Public Assessment Report

Decentralised Procedure

Vicks Cold & Flu Care Daymed Complete Hot Drink
Vicks Cold & Flu Care Daymed Plus Hot Drink

Paracetamol, Phenylephrine Hydrochloride, Guaifenesin

UK/H/1191&1588/01/DC

UK licence no: PL 00129/0349-50

Applicant: Procter & Gamble
(Health & Beauty Care) Limited
Vicks Cold & Flu Care Daymed Complete Hot Drink

Vicks Cold & Flu Care Daymed Plus Hot Drink

LAY SUMMARY

On 19th February 2010, the MHRA granted Procter & Gamble (Health & Beauty Care) Limited Marketing Authorisations (licences) for the medicinal products Vicks Cold and Flu Daymed complete Hot Drink and Vicks Cold and Flu Care Daymed Plus Hot Drink (PL 00129/0349-50). These are General Sale Licences (GSL) used in the treatment of short term symptomatic relief of mild to moderate pain, fever, nasal congestion with an expectorant effect on chesty cough, associated with colds, chills and influenza.

Vicks Cold and Flu Daymed complete Hot Drink and Vicks Cold and Flu Care Daymed plus Hot Drink are designed for the relief of symptoms of colds and flu. They contain three active ingredients:

- Paracetamol is a well known pain killer (analgesic). It is effective against aches and pains including headache and sore throat and can also reduce fever (antipyretic).
- Guaifenesin (an expectorant) loosens phlegm which helps relieve chesty coughs.
- Phenylephrine hydrochloride (a nasal decongestant) reduces swelling in the passages of the nose and so relieves a blocked nose.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Vicks Cold and Flu Daymed complete Hot Drink and Vicks Cold and Flu Care Daymed plus Hot Drink outweigh the risks, hence Marketing Authorisations have been granted.
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## Module 1

| **Product Name** | Vicks Cold & Flu Care Daymed Complete Hot Drink  
| | Vicks Cold & Flu Care Daymed Plus Hot Drink |
| **Type of Application** | Hybrid application, Article 10.3 |
| **Active Substance** | Paracetamol, Phenylephrine hydrochloride, Guaifenesin |
| **Form** | Powder for oral solution |
| **Strength** | Paracetamol 500 mg  
| | Phenylephrine hydrochloride 10 mg  
| | Guaifenesin 200mg |
| **MA Holder** | Procter & Gamble (Health & Beauty Care) Limited  
| | The Heights  
| | Brooklands, Weybridge  
| | Surrey KT 13 0XP  
| | United Kingdom |
| **RMS** | UK |
| **CMS** | AT, CZ, DE, ES, HU, IE, IT, PL, PT |
| **Procedure Number** | UK/H/1191&1588/01/DC |
| **Timetable** | Day 210 – 19th January 2010 |
Module 2
Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Vicks Cold & Flu Care Daymed Complete Hot Drink
Paracetamol 500mg, Phenylephrine HCl 10mg, Guaifenesin 200mg
Powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One sachet contains:
500mg Paracetamol
200mg Guaifenesin
10mg Phenylephrine hydrochloride
Excipients:
Sucrose 2000 mg
Aspartame 6 mg
Sodium 157 mg
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Powder for oral solution, sachet
Off-white powder

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Short term symptomatic relief of mild to moderate pain, fever, nasal congestion with an expectorant effect on chesty cough, associated with colds, chills and influenza.

4.2 Posology and method of administration
Dissolve the contents of one sachet in a standard mug of hot, but not boiling, water (approx. 250ml). Allow to cool to a drinkable temperature.

Adults, the Elderly and children aged 12 years and over: One sachet
Repeat every four hours as required, but do not exceed four doses (sachets) in any 24 hours.
Do not give to children under 12 years, except on medical advice.
Do not give to patients with hepatic or severe renal impairment (see Section 4.3).
Seek medical advice if symptoms persist for more than 3 days

4.3 Contraindications
Hypersensitivity to paracetamol, guaifenesin, phenylephrine hydrochloride or any of the other ingredients.
Hepatic or severe renal impairment
Hypertension
Hyperthyroidism,
Diabetes,
Heart disease,
Narrow-angle glaucoma
Porphyria
Use in patients taking tricyclic antidepressants
Use in patients who are currently taking or have taken monoamine oxidase inhibitors (MAOIs) within the last 2 weeks
Use in patients taking beta-blocking drugs
Use in patients who are currently taking other sympathomimetic drugs
Children under 12 years

4.4 Special warnings and precautions for use
Long term use of the product is not recommended.
Patients should be advised not to take with other paracetamol-containing products or other products containing the same active ingredients as this preparation. They should also be advised not to take other cough, cold or decongestant products concurrently, or alcohol. The physician or pharmacist
should check that sympathomimetic-containing preparations are not simultaneously administered by several routes, i.e. orally and topically (nasal, aural and eye preparations).

This medicine should only be recommended if all symptoms (pain and/or fever, nasal congestion and chesty cough) are present.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Use with caution in patients receiving digitalis, beta-adrenergic blockers, methyldopa or other anti-hypertensive agents (see section 4.5)

Use with caution in patients with prostatic hypertrophy as they may be susceptible to urinary retention.

Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines.

Use in patients with Raynaud’s phenomenon.

Contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Contains sodium 157 mg per dose. To be taken into consideration by patients on a controlled sodium diet.

Contains aspartame (E951) a source of phenylalanine. May be harmful for people with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction

The hepatotoxicity of paracetamol may be potentiated by excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

Isoniazid reduces the paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver.

Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors. Phenylephrine may adversely interact with sympathomimetic agents and may reduce the efficacy of beta-blocking drugs, methyldopa and other antihypertensive drugs (see section 4.4). Conditions where these drugs are used are contraindications for the product.

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.

Pharmacological interactions involving paracetamol with a number of other drugs have been reported. These are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Salicylates/aspirin may prolong the elimination t1/2 of paracetamol.

Paracetamol may decrease the bioavailability of lamotrigine, with possible reduction of its effect, due to a possible induction of its metabolism in the liver.

There is a possibility that digitalis may sensitise the myocardium to effects of sympathomimetic drugs.

Paracetamol may affect phosphotungstate uric acid tests and blood sugar tests.

4.6 Pregnancy and lactation

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.
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. There are limited data on the use of phenylephrine in pregnant women. Vasoconstriction of uterine vessels and reduced uterine blood flow associated with use of phenylephrine may result in foetal hypoxia. Until more information is available, use of phenylephrine should be avoided during pregnancy, unless considered essential by the physician.

There are no data available on whether phenylephrine is released into breast milk and no reports on the effects of phenylephrine on the nursing infant. Until more data are available, use of phenylephrine should be avoided in lactating women, unless considered essential by the physician.

The safety of guaifenesin in pregnancy and lactation has not been fully established. The product should only be used in pregnancy when considered essential by the doctor.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. When performing these activities, the possibility of adverse effects, such as dizziness and confusion should be taken into account.

4.8 Undesirable effects
The frequency of occurrence of undesirable effect is usually classified as follows:

Very common (> 1/10)
Common (> 1/100 to < 1/10)
Uncommon (> 1/1,000 to < 1/100)
Rare (> 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (incidence cannot be assessed on the basis of the available data).

Cardiac disorders: Phenylephrine may rarely be associated with tachycardia (≥1/10,000 to ≤1 in 1000).

Blood and lymphatic system disorders; Very rarely (<1 in 10,000) blood dyscrasias e.g. thrombocytopenia, agranulocytosis, haemolytic anaemia, neutropenia, leucopenia, pancytopenia have been reported with paracetamol, but these were not necessarily causally related.

Nervous system disorders: As with other sympathomimetic amines insomnia, nervousness, tremor, anxiety, restlessness, confusion, irritability and headache may rarely occur (≥1/10,000 to ≤1 in 1000). Headache and dizziness are also known to occur rarely with Guaifenesin (≥1/10,000 to ≤1 in 1000).

Gastrointestinal disorders: Anorexia, nausea and vomiting are common with sympathomimetics (≥1 in 100 to ≤1 in 10) and may occur with phenylephrine. Gastrointestinal discomfort, nausea, vomiting and diarrhoea are the most common side effects associated with Guaifenesin but these occur rarely (≥1/10,000 to ≤1 in 1000). Gastro-intestinal effects of paracetamol are very rare but there have been reports of acute pancreatitis after ingestion of above normal dosage.

Renal and urinary disorders: Interstitial nephritis has been reported incidentally after prolonged use of high doses of paracetamol.

Skin and subcutaneous disorders: Hypersensitivity including skin rash and urticaria may occur rarely (≥1/10,000 to ≤1 in 1000) with paracetamol.

Vascular disorders: High blood pressure with headache, vomiting and palpitations may occur rarely (≥1/10,000 to ≤1 in 1000) with phenylephrine.

Immune system disorders: There are rare reports (≥1/10,000 to ≤1 in 1000) of allergic or hypersensitivity reactions with both phenylephrine and paracetamol, including skin rashes, urticaria, anaphylaxis and bronchospasm.

Hepatobiliary disorders: Rarely (> 1/10,000 to < 1/1000) Liver function test abnormal (increase in hepatic transaminases).
4.9  **Overdose**

**PARACETAMOL**

There is a risk of poisoning, particularly in elderly patients, young children, in patients with liver disease, in case of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal in these cases.

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 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 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.

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 local National Poison Centre or a liver unit.

**PHENYLEPHRINE HYDROCHLORIDE**

Symptoms of phenylephrine overdose include irritability, headache, an increase in blood pressure and associated reflex bradycardia and arrhythmias. Raised blood pressure should be treated with an alpha receptor antagonist such as intravenous phentolamine. Reduction of blood pressure should, by reflex mechanism, increase the heart rate but, if necessary, this can be facilitated by the administration of atropine.

**GUAFENESIN**

Mild to moderate overdose may cause dizziness and gastrointestinal disturbances. Very high doses may produce excitation, confusion and respiratory depression. Urinary calculi have been reported in patients consuming large quantities of preparations containing guaifenesin. Treatment is symptomatic, involving gastric lavage and general supportive measures.

5  **PHARMACOLOGICAL PROPERTIES**

5.1  **Pharmacodynamic properties**

Pharmacotherapeutic Group: Other cold combination preparations

ATC code: R05X
Paracetamol has both analgesic and antipyretic activity which is mediated principally through its inhibition of prostaglandin synthesis in the central nervous system. Guaifenesin has an expectorant action. Expectorants are believed to alleviate cough discomfort by stimulating receptors in the gastric mucosa that initiate a reflex secretion of respiratory tract fluid, thereby increasing the volume and decreasing the viscosity of bronchial secretions. This facilitates removal of mucus and reduces irritation to the bronchial tissue. Phenylephrine hydrochloride mainly acts directly on adrenergic receptors. It has predominantly α-adrenergic activity and is without significant stimulating effects on the central nervous system at usual doses. It has recognised decongestant activity and acts by vasoconstriction to reduce oedema of the nasal mucosa.

The active ingredients are not known to cause sedation.

5.2 Pharmacokinetic properties
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are attained 10-60 minutes following oral dosing. Paracetamol is primarily metabolised in the liver via three pathways: glucuronidation, sulphation and oxidation. It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life ranges from 1 to 3 hours.

Guaifenesin is rapidly absorbed from the gastrointestinal tract after oral administration with maximum blood levels occurring within 15 minutes of administration. It is rapidly metabolised in the kidneys by oxidation to β-(2 methoxy-phenoxy) lactic acid, which is excreted in the urine. The elimination half life is one hour.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate. Peak plasma levels occur between 1 and 2 hours and the plasma half life ranges from 2 to 3 hours.

5.3 Preclinical safety data
Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use in the product and which have not already been mentioned elsewhere in this Summary.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sucrose
Citric Acid
Tartaric Acid
Sodium Cyclamate
Sodium Citrate
Aspartame (E951)
Acesulfame Potassium (E950)
Powdered Menthol
Lemon Flavour
Lemon Juice Flavour
Quinoline Yellow (E104)

6.2 Incompatibilities
None known

6.3 Shelf life
3 years

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
The sachet laminate comprises:
6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER
Procter & Gamble (Health & Beauty Care) Ltd.
The Heights
Brooklands
Weybridge
Surrey
KT13 0XP
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 00129/0349

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19/02/2010

10 DATE OF REVISION OF THE TEXT
19/02/2010
1 NAME OF THE MEDICINAL PRODUCT
Vicks Cold & Flu Care Daymed Plus Hot Drink
Paracetamol 500mg, Phenylephrine HCl 10mg, Guaifenesin 200mg
Powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One sachet contains:
500mg Paracetamol
200mg Guaifenesin
10mg Phenylephrine hydrochloride
Excipients:
Sucrose 2000 mg
Aspartame 6 mg
Sodium 157 mg
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Powder for oral solution, sachet
Off-white powder

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Short term symptomatic relief of mild to moderate pain, fever, nasal congestion with an expectorant effect on chesty cough, associated with colds, chills and influenza.

4.2 Posology and method of administration
Dissolve the contents of one sachet in a standard mug of hot, but not boiling, water (approx. 250ml). Allow to cool to a drinkable temperature.

Adults, the Elderly and children aged 12 years and over: One sachet
Repeat every four hours as required, but do not exceed four doses (sachets) in any 24 hours.
Do not give to children under 12 years, except on medical advice.
Do not give to patients with hepatic or severe renal impairment (see Section 4.3).
Seek medical advice if symptoms persist for more than 3 days

4.3 Contraindications
Hypersensitivity to paracetamol, guaifenesin, phenylephrine hydrochloride or any of the other ingredients.
Hepatic or severe renal impairment
Hypertension
Hyperthyroidism,
Diabetes,
Heart disease,
Narrow-angle glaucoma
Porphyria
Use in patients taking tricyclic antidepressants
Use in patients who are currently taking or have taken monoamine oxidase inhibitors (MAOIs) within the last 2 weeks
Use in patients taking beta-blocking drugs
Use in patients who are currently taking other sympathomimetic drugs
Children under 12 years

4.4 Special warnings and precautions for use
Long term use of the product is not recommended.
Patients should be advised not to take with other paracetamol-containing products or other products containing the same active ingredients as this preparation. They should also be advised not to take other cough, cold or decongestant products concurrently, or alcohol. The physician or pharmacist should check that sympathomimetic-containing preparations are not simultaneously administered by several routes, i.e. orally and topically (nasal, aural and eye preparations).
PAR Vicks Cold & Flu Care Daymed Complete Hot Drink and Vicks Cold &
Flu Care Daymed Plus Hot Drink

This medicine should only be recommended if all symptoms (pain and/or fever, nasal congestion and chesty cough) are present.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
Use with caution in patients receiving digitalis, beta-adrenergic blockers, methyldopa or other anti-hypertensive agents (see section 4.5)
Use with caution in patients with prostatic hypertrophy as they may be susceptible to urinary retention. Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines.
Use in patients with Raynaud’s phenomenon.

Contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.
Contains sodium 157 mg per dose. To be taken into consideration by patients on a controlled sodium diet.
Contains aspartame (E951) a source of phenylalanine. May be harmful for people with phenylketonuria.

4.5 Interaction with other medicinal products and other forms of interaction
The hepatotoxicity of paracetamol may be potentiated by excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdose.

Isoniazid reduces the paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver.

Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors. Phenylephrine may adversely interact with sympathomimetic agents and may reduce the efficacy of beta-blocking drugs, methyldopa and other antihypertensive drugs (see section 4.4). Conditions where these drugs are used are contraindications for the product.

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.

Pharmacological interactions involving paracetamol with a number of other drugs have been reported. These are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Salicylates/aspirin may prolong the elimination t1/2 of paracetamol.

Paracetamol may decrease the bioavailability of lamotrigine, with possible reduction of its effect, due to a possible induction of its metabolism in the liver

There is a possibility that digitalis may sensitise the myocardium to effects of sympathomimetic drugs.

Paracetamol may affect phosphotungstate uric acid tests and blood sugar tests

4.6 Pregnancy and lactation
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.
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. There are limited data on the use of phenylephrine in pregnant women. Vasoconstriction of uterine vessels and reduced uterine blood flow associated with use of phenylephrine may result in foetal hypoxia. Until more information is available, use of phenylephrine should be avoided during pregnancy, unless considered essential by the physician.

There are no data available on whether phenylephrine is released into breast milk and no reports on the effects of phenylephrine on the nursing infant. Until more data are available, use of phenylephrine should be avoided in lactating women, unless considered essential by the physician.

The safety of guaifenesin in pregnancy and lactation has not been fully established. The product should only be used in pregnancy when considered essential by the doctor.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. When performing these activities, the possibility of adverse effects, such as dizziness and confusion should be taken into account.

4.8 Undesirable effects

The frequency of occurrence of undesirable effect is usually classified as follows:

- Very common (> 1/10)
- Common (> 1/100 to < 1/10)
- Uncommon (> 1/1,000 to < 1/100)
- Rare (> 1/10,000 to < 1/1,000)
- Very rare (< 1/10,000)
- Not known (incidence cannot be assessed on the basis of the available data).

Cardiac disorders: Phenylephrine may rarely be associated with tachycardia (≥1/10,000 to ≤1 in 1000).

Blood and lymphatic system disorders: Very rarely (<1 in 10,000) blood dyscrasias e.g. thrombocytopenia, agranulocytosis, haemolytic anaemia, neutropenia, leucopenia, pancytopenia have been reported with paracetamol, but these were not necessarily causally related.

Nervous system disorders: As with other sympathomimetic amines insomnia, nervousness, tremor, anxiety, restlessness, confusion, irritability and headache may rarely occur (≥1/10,000 to ≤1 in 1000). Headache and dizziness are also known to occur rarely with Guaifenesin (≥1/10,000 to ≤1 in 1000).

Gastrointestinal disorders: Anorexia, nausea and vomiting are common with sympathomimetics (≥1 in 100 to ≤1 in 10) and may occur with phenylephrine. Gastrointestinal discomfort, nausea, vomiting and diarrhoea are the most common side effects associated with Guaifenesin but these occur rarely (≥1/10,000 to ≤1 in 1000). Gastro-intestinal effects of paracetamol are very rare but there have been reports of acute pancreatitis after ingestion of above normal dosage.

Renal and urinary disorders: Interstitial nephritis has been reported incidentally after prolonged use of high doses of paracetamol.

Skin and subcutaneous disorders: Hypersensitivity including skin rash and urticaria may occur rarely (≥1/10,000 to ≤1 in 1000) with paracetamol.

Vascular disorders: High blood pressure with headache, vomiting and palpitations may occur rarely (≥1/10,000 to ≤1 in 1000) with phenylephrine.

Immune system disorders: There are rare reports (≥1/10,000 to ≤1 in 1000) of allergic or hypersensitivity reactions with both phenylephrine and paracetamol, including skin rashes, urticaria, anaphylaxis and bronchospasm.

Hepatobiliary disorders: Rarely (> 1/10,000 to < 1/1000) Liver function test abnormal (increase in hepatic transaminases).
4.9 Overdose
PARACETAMOL
There is a risk of poisoning, particularly in elderly patients, young children, in patients with liver disease, in case of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal in these cases.

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 overdosage 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 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.

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 local National Poison Centre or a liver unit.

PHENYLEPHRINE HYDROCHLORIDE
Symptoms of phenylephrine overdose include irritability, headache, an increase in blood pressure and associated reflex bradycardia and arrhythmias. Raised blood pressure should be treated with an alpha receptor antagonist such as intravenous phentolamine. Reduction of blood pressure should, by reflex mechanism, increase the heart rate but, if necessary, this can be facilitated by the administration of atropine.

GUAIFENESIN
Mild to moderate overdose may cause dizziness and gastrointestinal disturbances. Very high doses may produce excitation, confusion and respiratory depression. Urinary calculi have been reported in patients consuming large quantities of preparations containing guaifenesin. Treatment is symptomatic, involving gastric lavage and general supportive measures.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Other cold combination preparations
ATC code: R05X
Paracetamol has both analgesic and antipyretic activity which is mediated principally through its inhibition of prostaglandin synthesis in the central nervous system. Guaiifenesin has an expectorant action. Expectorants are believed to alleviate cough discomfort by stimulating receptors in the gastric mucosa that initiate a reflex secretion of respiratory tract fluid, thereby increasing the volume and decreasing the viscosity of bronchial secretions. This facilitates removal of mucus and reduces irritation to the bronchial tissue. Phenylephrine hydrochloride mainly acts directly on adrenergic receptors. It has predominantly α-adrenergic activity and is without significant stimulating effects on the central nervous system at usual doses. It has recognised decongestant activity and acts by vasoconstriction to reduce oedema of the nasal mucosa.

The active ingredients are not known to cause sedation.

### 5.2 Pharmacokinetic properties
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are attained 10-60 minutes following oral dosing. Paracetamol is primarily metabolised in the liver via three pathways: glucuronidation, sulphation and oxidation. It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life ranges from 1 to 3 hours.

Guaiifenesin is rapidly absorbed from the gastrointestinal tract after oral administration with maximum blood levels occurring within 15 minutes of administration. It is rapidly metabolised in the kidneys by oxidation to β-(2 methoxy-phenoxy) lactic acid, which is excreted in the urine. The elimination half life is one hour.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate. Peak plasma levels occur between 1 and 2 hours and the plasma half life ranges from 2 to 3 hours.

### 5.3 Preclinical safety data
Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use in the product and which have not already been mentioned elsewhere in this Summary.

### 6 PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients
- Sucrose
- Citric Acid
- Tartaric Acid
- Sodium Cyclamate
- Sodium Citrate
- Aspartame (E951)
- Acesulfame Potassium (E950)
- Powdered Menthol
- Lemon Flavour
- Lemon Juice Flavour
- Quinoline Yellow (E104)

#### 6.2 Incompatibilities
None known

#### 6.3 Shelf life
3 years

#### 6.4 Special precautions for storage
Do not store above 25°C.

#### 6.5 Nature and contents of container
The sachet laminate comprises:
- Low density polyethylene 30 gm2/aluminium foil 15 micron/Low density polyethylene 12 gm2/paper 40 gm2 (outer layer).
A pack size of five and ten sachets is available. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORIZATION HOLDER
Procter & Gamble (Health & Beauty Care) Ltd.
The Heights
Brooklands
Weybridge
Surrey
KT13 0XP
United Kingdom

8 MARKETING AUTHORIZATION NUMBER(S)
PL 00129/0350

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
19/02/2010

10 DATE OF REVISION OF THE TEXT
19/02/2010
Module 3

PACKAGE LEAFLET: INFORMATION FOR THE USER

Vicks Cold & Flu Care Daymed Complete Hot Drink
Paracetamol 500mg, Guaifenesin 200mg, Phenylephrine HCl 10mg. Powder for oral solution

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to use Vicks Cold & Flu Care Daymed Complete Hot Drink carefully to get the best results from it.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 3 days
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Vicks Cold & Flu Care Daymed Complete Hot Drink is and what it is used for
2. Before you take Vicks Cold & Flu Care Daymed Complete Hot Drink
3. How to take Vicks Cold & Flu Care Daymed Complete Hot Drink
4. Possible side effects
5. How to store Vicks Cold & Flu Care Daymed Complete Hot Drink
6. Further information

1. WHAT VICKS COLD & FLU CARE DAYMED COMPLETE HOT DRINK IS AND WHAT IT IS USED FOR

Vicks Cold & Flu Care Daymed Complete Hot Drink is designed for the relief of symptoms of colds and flu. It contains three active ingredients:
- Paracetamol is a well known pain killer (analgesic). It is effective against aches and pains including headache and sore throat and can also reduce fever (antipyretic).
- Guaifenesin (an expectorant) loosens phlegm which helps relieve chesty coughs.
- Phenylephrine hydrochloride (a nasal decongestant) reduces swelling in the passages of the nose and so relieves a blocked nose.

You should only use Vicks Cold & Flu Care Daymed Complete Hot Drink if you have pain or fever, nasal congestion and chesty cough.

2. BEFORE YOU TAKE VICKS COLD & FLU CARE DAYMED COMPLETE HOT DRINK

Do not take Vicks Cold & Flu Care Daymed Complete Hot Drink if you:
- are allergic to paracetamol, guaifenesin, phenylephrine hydrochloride, or to any of the ingredients (see section 6)
- have heart disease
- have high blood pressure (hypertension)
- have a problem with your liver or severe kidney disease
- have overactivity of the thyroid gland
- are diabetic
- have glaucoma (increased pressure in the eye) of the narrow-angle type
- have porphyria, which is a hereditary disorder of characterised by excessive amounts of pigments in the urine
- are taking tricyclic antidepressants
- are taking beta blockers
- are taking monoamine oxidase inhibitors (MAOIs) - used in treatment of depression or Parkinson's disease or have taken them in the last 14 days
- are taking medicines to lower your blood pressure or treat angina.
Do not give Vicks Cold & Flu Care Daymed Complete Hot Drink to children under 12 years of age.

Important: Contains Paracetamol. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage. Do not take with any other flu, cold or decongestant products.

Ask your doctor or pharmacist before taking Vicks Cold & Flu Care Daymed Complete Hot Drink if you:

- have a problem with your liver functions
- are male and have an enlarged prostate gland, as you may have more difficulty passing water
- have a blood circulation problem (including Raynaud’s syndrome)

Taking other medicines
Please inform your doctor or pharmacist before you take Vicks Cold & Flu Care Daymed Complete Hot Drink if you are taking:

- medicine containing paracetamol or other decongestants for colds and flu.
- monoamine oxidase inhibitors (MAOIs) used in the treatment of depression or Parkinson’s disease. Do not take Vicks Cold & Flu Care Daymed Complete Hot Drink if you have taken MAOIs in the last 14 days.
- tricyclic antidepressants for depression, such as amitriptyline or imipramine.
- medicine for high blood pressure (antihypertensives), including beta-blockers, or for improving heart function or correcting abnormal heart rhythms (digoxin, lanoxic, digitoxin).
- phenothiazines (which are used either as antipsychotic drugs to treat conditions such as schizophrenia or paranoia, or to prevent nausea and vomiting).
- medicine for nausea and vomiting (such as metoclopramide or domperidone).
- medicine for thinning the blood (anticoagulants), such as warfarin or other coumarins.
- medicine for high cholesterol (such as cholestyramine).
- sedatives (barbiturates).
- probenecid or AZT (zidovudine).
- isoniazid (used to treat or prevent tuberculosis).

Taking Vicks Cold & Flu Care Daymed Complete Hot Drink with food and drink
Do not take this product with alcoholic drinks.

Pregnancy and breast-feeding
Taking Vicks Cold & Flu Care Daymed Complete Hot Drink during pregnancy or breast feeding is not recommended; you should ask your doctor or pharmacist for advice before use.

Driving and using machines
This product may cause dizziness or confusion. If you are affected do not drive or operate machinery.

Important information about some of the ingredients of Vicks Cold & Flu Care Daymed Complete Hot Drink
This product contains:

- Aspartame (E951), a source of phenylalanine. May be harmful for people with phenylketonuria.
- Sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
- Sodium (157 mg per dose). To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE VICKS COLD & FLU CARE DAYMED COMPLETE HOT DRINK

Always take Vicks Cold & Flu Care Daymed Complete Hot Drink exactly as your doctor or pharmacist has told you; check with them if you are not sure about anything.
Dosage
This medicine is a powder to be dissolved in water and taken as a hot drink.
Pour one sachet of powder into a mug of standard size and fill with hot, but not boiling water (approx.
250ml). Allow to cool to a drinkable temperature.

Adults and children over 12 years:
1 sachet every 4-6 hours as required. Do not take more than 4 sachets in any 24 hour period.

Do not give to children under 12 years of age

Do not exceed the stated dose.

Do not take this medicine with alcoholic drinks.

Long term use of the product is not recommended.
If symptoms persist for more than 3 days or worsen, consult your doctor.

If you take more Vicks Cold & Flu Care Daymed Complete Hot Drink than you should:

Seek medical advice immediately if you accidentally take more than you should or give a child more than
is recommended, even if you think they feel well because of the risk of delayed, serious liver damage.

If you have any further questions on the use of this product, ask your pharmacist.

4 POSSIBLE SIDE EFFECTS

Like all medicines, Vicks Cold & Flu Care Daymed Complete Hot Drink can cause side effects, although not
everybody gets them. If you experience any of the following side effects, or anything else unusual happens,
stop taking the medicine immediately.

Certain disorders of the blood cells and pancreatitis (inflammation of the pancreas) may occur very rarely
with paracetamol (affect less than 1 in 10,000 people).

Allergic reactions (such as skin rashes or hives), severe allergic reactions (anaphylaxis), wheezing or
breathing difficulties may occur rarely (affect less than 1 in 1000 people, but more than 1 in 10,000 people).

Rarely, headache, dizziness and gastrointestinal disturbances, such as stomach ache, nausea, vomiting and
diarrhoea have been reported with guarana. (affect less than 1 in 1000 people, but more than 1 in 10,000
people).

Phenylephrine may rarely cause a rapid heartbeat (palpitations).
High blood pressure with headache, dizziness and palpitations may also occur rarely.
Phenylephrine may also cause trouble sleeping (insomnia), nervousness, shaking (tremor), irritability,
restlessness, confusion or anxiety. These side effects are rare (affect less than 1 in 1000 people, but more
than 1 in 10,000 people). Loss of appetite, nausea or vomiting are common with phenylephrine (affect less
than 1 in 10 people, but more than 1 in 100 people).

Loss of appetite, nausea or vomiting are common with phenylephrine (affect less than 1 in 10 people, but
more than 1 in 100 people).

If any side effects you experience become serious, or if you notice any side effects not listed in this
leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE VICKS COLD & FLU CARE DAYMED COMPLETE HOT DRINK

Keep out of the reach and sight of children
Store below 25 °C.

Do not take Vicks Cold & Flu Care Daymed Complete Hot Drink after the expiry date which is printed on the sachet or carton. The expiry date refers to the last day of the month stated.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Vicks Cold & Flu Care Daymed Complete Hot Drink contains

Each sachet of this medicine provides a single dose containing the active ingredients: paracetamol 500mg, guaifenesin 200mg and phenylephrine hydrochloride 10 mg.

The other ingredients are: sucrose, citric acid, tartaric acid, sodium cyclamate, sodium citrate, aspartame (E951), acesulfame potassium (E950), powdered menthol, lemon flavour, lemon juice flavour, quinoline Yellow (E104). See end of section 2.

What Vicks Cold & Flu Care Daymed Complete Hot Drink looks like and contents of the pack

Vicks Cold & Flu Care Daymed Complete Hot Drink is an off-white coloured powder which is packed in laminated sachets in a carton box. The product is available in cartons of 5 and 10 sachets.

Not all pack sizes may be marketed

Marketing Authorisation Holder

To be completed nationally

Manufacturer

Wrafton Laboratories Limited
Braunton,
Devon,
EX33 2DL
UK

This leaflet was approved in MM/YYYY

<Member state> <Name of the medicinal product>
PACKAGE LEAFLET: INFORMATION FOR THE USER

Vicks Cold & Flu Care Daymed Plus Hot Drink
Paracetamol 500mg, Guaifenesin 200mg, Phenylephrine HCl 10mg. Powder for oral solution

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to use Vicks Cold & Flu Care
Daymed Plus Hot Drink carefully to get the best results from it.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 3 days.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet,
  please tell your doctor or pharmacist.

In this leaflet:
1. What Vicks Cold & Flu Care Daymed Plus Hot Drink is and what it is used for
2. Before you take Vicks Cold & Flu Care Daymed Plus Hot Drink
3. How to take Vicks Cold & Flu Care Daymed Plus Hot Drink
4. Possible side effects
5. How to store Vicks Cold & Flu Care Daymed Plus Hot Drink
6. Further information

1. WHAT VICKS COLD & FLU CARE DAYMED PLUS HOT DRINK IS AND WHAT IT IS
   USED FOR Plus

Vicks Cold & Flu Care Daymed Plus Hot Drink is designed for the relief of symptoms of colds and flu.
It contains three active ingredients:
- Paracetamol is a well known pain killer (analgesic). It is effective against aches and pains including
  headache and sore throat and can also reduce fever (antipyretic).
- Guaifenesin (an expectorant) loosens phlegm which helps relieve chesty coughs.
- Phenylephrine hydrochloride (a nasal decongestant) reduces swelling in the passages of the nose and
  so relieves a blocked nose.
You should only use Vicks Cold & Flu Care Daymed Plus Hot Drink if you have pain or fever, nasal
congestion and chesty cough.

2. BEFORE YOU TAKE VICKS COLD & FLU CARE DAYMED PLUS HOT DRINK Plus

Do not take Vicks Cold & Flu Care Daymed Plus Hot Drink if you:
- are allergic to paracetamol, guaifenesin, phenylephrine hydrochloride, or to any of the
  ingredients (see section 6)
- have heart disease
- have high blood pressure (hypertension)
- have a problem with your liver or severe kidney disease
- have overactivity of the thyroid gland
- are diabetic
- have glaucoma (increased pressure in the eye) of the narrow-angle type
- have porphyria, which is a hereditary disorder of characterised by excessive amounts of
  pigments in the urine
- are taking tricyclic antidepressants
- are taking beta blockers
- are taking monoamine oxidase inhibitors (MAOIs) - used in treatment of depression or
  Parkinson's disease or have taken them in the last 14 days
- are taking medicines to lower your blood pressure or treat angina.
Do not give Vicks Cold & Flu Care Daymed Plus Hot Drink to children under 12 years of age.

Important: Contains Paracetamol. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage. Do not take with any other flu, cold or decongestant products.

Ask your doctor or pharmacist before taking Vicks Cold & Flu Care Daymed Plus Hot Drink if you:

- have a problem with your liver functions
- are male and have an enlarged prostate gland, as you may have more difficulty passing water
- have a blood circulation problem (including Raynaud’s syndrome)

**Taking other medicines**

Please inform your doctor or pharmacist before you take Vicks Cold & Flu Care Daymed Plus Hot Drink if you are taking:

- medicine containing **paracetamol or other decongestants for colds and flu**. If you are taking these, do not take Vicks Cold & Flu Care Daymed Plus Hot Drink.
- **monoamine oxidase inhibitors** (MAOIs) used in the treatment of depression or Parkinson’s disease. Do not take Vicks Cold & Flu Care Daymed Plus Hot Drink if you have taken MAOIs in the last 14 days.
- **tricyclic antidepressants** for depression, such as amitriptyline or imipramine.
- medicine for **high blood pressure** (antihypertensives), including beta-blockers, or for improving heart function or correcting abnormal heart rhythms (digoxin, lanoxin, digitoxin).
- phenothiazines (which are used either as antipsychotic drugs to treat conditions such as schizophrenia or paranoia, or to prevent nausea and vomiting).
- **medicine for nausea and vomiting** (such as metoclopramide or domperidone)
- medicine for **thinning the blood** (anticoagulants), such as warfarin or other coumarins
- **medicine for high cholesterol** (such as cholestryamine)
- **sedatives (barbiturates)**
- **probenecid or AZT (zidovudine)**
- **isoniazid (used to treat or prevent tuberculosis)**

**Taking Vicks Cold & Flu Care Daymed Plus Hot Drink with food and drink**

Do not take this product with alcoholic drinks.

**Pregnancy and breast-feeding**

Taking Vicks Cold & Flu Care Daymed Plus Hot Drink during pregnancy or breast feeding is **not recommended**: you should ask your doctor or pharmacist for advice before use. Plus

**Driving and using machines**

This product may cause dizziness or confusion. If you are affected do not drive or operate machinery.

**Important information about some of the ingredients of Vicks Cold & Flu Care Daymed Plus Hot Drink**

This product contains:

- Aspartame (E951), a source of phenylalanine. May be harmful for people with phenylketonuria.
- Sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
- Sodium (157 mg per dose). To be taken into consideration by patients on a controlled sodium diet.

**3. HOW TO TAKE VICKS COLD & FLU CARE DAYMED PLUS HOT DRINK**

Always take Vicks Cold & Flu Care Daymed Plus Hot Drink exactly as your doctor or pharmacist has told you; check with them if you are not sure about anything.
Dosage
This medicine is a powder to be dissolved in water and taken as a hot drink.
Pour one sachet of powder into a mug of standard size and fill with hot, but not boiling water (approx 250ml). Allow to cool to a drinkable temperature.

Adults and children over 12 years:
1 sachet every 4-6 hours as required. Do not take more than 4 sachets in any 24 hour period.

Do not give to children under 12 years of age

Do not exceed the stated dose.

Do not take this medicine with alcoholic drinks.

Long term use of the product is not recommended.
If symptoms persist for more than 3 days or worsen, consult your doctor.

If you take more Vicks Cold & Flu Care Daymed Plus Hot Drink than you should:

Seek medical advice immediately if you accidentally take more than you should or give a child more than is recommended, even if you/ the child feel well because of the risk of delayed, serious liver damage.

If you have any further questions on the use of this product, ask your pharmacist.

4 POSSIBLE SIDE EFFECTS

Like all medicines, Vicks Cold & Flu Care Daymed Plus Hot Drink can cause side effects, although not everybody gets them. If you experience any of the following side effects, or anything else unusual happens, stop taking the medicine immediately.

Certain disorders of the blood cells and pancreatitis (inflammation of the pancreas) may occur very rarely with paracetamol (affect less than 1 in 10,000 people).

Allergic reactions (such as skin rashes or hives), severe allergic reactions (anaphylaxis), wheezing or breathing difficulties may occur rarely (affect less than 1 in 1000 people, but more than 1 in 10,000 people).

Rarely, headache, dizziness and gastrointestinal disturbances, such as stomach ache, nausea, vomiting and diarrhoea have been reported with guaifenesin. (affect less than 1 in 1000 people, but more than 1 in 10,000 people).

Phenylephrine may rarely cause a rapid heartbeat (palpitations).
High blood pressure with headache, dizziness and palpitations may also occur rarely.
Phenylephrine may also cause trouble sleeping (insomnia), nervousness, shaking (tremor), irritability, restlessness, confusion or anxiety. These side effects are rare (affect less than 1 in 1000 people, but more than 1 in 10,000 people). Loss of appetite, nausea or vomiting are common with phenylephrine (affect less than 1 in 10 people, but more than 1 in 100 people).

Loss of appetite, nausea or vomiting are common with phenylephrine (affect less than 1 in 10 people, but more than 1 in 100 people).

If any side effects you experience become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE VICKS COLD & FLU CARE DAYMED PLUS HOT DRINK

Keep out of the reach and sight of children
Store below 25 °C.

Do not take Vicks Cold & Flu Care Daymed Plus Hot Drink after the expiry date which is printed on the sachet or carton. The expiry date refers to the last day of the month stated.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Vicks Cold & Flu Care Daymed Plus Hot Drink contains

Each sachet of this medicine provides a single dose containing the active ingredients: paracetamol 500mg, guaifenesin 200mg and phenylephrine hydrochloride 10 mg.

The other ingredients are: sucrose, citric acid, tartaric acid, sodium cyclamate, sodium citrate, aspartame (E951), acesulfame potassium (E950), powdered menthol, lemon flavour, lemon juice flavour, quinoline Yellow (E104). See end of section 2.

What Vicks Cold & Flu Care Daymed Plus Hot Drink looks like and contents of the pack

Vicks Cold & Flu Care Daymed Plus Hot Drink is an off-white coloured powder which is packed in laminated sachets in a carton box. The product is available in cartons of 5 and 10 sachets.

Not all pack sizes may be marketed

Marketing Authorisation Holder

To be compelted nationally

Manufacturer

Wrafton Laboratories Limited
Braunton,
Devon,
EX33 2DL
UK

This leaflet was approved in MM/YYYY

<Member state> <Name of the medicinal product>
Module 4
Labelling

### PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

**CARTON**

### 1. NAME OF THE MEDICINAL PRODUCT

Vicks Cold & Flu Care Daymed Complete Hot Drink  
Paracetamol 500mg, Phenylephrine hydrochloride 10mg, Guaifenesin 200mg  
Powder for oral solution

### 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains:  
500mg Paracetamol  
200mg Guaifenesin  
10mg Phenylephrine hydrochloride

### 3. LIST OF EXCIPIENTS

Also contains:  
Sucrose  
Sodium  
Aspartame (E951)

See leaflet for further information

### 4. PHARMACEUTICAL FORM AND CONTENTS

Powder for oral solution  
5 sachets

### 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.  
For oral use.

### 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.

### 7. OTHER SPECIAL WARNING(S), IF NECESSARY

### 8. EXPIRY DATE
9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

Lot No:

14. GENERAL CLASSIFICATION FOR SUPPLY

<Medicinal product not subject to medical prescription> / <Medicinal product subject to medical prescription>

15. INSTRUCTIONS ON USE

Vicks Cold & Flu Daymed Complete Hot Drink is for effective relief of cold and flu symptoms of headache, body aches and pains, sore throat, fever, blocked nose and chesty cough.

Directions:

Dissolve the contents of one sachet in a standard mug of hot, but not boiling water (approx. 250ml). Allow to cool to a drinkable temperature.

Adults and children aged 12 years and over:

1 sachet every 4-6 hours as required, up to a maximum of 4 sachets in any 24 hours.

Do not give to children under 12 years of age.

DO NOT EXCEED THE STATED DOSE

CONTAINS PARACETAMOL. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Do not take with any other flu, cold or decongestant products.
If you are pregnant or breast-feeding, taking other medication, or are under medical care, consult your doctor before taking this product.

If symptoms persist for more than 3 days or worsen, consult your doctor.

16. INFORMATION IN BRAILLE

To be completed nationally
PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Vicks Cold & Flu Care Daymed Complete Hot Drink
Paracetamol 500mg, Phenytoin hydrochloride 10mg, Guaifenesin 200mg
Powder for oral solution

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains:
500mg Paracetamol
200mg Guaifenesin
10mg Phenytoin hydrochloride

3. LIST OF EXCIPIENTS

Also contains:
Sucrose
Sodium
Aspartame (E951)

See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for oral solution
10 sachets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp Date:
9. **SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

To be completed nationally

12. **MARKETING AUTHORISATION NUMBER(S)**

To be completed nationally

13. **BATCH NUMBER**

Lot No:

14. **GENERAL CLASSIFICATION FOR SUPPLY**

<Medicinal product not subject to medical prescription>/ <Medicinal product subject to medical prescription>

15. **INSTRUCTIONS ON USE**

Vicks Cold & Flu Daymed Complete Hot Drink is for effective relief of cold and flu symptoms of headache, body aches and pains, sore throat, fever, blocked nose and chesty cough.

Directions:

Dissolve the contents of one sachet in a standard mug of hot, but not boiling water (approx. 250ml). Allow to cool to a drinkable temperature.

Adults and children aged 12 years and over:

1 sachet every 4-6 hours as required, up to a maximum of 4 sachets in any 24 hours.

Do not give to children under 12 years of age.

DO NOT EXCEED THE STATED DOSE

CONTAINS PARACETAMOL. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Do not take with any other flu, cold or decongestant products.
If you are pregnant or breast-feeding, taking other medication, or are under medical care, consult your doctor before taking this product.

If symptoms persist for more than 3 days or worsen, consult your doctor.

16. INFORMATION IN BRAILLE

To be completed nationally.
PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

SACHET

1. NAME OF THE MEDICINAL PRODUCT

Vicks Cold & Flu Care Daymed Complete Hot Drink
Paracetamol 500mg, Phenylephrine hydrochloride 10mg, Guaifenesin 200mg
Powder for oral solution

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains:
500mg Paracetamol
200mg Guaifenesin
10mg Phenylephrine hydrochloride

3. LIST OF EXCIPIENTS

Also contains:
Sucose
Sodium
Aspartame (E951)

See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for oral solution
4.36g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp Date:
9. **SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER**

To be completed nationally

12. **MARKETING AUTHORIZATION NUMBER(S)**

To be completed nationally

13. **BATCH NUMBER**

Lot No:

14. **GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product not subject to medical prescription

15. **INSTRUCTIONS ON USE**

Vicks Cold & Flu Daymed Complete Hot Drink is for effective relief of cold and flu symptoms of headache, body aches and pains, sore throat, fever, blocked nose and chesty cough.

Directions:

Dissolve the contents of one sachet in a standard mug of hot, but not boiling water (approx. 250ml). Allow to cool to a drinkable temperature.

Adults and children aged 12 years and over:

1 sachet every 4-6 hours as required, up to a maximum of 4 sachets in any 24 hours.

Do not give to children under 12 years of age.

DO NOT EXCEED THE STATED DOSE

CONTAINS PARACETAMOL. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Do not take with any other flu, cold or decongestant products.

If you are pregnant or breast-feeding, taking other medication, or are under medical care, consult your doctor before taking this product.
If symptoms persist for more than 3 days or worsen, consult your doctor.

16. INFORMATION IN BRAILLE

To be completed nationally
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the RMS considered that the applications for Vicks Cold and Flu Care Daymed Complete Hot Drink and Vicks Cold and Flu Care Daymed Plus Hot Drinks (PL 00129/0349-50; UK/H/1191&1588/01/DC) could be approved. The products are General Sale Licence (GSL) in the treatment of symptoms associated with cold and flu.

These are applications made under the decentralised procedure (DCP), according to Article 10.3 of 2001/83 EC, as amended, claiming to be generic medicinal products of Beechams All-in-One (PL 00079/0320).

The product contains a combination of paracetamol, phenylephrine hydrochloride and guaifenesin.

Paracetamol is a well established medicinal product which has been in clinical usage for many years. Paracetamol has analgesic and antipyretic activity, which are mediated through inhibition of prostaglandin synthesis in the CNS.

Phenylephrine hydrochloride is a post-synaptic $\alpha$-receptor agonist, with low cardioselective $\beta$-receptor affinity. It has a recognised decongestant activity, by vasoconstriction to reduce oedema of the nasal mucosa.

Guaifenesin the glyceryl ether of guaiacol, is an expectorant.Expectorants are believed to alleviate cough discomfort by stimulating receptors in the gastric mucosa that initiate a reflex secretion of respiratory tract fluid, thereby increasing the volume and decreasing the viscosity of bronchial secretions. This facilitates removal of mucus and reduces irritation to the bronchial tissue.

No new preclinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

No new clinical studies were conducted, which is acceptable given that the applications were based on being generic medicinal products of originator products that have been licensed for over 10 years.

Given that the proposed product and the reference product are both oral solutions at the time of administration; in accordance with 5.1.2 of the CPMP Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98), bioequivalence studies have not been performed in support of the proposed applications. The powdered product is dissolved in hot water prior to administration, to produce an oral solution having the same qualitative and quantitative composition per dose as the reference medicinal product, Beechams All-in-One.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture, assembly and batch release of these products.
## II. ABOUT THE PRODUCT

| Name of the product in the Reference Member State | Vicks Cold & Flu Care Daymed Complete Hot Drink  
Vicks Cold & Flu Care Daymed Plus Hot Drink |
<table>
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<tr>
<td>Name(s) of the active substance(s) (USAN)</td>
<td>Paracetamol, Phenylephrine hydrochloride, Guaifenesin</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>R05X  Other cold combination products</td>
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</tbody>
</table>
| Pharmaceutical form and strength(s)              | Powder for oral solution  
Paracetamol 500 mg  
Phenylephrine hydrochloride 10 mg  
Guaifenesin 200 mg |
| Reference numbers for the Mutual Recognition Procedure | UK/H/1191 & 1588/01/DC                                                                         |
| Reference Member State                           | United Kingdom                                                                                   |
| Member States concerned                          | AT, CZ, DE, ES, HU, IE, IT, PL, PT                                                                |
| Marketing Authorisation Number(s)                | PL 00129/0349-50                                                                                 |
| Name and address of the authorisation holder      | Proctor & Gamble (Health & Beauty Care) Limited  
The Heights  
Brooklands, Weybridge  
Surrey KT 13 0XP  
United Kingdom |
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

INN: Paracetamol

Chemical Names: 4-Hydroxyacetanilide

Structure:

![Paracetamol Structure](image)

Molecular formula: $\text{C}_8\text{H}_9\text{NO}_2$
Molecular weight: 151.2

Physical form: Paracetamol is a white crystalline powder which is sparingly soluble in water, freely soluble in alcohol and very slightly soluble in methylene chloride.

All aspects of the manufacture and control of the active substance Paracetamol are covered by a European Directorate for the Quality of Medicines (EDQM) certificate of suitability.

INN: Phenylephrine hydrochloride

Chemical Names: (1R)-1-(3-hydroxyphenyl)-2-(methylamino)ethanol hydrochloride

Structure:

![Phenylephrine Structure](image)

Molecular formula: $\text{C}_9\text{H}_{13}\text{NO}_2, \text{HCl}$
Molecular weight: 203.7

Physical form: Phenylephrine hydrochloride is a white or almost white, odourless crystalline powder which is freely soluble in water and alcohol.

All aspects of the manufacture and control of the drug substance Phenylephrine hydrochloride are covered by a European Directorate for the Quality of Medicines (EDQM) certificate of suitability.

INN: Guaifenesin

Chemical Names: 3(2-methoxyphenoxy)-1,2-propanediol
Structure:

\[
\begin{align*}
\text{Molecular formula:} & \quad \text{C}_{10}\text{H}_{14}\text{O}_{4} \\
\text{Molecular weight:} & \quad 198.22
\end{align*}
\]

Physical form: White or almost white, crystalline powder

All aspects of the manufacture and control of the drug substance Guaifenesin are covered by a European Directorate for the Quality of Medicines (EDQM) certificate of suitability.

**DRUG PRODUCT**

**Other ingredients**
Other ingredients consist of pharmaceutical excipients sucrose, citric acid, sodium citrate, aspartame, acesulfame potassium, tartaric acid, sodium cyclamate, lemon flavour 8476, quinoline yellow, menthol flavour and lemon juice FLAV-O-LOK.

All excipients are controlled to their respective European Pharmacopoeia monograph with the exception of lemon flavour 8476, quinoline yellow, menthol flavour and lemon juice FLAV-O-LOK which comply with in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients. None of the excipients used are sourced from materials of animal or human origin.

**Pharmaceutical Development**
A suitable pharmaceutical development data have been provided for this application.

**Manufacture**
A description and flow-chart of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of the product. The results appear satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

**Container Closure System**
The finished product is supplied in sachet laminate comprises low density polyethylene 30 gm2/aluminium foil 15 micron/Low density polyethylene 12 gm2/paper 40 gm2 (outer layer).
Pack sizes are 5 and 10 sachets.

Specifications and Certificates of Analysis for the primary packaging material have been provided. These are satisfactory. All primary packaging is controlled to European Pharmacopoeia standards and complies with guidelines concerning materials in contact with parenteral products.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 3 years has been set when the product is unopened, with the storage conditions “Do not store above 25 degree C”.

**Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and Labelling**
The SPC, PIL and labelling are pharmaceutically satisfactory.

The applicant has submitted results of PIL user testing. The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**MAA Form**
The MAA form is pharmaceutically satisfactory.

**Expert Report**
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
It is recommended that Marketing Authorisation is granted for these applications.

### III.2 PRE-CLINICAL ASPECTS
**PHARMACODYNAMICS, PHARMACOKINETICS, TOXICOLOGY**
No new non-clinical data have been provided, which is acceptable for this type of application. The pharmacodynamics, pharmacokinetics and toxicology of paracetamol, guaifenesin and phenylephrine hydrochloride are well established and are adequately discussed in the non-clinical overview.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the products’ pharmacology and toxicology.

A suitable justification has been provided for non-submission of an environmental risk assessment.
III.3 CLINICAL ASPECTS

Pharmacokinetics
No new data have been submitted and none are required for an application of this type.

Vicks Cold and Flu Care Daymed Complete Hot Drink and Vicks Cold and Flu Care Daymed Plus Hot Drinks is the generic version of Beechams All-in-One. The use of the reference product is well-established in the UK. Both products contain the same quantitative and qualitative composition of the active ingredients.

According to CPMP guidelines, the applicant is not required to submit a bioequivalence study if the product is an oral solution containing the same active substance, in the same concentration as the currently authorised product (CPMP/EWP/1401/98, subpoint 5.1.6, Parenteral solutions).

Pharmacodynamics
No new data have been submitted and none are required for an application of this type.

Clinical efficacy
No new data have been submitted and none are required for an application of this type.

Clinical safety
No new clinical data have been provided.

These active ingredients have been in clinical use separately and in combinations for many years and their safety profile is well recognised. When used at the recommended doses and dosing schedules they are relatively safe.

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and labelling
The SPC, PIL and labelling are medically satisfactory and consistent with those for the reference products.

Risk Management Plan
The applicant has concluded that there is no need for a risk management plan.

Clinical Expert Report
The clinical expert report is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

MAA Form
The MAA Form is medically satisfactory.

Clinical Conclusion
The grant of Marketing Authorisations is recommended.
IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Vicks Cold and Flu Care Daymed Complete Hot Drink and Vicks Cold and Flu Care Daymed Plus Hot Drinks are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
No new data have been submitted and none are required for an application of this type.

Vicks Cold and Flu Care Daymed Complete Hot Drink and Vicks Cold and Flu Care Daymed Plus Hot Drinks is the generic version of Beechams All-in-one (PL 00079/0320). The use of the reference product is well-established in the UK. Both products contain the same quantitative and qualitative composition of the active ingredients.

According to CPMP guidelines, the applicant is not required to submit a bioequivalence study if the product is oral solution containing the same active substance, in the same concentration as the currently authorised product (CPMP/EWP/1401/98 rev. 1, Appendix II).

No new safety data are supplied or required for this generic application.

The SPC, PIL and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable, and no new preclinical or clinical safety concerns have been identified. The data supplied supports the claim that the applicant’s product and the innovator product are interchangeable. Extensive clinical experience with the drug substances is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

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<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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