SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Wockhardt Cold Relief Capsules with Decongestant
Wockhardt Sinus Dual Relief Capsules
Health Essentials Cold Relief with Decongestant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol	300mg
Caffeine	25mg
Phenylephrine hydrochloride	5mg

Excipient(s) with known effect
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules

Hard gelatine green and yellow capsules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For relief of cold and flu, also acts as decongestant for catarrh, blocked nose and sinuses.

4.2 Posology and method of administration

Posology

ADULTS AND CHILDREN OVER 12 YEARS:

One to two capsules every four hours as required up to a maximum of eight capsules in any 24 hour period.

Maximum daily dose: eight capsules in divided doses in any 24 hour period.

Do not take continuously for more than 3 days without medical advice.

CHILDREN UNDER 12 YEARS:
Do not give to children under twelve years unless your doctor tells you to.

Method of administration
For oral administration. The capsules are to be taken with water.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine, phenylephrine or to any of the excipients listed in section 6.1.

Caffeine:

Hypersensitivity to caffeine.

Do not give to patients with a history of peptic ulceration.

Phenylephrine hydrochloride

- Hyper susceptible patients
- Hyperthyroidism
- Closed angle glaucoma
- Aneurysm
- Arteriosclerosis
- Phaeochromocytoma
- Hypertension
- Prostatic enlargement
- Cardiovascular disease
- Diabetes
- Concomitant use with other sympathomimetic decongestants
- Monoamine oxidase inhibitors, including moclobemide or within the last two weeks
- Tricyclic antidepressants
- Beta blockers

4.4 Special warnings and precautions for use

Paracetamol
Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with alcoholic liver disease. Paracetamol should be given with care to patients with alcoholic dependence.

Paracetamol is well tolerated by the majority of people with asthma. However, a small percentage of aspirin sensitive asthmatics are also sensitive to paracetamol. The likelihood of a reaction to paracetamol increases with a patient's level of sensitivity to aspirin (see section 4.8 Undesirable Effects).

Caution should be exercised when using paracetamol prior to (less than 72 hours) or concurrently with intravenous busulfan.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Caffeine
Care is advised in the administration of caffeine to patients with cardiac disease.

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

Phenylephrine
Care is advised in the administration of phenylephrine in patients with cardiovascular conditions such as hypertension, Prinzmetal's angina, thromboembolic disorders, following myocardial infarction or a history of ischaemic heart disease.
Phenylephrine should be used with caution in elderly patients.

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

The following warnings appear in the leaflet and on the label:

Label-

Contains paracetamol.
Do not take more medicine than the label tells you to. If you do not get better, talk to your doctor.
Do not take anything else containing paracetamol while taking this medicine.
Talk to a doctor at once if you take too much of this medicine, even if you feel well.

Leaflet-

Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.

Generally:

- Do not exceed the recommended dose.
- If symptoms persist consult your doctor.
- Do not give to children under twelve years except on advice from a doctor.
- Keep out of the reach and sight of children.

Patients should be advised not to take other paracetamol-containing products concurrently.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol

Alcohol:	Paracetamol should be given with care to patients with alcohol dependence (see Section 4.4).
Analgesics	Diflunisal increases blood concentrations of paracetamol.
Anion–exchange resins:	Absorption reduced by colestyramine; administration should be separated by at least 1 hour.
Antibacterials	Isoniazid may increase the risk of hepatotoxicity with therapeutic doses of paracetamol. Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).
Anticoagulants	The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Antiepileptics	Carbamazepine, phenobarbital, phenytoin and primidone can reduce the effects of paracetamol and increase the risk of hepatotoxicity. Paracetamol may increase lamotrigine

	metabolism.
Motility stimulants	The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.
Oral Contraceptives	Paracetamol is cleared from the body more quickly in women taking oral contraceptives and the analgesic effects may be reduced.
Uricosurics	Probenecid can reduce the loss of paracetamol from the body.

Caffeine

Antibacterials:	Some quinolone antibiotics, including enoxacin, pipemidic acid and ciprofloxacin can reduce the clearance of caffeine and prolong its plasma half-life.
Antidepressants	Fluvoxamine can reduce the clearance of caffeine and increase its stimulant and side effects.
Antiepileptics	Phenytoin may increase the clearance of caffeine.
Benzodiazepines	Caffeine can reduce the sedative effects of diazepam.
Disulfiram	May reduce the clearance of caffeine.
Lithium	Caffeine may increase the clearance of lithium.
Mexiletine	May reduce the clearance of caffeine.
Oestrogens and progestogens	Oral contraceptives or oestrogen replacement therapy may reduce the clearance of caffeine.
Phenylpropanolamine	Concomitant administration may increase blood pressure, resulting in hypertensive crises in a few susceptible individuals. Manic psychosis has occurred. Phenylpropanolamine can increase serum caffeine levels.
Theophylline	Concomitant administration can increase plasma theophylline and plasma caffeine levels.

Phenylephrine Hydrochloride

Phenylephrine should be used with caution in combination with the following drugs as interactions have been reported.

Adrenergic neurone blockers	May enhance the hypertensive effect of phenylephrine.
Atropine	There is an increased risk of hypertension when used with atropine.
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.
Digoxin and cardiac glycosides	Increase the risk of irregular heartbeat or heart attack
Ergot alkaloids	E.g. (ergotamine and methylsergide) increased risk of ergotism.
Monoamine oxidase inhibitors (including moclobemide)	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors (see contraindications).
Oxytocin	Potential increased risk of hypertension with oxytocin.
Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects (hypertensive effects).
Tricyclic antidepressants (e.g. amitriptyline)	There is an increased risk of hypertension when used with tricyclic antidepressants e.g. imipramine.

4.6 Fertility, pregnancy and lactation

Paracetamol:
Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use. A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast-feeding.

Caffeine:
Taken during pregnancy, it appears that the half-life of caffeine is prolonged. This is a possible contributing factor in hypermesis gravidarum. Caffeine crosses the placenta, and foetal blood and tissue levels similar to maternal concentrations are achieved. Cardiac dysrhythmias have been noted in the

foetuses and neonates of mothers consuming varying levels of caffeine during pregnancy. Decreased birth weight may be associated with maternal caffeine intake and cigarette smoking. Limited evidence suggests that high maternal caffeine intake may be associated with fetotoxicity including spontaneous abortion, however, other factors may have contributed to the findings. Decreased fertility may be associated with maternal caffeine intake. Caffeine intake during pregnancy should be kept to a minimum.

Caffeine is excreted in breast milk, but with moderate intake amounts are probably too low to be clinically significant. Regular intake of large amounts of caffeine by nursing mothers can affect the infant including irritability and poor sleeping patterns.

Phenylephrine Hydrochloride:
The safety of phenylephrine during pregnancy has not been established but there is some evidence suggesting a possible association of foetal abnormalities with first trimester exposure to phenylephrine. As an alpha-adrenoceptor stimulant, phenylephrine might provoke uterine changes, which can result in foetal asphyxia and/or foetal bradycardia. There is no information on the excretion of phenylephrine into breast milk; however no clinical problems have been documented.

In view of the above, this product should be avoided during pregnancy and lactation unless prescribed by a doctor.

4.7 Effects on ability to drive and use machines

Paracetamol:
Paracetamol has no or negligible influence on the ability to drive and use machines.

Caffeine:
Caffeine has no or negligible influence on the ability to drive and use machines.

Phenylephrine Hydrochloride:
May cause dizziness, if affected, do not drive or operate machinery.

4.8 Undesirable effects

a) Summary of the safety profile

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. The frequency of these adverse events is not known (cannot be estimated from available data).

Paracetamol:

Body System	**Adverse effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis These are not necessarily causally related to paracetamol.
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome, toxic epidermal necrolysis. A small percentage of aspirin-sensitive asthmatics are also sensitive to paracetamol. In such cases, the deterioration in respiratory function induced by paracetamol is milder and shorter than with aspirin (see section 4.4).
Metabolism and nutrition disorders	High anion gap metabolic acidosis
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction
Renal and urinary disorders	Nephropathy has been associated with chronic high dose use.

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

Caffeine:

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

Central Nervous system	Nervousness and anxiety Irritability, Restlessness and Excitability Dizziness

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 such as insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

Phenylephrine Hydrochloride:

The following adverse events have been observed in clinical trials and post-marketing reports 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, diarrhoea

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

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	Allergic reactions (e.g. rash, urticaria, allergic dermatitis). Hypersensitivity reactions – including that cross-sensitivity may occur with other sympathomimetics
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Paracetamol

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, phenobarbital, 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 overdose in the first 24 hours are sweating, 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, hypotension, cerebral oedema, coma and death. Prothrombin time may increase with deteriorating liver function. 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 arrythmias 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 eight 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 24 hours from ingestion should be discussed with the NPIS or a liver unit.

Caffeine

Symptoms: Large doses may cause restlessness, excitement, psychosis, muscle tremor, tinnitus, hyperglycaemia, hypokalaemia, diuresis, dehydration, tachycardia and extrasystoles. Emesis and convulsions may occur.

Treatment
No specific antidote. Elimination may be enhanced by repeated oral doses of activated charcoal. Symptomatic and supportive treatment.

Hypokalemia should be corrected by intravenous infusion of potassium chloride.

Intravenous diazepam or barbiturates may be used to control convulsions.

Phenylephrine Hydrochloride

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

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol

Paracetamol is an effective analgesic and antipyretic agent but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical simulation. Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of

prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems and unlike salicylates it does not cause gastric irritation or bleeding.

Caffeine

Acts on the central nervous system, on muscle including cardiac muscle and the kidneys. Its action on the central nervous system is mainly on the higher centres and produces a condition of wakefulness and increased mental activity. It facilitates the performance of muscular work and increases the total work that can be performed by a muscle. It may stimulate the respiratory centre, increasing the rate and depths of respiration. Its stimulant action on the medullary vasomotor centre is usually compensated by its peripheral vasodilator effect on the arterioles, so that the blood pressure usually remains unchanged. The diuretic action of caffeine has been accounted for in many ways. It may increase renal blood flow and glomerular filtration rate, but its main action may be due to the regulation of the normal tubular absorption. It is less effective as a diuretic than theobromine, which has less central stimulating effect and does not cause insomnia. The xanthines are rarely of great value in promoting increased renal function when this is depressed. Caffeine is claimed to enhance the action of ergotamine and is frequently given with ergotamine in the treatment of migraine.

Phenylephrine Hydrochloride

It is a sympathomimetic with many direct effects on adrenergic receptors. It has predominantly alpha-adrenergic activity and is without stimulating effects on the central nervous system. Its pressor activity is weaker than that of noradrenaline but of longer duration. After injection it produces peripheral vasoconstriction and increased arterial pressure; it also causes reflex bradycardia. It reduces blood flow to the skin and to the kidney. It has been used in the treatment of hypotensive states e.g. circulatory failure, spinal anaesthesia; or hypertension following the use of chlorpromazine and other phenothiazines. Phenylephrine hydrochloride may be given in preparations for the relief of nasal congestion. Locally it is used as a nasal decongestant in rhinitis and sinusitis. In opthalmology, phenylephrine hydrochloride is employed as a mydriatic and conjunctival decongestant. In open angle glaucoma, it is sometimes used to lower intra-ocular pressure temporarily.

There is no pharmacological information with regard to the compound preparation. However, there is no evidence to suggest that any of the actions described above are in any way impinged upon by the other active drugs.

5.2 Pharmacokinetic properties

Paracetamol

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma metabolised in the liver (90-95%) and excreted in the urine, mainly as the glucuronide concentrations occurring about 30 minutes to 2 hours after ingestion. It is and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1-4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) (which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione) may accumulate following paracetamol overdosage and cause liver damage. The time to peak concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

Caffeine

It is absorbed readily after oral, rectal, or parenteral administration but absorption from the gastro-intestinal tract may be erratic. There is little evidence of accumulation in any particular tissue. Caffeine passes readily into the central nervous system and into saliva. Concentrations have also been detected in breast milk. It is metabolised almost completely and is excreted in the urine as 1-methyluric acid, 1-methylxanthine and other metabolites with only about 1% unchanged.

Phenylephrine Hydrochloride

It has reduced bioavailability from the gastro-intestinal tract owing to first pass metabolism by monoamine oxidase in the gut and liver. When injected intramuscularly, it takes 10-15 minutes to act and subcutaneous and intramuscular injections are effective for about an hour. Intravenous injections are effective for about 20 minutes.

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch

Colloidal anhydrous silica

Magnesium stearate

Capsule contains:

Gelatin

Colours: E131, E171, E172 and E104

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a dry place below 25°C.

Protect from light.

6.5 Nature and contents of container

Blister packs:

8, 10, 12, 16 (GSL)

20, 24, 28, 30, 32 (Pharmacy)

Blister strips consist of a 35gsm paper/9µ soft tempered aluminium foil lid and 250µ PVC film base in cartons.

6.6 Special precautions for disposal

Return any leftover capsules to the pharmacist

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd

Ash Road North

Wrexham LL13 9UF

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0173

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

02/05/2025