MECURE INDUSTRIES PLC

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. Name of the medicinal product

Me Cure's Cold Free Tablets

2. Qualitative and quantitative composition

- *Cold tablet*

  Each uncoated tablet contains 500mg Paracetamol, 5mg Phenylepherine, 4mg Chlorpheniramine Maleate and 30mg Caffeine.

  Excipients q.s

- *Vitamin C tablet*

  Each uncoated tablet contains 50mg Ascorbic acid

  Excipients q.s

  For full list of excipients, see section

3. Pharmaceutical form

Tablet

- *Cold tablet*
  Orange circular flat beveled edge uncoated tablets, having embossed with **"COLD**

  FREE "on one side and other side is **"MECURE ".**

- *Vitamin C tablet*

  Almost white circular biconvex uncoated tablets, having embossed with "VIT C" on

  one side and other is plain.

4. Clinical particulars

4.1 Therapeutic indications

This product is recommended for fast relief of fever, headache, nasal congestion and sneezing associated with cold and catarrh.

4.2 Posology and method of administration

Adult: One Cold tablet + One Vitamin C tablet 3 - 4 times a day.

Children (6 – 12 years): Half Cold tablet + One Vitamin C Tablets 3 – 4 times a day.

For Oral administration

4.3 Contraindications

Concomitant use of other sympathomimetic decongestants.

Phaeochromocytoma

Closed angle glaucoma

Known hypersensitivity to paracetamol or any of the other constituents.

Hepatic or severe renal impairment, hypertension, hyperthyroidism, diabetes, and heart disease. Patients taking tricyclic antidepressants, or beta-blocking drugs and those who are taking or who have taken within the last two weeks monoamine oxidase inhibitors (see section 4.5).

4.4 Special warnings and precautions for use

Contains paracetamol. Patients should be advised not to take other paracetamol-containing products concurrently. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Concomitant use of other decongestants or cold and flu medicines should be avoided.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Underlying liver disease increases the risk of paracetamol-related liver damage.

- Medical advice should be sought before using this product in patients with these conditions:
- Medical advice should be sought before taking this medicine in patients with: glutathione depletion due to metabolic deficiencies. An enlargement of the prostate gland
- Occlusive vascular disease (e.g. Raynaud's phenomenon)
- Cardiovascular disease

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see interactions).

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.

Do not exceed the stated dose.

If symptoms persist consult your doctor.

Keep out of the sight and reach of children.

Consult your doctor if you are taking warfarin.

Contains Colour Sunset Yellow which may cause an allergic reaction.

4.5 Interaction with other medicinal products and other forms of interaction

Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopromide or domperidone and absorption reduced by colestyramine. These interactions are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Medical advice should be sought before taking paracetamol-caffeine phenylephrine in combination with the following drugs:

Monoamine oxidase inhibitors (including moclobemide)	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine Oxidase inhibitors (see contraindications).
Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetics amines can increase the risk of cardiovascular side effects (see warnings and precautions).
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)	Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased (see contraindications).
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (see contraindications).
Digoxin and cardiac glycosides	Concimitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of irregular heartbeat or heart attack.
Ergot alkaloids (e.g. ergotamine and methylsergide)	Concomitant use of phenylephrine hydrochloride may cause an increased risk of ergotism *(see Warnings and Precautions).*
Warfarin and other coumarins	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.
Lithium	Caffeine can increase the elimination of lithium from the body. If taken concomitantly, it is recommended to reduce or moderate the intake of caffeine.

4.6 Pregnancy and lactation

Pregnancy

This product is not recommended for use in pregnancy due to the phenylephrine and caffeine content. There is a potential increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption during pregnancy. Pregnant women should seek medical advice before taking paracetamol.

Breast-feeding

This product should not be used while breast-feeding without medical advice. Avoid the use of the product during lactation, unless the benefits to the mother outweigh the risks to the infant. If used, the lowest effective dose and shortest duration of treatment should be considered.

Paracetamol is excreted in breast milk but not in a clinically significant amount at recommended dosages.

Caffeine in breast milk may have a stimulating effect on breast-fed infants but significant toxicity has not been observed.

Phenylephrine may be excreted in breast milk.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable effects

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labeled dose and considered attributable are tabulated below by system class. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Paracetamol

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis These were not necessarily causally related to paracetamol.
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema Very rare cases of serious skin reactions have been reported.
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
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.

Chlorpheniramine Maleate

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Unknown: haemolytic anaemia, blood dyscrasias
Immune system disorders	Unknown: allergic reaction, angioedema, anaphylactic reactions
Metabolism and nutritional disorders	Unknown: anorexia
Psychiatric disorders	Unknown: confusion*, excitation*, irritability*, nightmares*, depression
Respiratory, thoracic and	Unknown: thickening of bronchial secretions

mediastinal disorders	
Nervous system disorders*	Very common: sedation, somnolence Common: disturbance in attention, abnormal coordination, dizziness headache
Hepatobiliary disorders	Unknown: hepatitis, including jaundice

*Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (eg. increased energy, restlessness, nervousness).

Caffeine

Adverse reactions identified through post-marketing use with caffeine are listed below. The frequency of these reactions is unknown.

Body System	**Undesirable effect**
Central Nervous system	excitability, dizziness and headache
Psychiatric disorders	Nervousness, insomnia, restlessness, anxiety and irritability
Cardiac disorders	Palpitations
Gastrointestinal disorders	Gastrointestinal disturbances

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects.

Phenylephrine

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	**Undesirable effect**
Psychiatric disorders	Nervousness
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, Vomiting

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions is unknown

Body System	**Undesirable effect**
Immune system disorders	Hypersensitivity, allergic dermatitis, urticaria
Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma

Cardiac disorders	Tachycardia, palpitations
Skin and subcutaneous disorders	Rash
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Vitamin C

Nervous system disorders: headache.

Vascular disorders: flushing.

Gastrointestinal disorders: nausea, vomiting and stomach cramps. Large doses of ascorbic acid may cause diarrhea.

Skin and subcutaneous tissue disorders: redness of skin.

Renal and urinary disorders: Patients known to be at risk of hyperoxaluria should not ingest ascorbic acid doses exceeding 1g daily as there may be increased urinary oxalate excretion. However, such risk has not been demonstrated in normal, non-hyper oxaluric individuals. Ascorbic acid has been implicated in precipitating haemolytic anaemia in certain individuals deficient of glucose-6-phosphate dehydrogenase.

Increased intake of ascorbic acid over a prolonged period may result in increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly. Doses of more than 600mg daily have a diuretic effect.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continue monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reaction to the appropriate authority.

4.9 Overdose

Paracetamol

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.

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

Risk factors

If the patient

a. Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

   Or

b. Regularly consumes ethanol in excess of recommended amounts.

   Or

c. Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol over dosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion and have peaked after 4-6 days. 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.

Treatment

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to 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 hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

Caffeine

Symptoms

Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Treatment

No specific antidote is available, but supportive measures such as beta adrenoceptor antagonists to reverse the cardiotoxic effects may be used.

Chlorpheniramine Maleate

Symptoms

The estimated lethal dose of Chlorphenamine is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment

Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and fluid and electrolyte balance. If over dosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion). Treat hypotension and arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam. Haemoperfusion may be used in severe cases.

Phenylephrine

Symptoms

Phenylephrine over dosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include, irritability, restlessness, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to produce serious Phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

Treatment

Treatment should be as clinically appropriate. Severe hypertension may need to be treated with alpha blocking drugs such as phentolamine.

If overdose is confirmed or suspected, seek immediate advice from your Poison Centre and refer patient to nearest Emergency Medical Centre for management and expert treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage.

Vitamin C

Symptoms

At doses of over 3g per day unabsorbed ascorbic acid is mainly excreted unmetabolised in the faeces. Absorbed ascorbic acid additional to the body's needs is rapidly eliminated. Large doses of ascorbic acid may cause diarrhea and the formation of renal oxalate calculi. Symptomatic treatment may be required.

Ascorbic acid may cause acidosis or haemolytic anaemia in certain individuals with a deficiency of glucose 6-phosphate dehydrogenase. Renal failure can occur with massive ascorbic acid over dosage.

Treatment

Gastric lavage may be given if ingestion is recent otherwise general supportive measure should be employed as required.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC Code R06AB02

Chlorphenamine is a potent antihistamine (H_1-antagonist).

Paracetamol is a well established analgesic and antipyretic.

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors (predominantly alpha-adrenergic activity) producing nasal decongestion. Caffeine is the most active xanthine derivative in respect of stimulation of the central nervous system, producing a condition of wakefulness and increased mental activity.

5.2 Pharmacokinetic properties

Paracetamol is metabolized by the hepatic microsomal enzymes. It is rapidly and completely absorbed from the gastro-intestinal tract. Plasma concentration reaches a peak in half to one hour, the plasma half-life is one to three hours and it is uniformly distributed throughout the body.

Phenylephrine hydrochloride is irregularly absorbed from the gastro-intestinal tract. When injected intramuscularly it takes 10- *1* 5 minutes to act and subcutaneous and intramuscular injections are effective for about one hour. Intravenous injections are effective for about 20 minutes.

Caffeine is readily absorbed from the gastro-intestinal tract.

Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours.

Chlorphenamine is metabolized to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine.

Ascorbic acid is well absorbed from the gastrointestinal tract It is widely distributed to all tissues and is rapidly eliminated.

5.3 Preclinical safety data

Not applicable

6. Pharmaceutical particulars

6.1 List of excipients

Cold tablet contains: Microcrystalline Cellulose Powder, Starch, Colour Sunset Yellow, Gelatin, Methyl Paraben, Propyl Paraben, Sorbitol, Sodium Starch Glycolate, Colloidal Silicone Dioxide and Magnesium Stearate.

Vitamin C tablet contains: Starch, Lactose, Gelatin, Methyl Paraben, Propyl Paraben, Aerosil, Magnesium Stearate and Talcum.

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool dry place at temperature below 30°C. Store in the original packaging.

6.5 Nature and contents of container

Blister strip of 20 μm Aluminium foil and 250 μm PVC in a cardboard outer container. Pack sizes: 1 blister of 4 tablets each of cold tablet and Vitamin C.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorization holder

Me Cure Industries Limited

Plot 6 Block H, Debo Industries Compound,

Oshodi Industrial Scheme,

Oshodi,

Lagos,

Nigeria.

8.0 NAFDAC Registration Number: A4-1032