Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Day Nurse Capsules Paracetamol 500mg Pseudoephedrine Hydrochloride 30mg Pholcodine 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients	Quantity mg/cap
Paracetamol	500
Pseudoephedrine hydrochloride	30
Pholcodine	5

Also contains Allura Red (E129).

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard (Capsule)
The capsule has an orange cap and yellow body, printed with an identifier in black ink. It contains a white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of the major symptoms of colds and influenza.

4.2 Posology and method of administration

For oral administration only. To be taken during the day.
Adults and children aged 16 years and over: Two capsules every four to six hours, up to a maximum of 4 doses (8 capsules) in 24 hours if needed. Other products containing paracetamol may be taken at night, but the total daily dose of paracetamol must not exceed 4000mg (including this product) in any 24 hour period.

Maximum daily dose: 8 capsules for a total of 4000 mg Paracetamol, 240 mg Pseudoephedrine, 40 mg Pholcodine

Children under 16 years: Not to be given to children under 16 years of age.
Elderly: There is no specific requirement for dosage reduction in the elderly. Maximum duration of continued use without medical advice: 7 days. Minimum dosing interval: 4 hours.
Do not exceed the stated dose.

The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

Should not be used with other paracetamol containing products, decongestants or cough and cold medicines. If symptoms persist consult a doctor.
Hepatic Impairment: Patients who have been diagnosed with hepatic impairment must seek medical advice before taking this medication.
Renal Impairment: Pseudoephedrine is primarily excreted renally. This product should not be used by those with severe renal impairment and should be used with caution in those with mild to moderate renal impairment.

4.3 Contraindications

This product is contraindicated in people:

- With a hypersensitivity to paracetamol, pseudoephedrine, pholcodine or any of the excipients.
- With hypertension of either 180 mm Hg systolic or 120 mm Hg diastolic, or higher, or coronary artery disease.
- With, or at risk of developing, respiratory failure (e.g. those with chronic obstructive airways disease or pneumonia) or those with bronchiolitis or bronchiectasis, due to sputum retention.
- Who are receiving other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like medicines).
- Who are receiving Monoamine Oxidase Inhibitors (MAOIs), or for two weeks after stopping a MAOI drug.
- who are taking oxazolidinone class of antibiotics (including furazolidone and linezolid)
- With severe renal impairment.
- Children under 16 years of age.

4.4 Special warnings and precautions for use

Contains paracetamol. Do not use with any other paracetamol-containing products, antihistamines or cold and flu medicines. 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.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Label:
Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Leaflet or combined label/leaflet:
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of irreversible, serious liver damage.

Caution should be exercised:

- In patients taking beta-blockers or other antihypertensives, or vasoconstrictive agents such as ergot alkaloids
- in patients over the age of 60 years. Patients in this age group are at greater risk of adverse reactions due to decreased renal function, and unwanted reactions when using oral sympathomimetic agents.
- when planning surgery. Acute perioperative hypertension may occur if volatile halogenated anaesthetics are used simultaneously with indirect sympathomimetic agents. It is recommended that pseudoephedrine treatment is stopped 24 hours before anaesthesia.
- In patients taking other CNS depressants (including alcohol).

Medical advice should be sought before taking this medicine in patients with:

- mild to moderate kidney impairment
- hepatic impairment. Underlying liver disease increases the risk of paracetamol- related liver damage
- glutathione depleted due to metabolic deficiencies
- cardiovascular disease,
- arrhythmias,
- hypertension,
- hyperthyroidism,
- prostatic enlargement,
- diabetes,
- glaucoma,
- psychosis

- phaeochromocytoma,
- or in those with chronic or persistent cough, asthma, or where cough is accompanied by excessive secretions.
- taking tricyclic antidepressants

There have been reports of ischaemic colitis and ischaemic optic neuropathy with pseudoephedrine. The product should be discontinued immediately, and medical advice should be sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop and if sudden onset of severe headache, nausea, vomiting, and visual disturbances develop such as sudden loss of vision or decreased visual acuity such as scotoma occurs.

These may be indicative of posterior reversible encephalopathy syndrome(PRES)/reversible cerebral vasoconstriction syndrome (RCVS). There have been rare cases of PRES/RCVS reported with sympathomimetic drugs, including pseudoephedrine. Most cases improved or resolved within a few days following appropriate treatment

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of Day Nurse Capsules should be discontinued, and appropriate measures taken if needed.

Severe cutaneous adverse reactions (SCARs) including acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in patients treated with Day Nurse, most likely in the first week. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, Day Nurse should be discontinued immediately.

Pholcodine may enhance the CNS effects of alcohol or other CNS depressants.

Pseudoephedrine content of this product may result in a positive reaction during antidoping control tests.

If symptoms persist medical advice must be sought.
Do not exceed the stated dose.
Do not take with decongestants or cough medicines. Keep out of the sight and reach of children.

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 cholestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol-containing products with increased risk of bleeding; occasional doses have no significant effect.

Concomitant administration of pseudoephedrine hydrochloride-containing products and MAOIs (or within two weeks of stopping of MAOI) may lead to hypertensive crisis.

The oxazolidinone class of antibiotics (including furazolidone and linezolid) are known to cause a dose-related inhibition of monoamine oxidase. Therefore, they should not be taken with Day Nurse Capsules as there is a potential to cause hypertensive crisis

Concomitant use of this medication with sympathomimetic agents (such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine-like medicines) which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure.

Pseudoephedrine-containing products may antagonise the effect of certain classes of antihypertensives (e.g. beta blockers, methyl-dopa, reserpine, debrisoquine guanethidine) and increase the possibility of arrhythmias in digitalised patients.

Concomitant administration with vasoconstrictive agents (including ergot derivatives such as bromocriptine, pergolide, lisuride, cabergoline, ergotamine, dihydroergotamine and methylsergide) may cause an increased risk of ergotism

Pholcodine may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillizers (phenothiazines and tricyclic antidepressants).
Pseudoephedrine may interact with halogenated anaesthetics
Pholcodine may predispose patients to developing anaphylaxis with neuromuscular blocking agents.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

4.6 Fertility, pregnancy and lactation

Pregnancy
This product should not be used in pregnancy without medical advice.
Safe use of pseudoephedrine and pholcodine in pregnancy has not been established despite widespread use over many years.
Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, caution should be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus. If used, the lowest effective dose and shortest duration of treatment should be considered.

Lactation
This product should not be used whilst breastfeeding without medical advice, and only if 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.

Although paracetamol is excreted in breast milk, human studies with paracetamol have not identified any risk to lactation or the breast-fed offspring.
Pseudoephedrine is excreted in breast milk in small amounts but the effect of this on breast fed infants is unknown.
It is not known whether pholcodine is excreted into 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/labelled dose and considered attributable are tabulated below by System Organ Class and frequency.

The following convention has been utilised for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000)

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

Paracetamol

Body System	**Undesirable Effect**	**Frequency**
Blood and Lymphatic System Disorders	Thrombocytopaenia	Very rare
Immune System Disorders	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Toxic Epidermal Necrolysis and Steven Johnson syndrome.	Very rare
Respiratory, Thoracic and Mediastinal Disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary Disorders	Hepatic dysfunction	Very rare

Pseudoephedrine

Body System	Undesirable Effect	Frequency
Psychiatric Disorders	Nervousness, insomnia	Common
	Agitation, restlessness	Uncommon
	Hallucinations (particularly in children)	Rare
	Anxiety	Unknown
Nervous System Disorders	Dizziness	Common
	Headache, tremor	Unknown
Cardiac Disorders	Tachycardia, palpitations	Rare
Vascular Disorders	Increased blood pressure*	Rare
Gastrointestinal disorders	Vomiting, dry mouth, nausea	Common
	Ischaemic colitis	Unknown
Skin and Subcutaneous Tissue Disorders	Rash, allergic dermatitis**	Rare
	Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP)	Unknown
Renal and Urinary Disorders	Dysuria, urinary retention***	Uncommon
Eye disorders	Ischaemic optic neuropathy	Unknown

*Increases in systolic blood pressure have been observed. At therapeutic doses, the effects of pseudoephedrine on blood pressure are not clinically significant.
**A variety of allergic skin reactions, with or without systemic features such as bronchospasm and angioedema have been reported following use of pseudoephedrine. ***Urinary retention is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Pholcodine

Body System	Undesirable Effect	Frequency
Immune System Disorders	Hypersensitivity reactions including skin rashes, angioedema, anaphylaxis	Rare
Gastrointestinal disorders	Nausea, vomiting	Common
Skin and subcutaneous tissue disorders	Acute generalised exanthematous pustulosis (see section 4.4)	Unknown

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms and Signs
Paracetamol
Paracetamol overdose may cause liver failure, which may require liver transplant or lead to death.
There is a risk of poisoning with paracetamol particularly in elderly subjects, young children, patients with liver disease, cases of chronic alcoholism and in patients with chronic malnutrition. Overdosing may be fatal in these cases. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.
Overdose of paracetamol in a single administration in adults or in children can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may cause coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration. Liver damage is likely in adults who have taken more than the recommended amounts of paracetamol. It is considered that excess

quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue. Some patients may be at increased risk of liver damage from paracetamol toxicity. Risk Factors include: 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.
- Regularly consumes ethanol in excess of recommended amounts.
- Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Emergency Procedure:

Immediate transfer to hospital.

Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion. Administration of activated charcoal should be considered if>150mg/kg paracetamol has been taken within 1 hour.

The antidote N-acetylcysteine, should be administered as soon as possible in accordance with

National treatment guidelines

Symptomatic treatment should be implemented.

Pseudoephedrine
Pseudoephedrine overdose may result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement, restlessness, hallucinations, hypertension and arrhythmias. In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to extracellular to intracellular shifts in potassium.

Treatment:
Treatment should consist of standard supportive measures. Beta blockers should reverse the cardiovascular complications and the hypokalemia.

Pholcodine
Symptoms of pholcodine overdose may include nausea, drowsiness, restlessness, excitement and ataxia. Central nervous system depression, including respiratory depression, may develop but is unlikely to be severe unless other sedative agents have been co-ingested, including alcohol, or the overdose is very large.
Treatment:
Supportive and symptomatic care should be provided as required. If overdose is severe, naloxone may be helpful, particularly for patients with respiratory depression.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and antipyretic actions.
Pseudoephedrine is a sympathomimetic agent with both direct and indirect effects on adrenergic receptors. Pholcodine is a cough suppressant with little analgesic activity.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after oral administration. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma protein binding is negligible at usual therapeutic concentrations. Paracetamol is metabolised predominantly in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as

glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half life varies from about 1 to 4 hours.

Pseudoephedrine is rapidly and completely absorbed from the gastrointestinal tract after oral administration, with no presystemic metabolism. Peak plasma levels are achieved after 1-2 hours. The plasma half-life varies from 4.3-7.0 hours in adults. No protein binding data are available.
There is little metabolism of pseudoephedrine in man with approximately 90% being excreted in the urine unchanged. Approximately 1% is eliminated by hepatic metabolism, by N- demethylation to norpseudoephedrine.
As a weak base, the extent of renal excretion is dependent on urinary pH. At low urinary pH, tubular reabsorption is minimal and urine flow rate will not influence clearance of the drug. At high pH (>7.0), pseudoephedrine is extensively reabsorbed in the renal tubule and renal clearance will depend on urine flow rate.

Pholcodine is rapidly absorbed after oral administration and maximum plasma concentrations are attained at about 4-8 hours. The elimination half life ranges from 32 to 50 hours. The drug has a large volume of distribution and is only 23.5% protein bound. Pholcodine is metabolised in the liver but undergoes little conjugation with glucuronide and sulphate. Approximately 25-50% of the drug is recovered unchanged in the urine.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included.

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

Capsules contents
Sodium laurilsulfate
Sodium starch glycollate
Magnesium stearate

Hard gelatin capsule
(containing: Gelatin, Quinoline yellow (E104), Allura red (E129), Titanium dioxide (El71).)

Black print ink
(containing: Shellac, black iron oxide (E172), propylene glycol, ammonium hydroxide.)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package.

6.5 Nature and contents of container

PVC/PVdC blister tray with aluminium foil lid.
Pack sizes: 8, 10, 12, 16, 20 or 24 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Not applicable.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

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