification of the undesirable effects: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Very rare cases of serious skin reactions have been reported. Anaphylaxis Cutaneous hypersensitivity reactions including (amongst others) skin rashes and angioedema.
Respiratory, thoracic and mediastinal disorders	Bronchospasm- more likely in patients sensitive to aspirin and other NSAIDs
Hepatobiliary disorders	Hepatic dysfunction

There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs

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

Cetirizine

Signs and symptoms

Symptoms observed after an overdose of cetirizine are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect. Adverse events reported after an intake of at least 5 times the recommended daily dose are confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention.

Treatment

There is no known specific antidote to cetirizine. Should an overdose occur, symptomatic or supportive treatment is recommended.
Cetirizine is not effectively removed by dialysis, and dialysis will be ineffective unless a dialysable agent has been concomitantly ingested.

Paracetamol
Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors:
If the patient

• Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
Or
• Regularly consumes ethanol in excess of recommended amounts.
Or
• Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms
Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management
Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to the hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.
Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside the hospital. Management of patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be discussed with the NPIS or a liver unit.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Cetirizine, a human metabolite of hydroxyzine, is an antihistamine; its principal effects are mediated via selective inhibition of peripheral H_1 receptors. The antihistaminic activity of cetirizine has been clearly documented in a variety of animal and human models. *In vivo* and *ex vivo* animal models have shown negligible anticholinergic and antiserotonergic activity.

Paracetamol is a well established analgesic.

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.

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

Microcrystalline Cellulose
Croscarmellose Sodium
Starch
Starch (paste)
Povidone-K 30
Sodium Benzoate
Magnesium Stearate
Purified Talc
Croscarmellose Sodium

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: 3x10 tablets

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder and manufacturing site addresses

Simba Pharmaceuticals Ltd
1st Floor, Almont Park, Westlands.
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Manufacturing site address:

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E-Mail: aksharampharma@gmail.com

8. Marketing authorisation number(s)

CTD10404- Histamol

9. Date of first authorisation/renewal of the authorisation

Date of first authorization: 03-August-2023

10. Date of revision of the text

15-Sep-2023

11. Dosimetry:

Not Applicable

12. Instructions for preparation of radiopharmaceuticals:

Not Applicable