Public Assessment Report

Calcold
Calpol Night
Calcold Sachets

Paracetamol, diphenhydramine hydrochloride

15513/0145
15513/0146
15513/0151

McNeil Products Ltd
(formerly Pfizer Consumer Healthcare)

Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lay Summary</td>
<td>2</td>
</tr>
<tr>
<td>Scientific Discussion</td>
<td>3</td>
</tr>
<tr>
<td>Overall Conclusion And Risk Benefit/Analysis</td>
<td>8</td>
</tr>
<tr>
<td>Steps Taken During Assessment</td>
<td>9</td>
</tr>
<tr>
<td>Steps Taken After Assessment</td>
<td>10</td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td>11</td>
</tr>
<tr>
<td>Labels and Leaflet</td>
<td>32</td>
</tr>
</tbody>
</table>
Lay Summary

The MHRA has granted McNeil Products Ltd (formerly Pfizer Consumer Healthcare) marketing authorisations (licences) for the medicinal products Calcold, Calpol Night and Calcold Sachets. These are pharmacy only medications.

The products contain the active ingredients paracetamol and diphenhydramine hydrochloride and are for the treatment of mild to moderate pain in infants and children, including teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness, and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Calcold, Calcold Sachets and Calpol Night outweigh the risks, hence Marketing Authorisations have been granted.
Scientific Discussion

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted McNeil Products Ltd (formerly Pfizer Consumer Healthcare) marketing authorisations for the medicinal products for Calcold (PL 15513/0145) Calpol Night (PL 15513/0146) and Calcold Sachets (PL 15513/0151) on 12/01/2007. The Market Authorisation holder states that Calpol Sachets are not currently marketed and so the labelling contains the previous MA holder’s name (see section 6).

These applications were made under Article 10.1 of Directive 2001/83. The applicant claims these products to be generic medicinal products of Dozol Oral Solution (PL01648/0004) marketed by Ricesteele Manufacturing Ltd, granted 20 January 1977. The reference product is Medised Infant Oral Solution, paracetamol 120mg and diphenhydramine hydrochloride 12.5mg per 5ml (PL11314/0135), marketed by Seton Products Ltd., granted 13 September 1999.

The products contain two active substances, paracetamol and diphenhydramine hydrochloride.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

1. Paracetamol

The active substance paracetamol had the following characteristics

Structure:

\[
\begin{align*}
\text{H}_2\text{C} & \text{O} \\
\text{N} & \text{H}
\end{align*}
\]

Description: White crystalline powder

Molecular formula: \( \text{C}_8\text{H}_9\text{NO}_2 \)

Relative molecular mass: 151.2

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.
Paracetamol is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated supporting a retest period of 60 months, with no specific storage instructions.

**2. Diphenhydramine hydrochloride**

![Structure](image)

Structure:

Description: White or almost white crystalline powder

Molecular formula: \( \text{C}_{17}\text{H}_{22}\text{ClN} \)

Relative molecular mass: 291.8

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Diphenhydramine hydrochloride is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Appropriate stability data have been generated supporting a retest period of 60 months, with no specific storage instructions.

**DRUG PRODUCT**

**Other Ingredients.**

The other ingredients of these products are shown below:

- Propylene Glycol
- Polyethylene Glycol 4000
- Benzoic Acid (E210)
- Glycerol
- Liquid Sorbitol 70%
- Liquid Maltitol (Lycassin 80/55)
- Strawberry Flavour
- Base Sugar 555049E
- Sodium Cyclamate
- Saccharin Sodium
All excipients apart from strawberry flavour and base sugar 555049E have monographs in the European Pharmacopoeia. Satisfactory certificates of analysis are provided for the non-pharmacopoeial excipients. A TSE declaration for each excipient is provided by the finished product manufacturer.

**Dissolution and impurity profiles**
Dissolution and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

**Manufacture**
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been 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 product is packaged in 100ml, 150ml and 200ml Type III amber glass bottles with polypropylene child resistant closures with LDPE liner.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 36 months was accepted.

**ASSESSOR’S OVERALL CONCLUSIONS ON QUALITY AND ADVICE**
A Marketing Authorisation was granted.
PRECLINICAL ASSESSMENT

No preclinical data were provided and none were required for these applications.
MEDICAL ASSESSMENT

General
These products are for the treatment of mild to moderate pain in infants and children, including teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness, and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep.

Pharmacodynamic properties
Paracetamol (ATC Code: NO2B E01) is an antipyretic analgesic with a mechanism of action that is not fully elucidated. Diphenhydramine hydrochloride (ATC Code: RO6A A02) is an antihistamine with anti-cholinergic, anti-emetic, anti-allergic and sedative effects.

Pharmacokinetic properties
Paracetamol and diphenhydramine hydrochloride are both readily absorbed from the gastrointestinal tract. Both are widely distributed throughout the body, metabolised in the liver and excreted in the urine. As CalCold is an oral solution, the active ingredients are absorbed rapidly following ingestion.

Bioequivalence
Demonstration of bioequivalence was not necessary as the products are an oral solution.

Efficacy and Safety
Efficacy and safety were reviewed in the clinical expert report. The expert report is written by a medically qualified pharmaceutical consultant and is satisfactory.

Summary of Product Characteristics
This is satisfactory.

Patient Information Leaflet
This is satisfactory.

Conclusions.
Market authorisations may be granted.
Overall Conclusion and Risk/Benefit Analysis

**Quality**
The important quality characteristics of Calcold, Calcold Sachets and Calpol Night 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.

**Pre-Clinical**
No new preclinical data were submitted and none are required for applications of this type.

**Clinical**
A bioequivalence study was not necessary as the product is an oral solution.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the reference product.

**Risk/Benefit Analysis**
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk benefit is, therefore, considered to be positive.
Steps Taken During Assessment

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the application on 29/06/2005.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 13/09/2005.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 23/02/2006 and on the medical assessment on 27/11/2006.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant provided further information in regard to the quality assessment on 23/10/2006 and on the medical assessment on 07/01/2007.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 12/01/2007.</td>
</tr>
</tbody>
</table>
Steps Taken after Assessment

A variation was granted on 15/06/2007 to change the PSUR reporting period from 6 months to 3 years for all three products.

For Calcold Sachets (PL 15513/0151) a variation was granted on 19/10/2007 to change the name of the MA holder to McNeil Products Ltd, which is the new name for Pfizer Consumer Healthcare.
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
   CalCold

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
   CalCold contains Paracetamol 120mg and Diphenhydramine hydrochloride 12.5mg in each 5 ml. For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
   Oral Solution.
   Clear, alcohol-free, strawberry flavour solution.

4. CLINICAL INDICATIONS
   4.1 Therapeutic indications
   For the treatment of mild to moderate pain in infants and children, including teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness, and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep.

   4.2 Posology and method of administration
   For Oral Administration
   Dosage:
   3 months – under 1 year    2.5 ml to 5 ml three to four times daily
   1 year – under 6 years     5 ml – 10 ml three to four times daily
   6 years – 12 years         10 ml - 20 ml three times daily

   4.3 Contraindications
   Hypersensitivity to paracetamol, diphenhydramine hydrochloride or any of the other constituents.

   Large doses of anti-histamines may precipitate seizures in epileptics. CalCold is contraindicated in individuals with chronic or persistent cough, such as that which occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a doctor.
CalCold should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or those patients who have received treatment with MAOIs within the last two weeks.

4.4 Special warnings and precautions for use

Do not give this medication to babies under 3 months unless under the direction of a doctor.

Do not give with any other paracetamol-containing products.

Dose should not be repeated more frequently than four hour intervals. Not more than 4 doses should be taken in 24 hours. Dosage should not be continued for more than three days without consulting a doctor.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with (non-cirrhotic) alcoholic liver disease. Patients with moderate to severe renal or hepatic dysfunction or urinary retention should exercise caution when using this product (see Section 5.2 - Renal/Hepatic Dysfunction).

Immediate medical advice should be sought in the event of overdose, even if the child seems well, because of the risk of delayed serious liver disease.

Diphenhydramine should not be taken by patients with narrow-angle glaucoma or symptomatic prostatic hypertrophy unless directed by a doctor.

Alcohol or other potential sedating medicines should not be used concurrently with CalCold

Patients with rare hereditary problems of fructose intolerance should not take this medicine. CalCold contains Maltitol and Sorbitol which may have a mild laxative effect at high doses.

This product contains propylene glycol and may cause alcohol-like symptoms. Children should be supervised while on this medication.

Do not exceed the recommended dose.

If symptoms persist consult your doctor.

Keep out of the reach and sight of children.

Special label warnings

Do not give with any other paracetamol-containing products.

Immediate medical advice should be sought in the event of an overdose, even if the child seems well.
Special leaflet warnings
Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage. If you have been told by your doctor that your child has an intolerance to some sugars, contact your doctor before giving this medicinal product.

4.5 Interactions 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 colestyramine.

The anti-coagulant 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.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual’s ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

Diphenhydramine may potentiate the effect of alcohol, codeine, antihistamines and other CNS depressants. The effects of anticholinergics e.g. some psychotropic drugs and atropine may be potentiated by diphenhydramine giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. colic, urinary retention and headache.

4.6 Pregnancy and lactation.

Safety in pregnancy has not been established. Pregnant or lactating patients should not take this medication unless it is considered essential by a doctor.

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.

Diphenhydramine hydrochloride crosses the placenta and is excreted in breast milk.
4.7 Effects on ability to drive and operate machinery

May cause drowsiness, dizziness or blurred vision. If affected do not drive or operate machinery. Avoid alcoholic drink.

4.8 Undesirable effects.

Adverse effects of paracetamol are rare, but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Most reports of adverse reactions to paracetamol relate to overdosage with the drug.

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.

Nephrotoxicity following therapeutic doses of paracetamol is uncommon, but papillary necrosis has been reported after prolonged administration.

Diphenhydramine may cause drowsiness, dizziness, gastrointestinal disturbance, dry mouth, nose and throat, difficulty in urination or blurred vision. Less frequently it may cause palpitations, tremor, convulsions or paraesthesiae.

Hypersensitivity reactions to diphenhydramine have been reported, in particular, skin rashes, erythema, urticaria and angiodema.

4.9 Overdose.

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 overdo sage 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.

Symptoms of diphenhydramine overdose include drowsiness, hyperpyrexia and anticholinergic effects. In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

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, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the National Poisons Information Service (NPIS) or a liver unit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol (ATC Code: NO2B E01) is an antipyretic analgesic with a mechanism of action that is not fully elucidated. Diphenhydramine hydrochloride (ATC Code: RO6A A02) is an antihistamine with anti-cholinergic, anti-emetic, anti-allergic and sedative effects.
5.2 Pharmacokinetic properties

Paracetamol and diphenhydramine hydrochloride are both readily absorbed from the gastrointestinal tract. Both are widely distributed throughout the body, metabolised in the liver and excreted in the urine. As CalCold is an oral solution, the active ingredients are absorbed rapidly following ingestion.

5.3 Preclinical safety data

Paracetamol and diphenhydramine hydrochloride are well established drug substances whose preclinical profiles have been investigated and are thoroughly established.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Propylene Glycol
- Polyethylene Glycol 4000
- Benzoic Acid (E210)
- Glycerol
- Liquid Sorbitol 70%
- Liquid Maltitol (Lycassin 80/55)
- Strawberry Flavour
- Base Sugar 555049E
- Sodium Cyclamate
- Saccharin Sodium
- Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Keep bottle in the outer carton.

6.5 Nature and contents of container

Pharmaceutical grade III amber glass bottles with pilfer proof screw caps. Pack sizes: 100ml, 150ml, 200ml. All pack sizes may not 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.

No special requirements.

Administrative Data

7. MARKETING AUTHORISATION HOLDER

Pfizer Consumer Healthcare

*Alternative Trading Style:*

Warner-Lambert Consumer Healthcare
Walton Oaks
Dorking Road
Walton-on-the-Hill
Surrey KT20 7NS
United Kingdom

8. MARKETING AUTHORITY NUMBER

PL 15513/0145

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION.

10. DATE OF REVISION OF THE TEXT.

December 2006
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
Calpol Night

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Calpol Night contains Paracetamol 120mg and Diphenhydramine hydrochloride 12.5mg in each 5 ml.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Oral Solution.
Clear, alcohol-free, strawberry flavour solution.

4. CLINICAL INDICATIONS
4.1 Therapeutic indications
For the treatment of mild to moderate pain in infants and children, including teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness, and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep.

4.2 Posology and method of administration
For Oral Administration

<table>
<thead>
<tr>
<th>Dosage:</th>
<th>2.5 ml to 5 ml three to four times daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months - under 1 year</td>
<td>2.5 ml to 5 ml three to four times daily</td>
</tr>
<tr>
<td>1 year - under 6 years</td>
<td>5 ml - 10 ml three to four times daily</td>
</tr>
<tr>
<td>6 years - 12 years</td>
<td>10 ml - 20 ml three times daily</td>
</tr>
</tbody>
</table>

4.3 Contraindications
Hypersensitivity to paracetamol, diphenhydramine hydrochloride or any of the other constituents.

Large doses of anti-histamines may precipitate seizures in epileptics.

Calpol Night is contraindicated in individuals with chronic or persistent cough, such as that which occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a doctor.
Calpol Night should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or those patients who have received treatment with MAOIs within the last two weeks.

4.4 Special warnings and precautions for use

Do not give this medication to babies under 3 months unless under the direction of a doctor.

Do not give with any other paracetamol-containing products.

Dose should not be repeated more frequently than four hour intervals. Not more than 4 doses should be taken in 24 hours. Dosage should not be continued for more than three days without consulting a doctor.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with (non-cirrhotic) alcoholic liver disease. Patients with moderate to severe renal or hepatic dysfunction or urinary retention should exercise caution when using this product (see Section 5.2 - Renal/Hepatic Dysfunction).

Immediate medical advice should be sought in the event of overdose, even if the child seems well, because of the risk of delayed serious liver disease.

Diphenhydramine should not be taken by patients with narrow-angle glaucoma or symptomatic prostatic hypertrophy unless directed by a doctor.

Alcohol or other potential sedating medicines should not be used concurrently with Calpol Night.

Patients with rare hereditary problems of fructose intolerance should not take this medicine. Calpol Night contains Maltitol and Sorbitol which may have a mild laxative effect at high doses.

This product contains propylene glycol and may cause alcohol-like symptoms. Children should be supervised while on this medication.

Do not exceed the recommended dose.

If symptoms persist consult your doctor.

Keep out of the reach and sight of children.

Special label warnings
Do not give with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if the child seems well.
Special leaflet warnings
Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage. If you have been told by your doctor that your child has an intolerance to some sugars, contact your doctor before giving this medicinal product.

4.5 Interactions 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 colestyramine.

The anti-coagulant 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.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual’s ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

Diphenhydramine may potentiate the effect of alcohol, codeine, antihistamines and other CNS depressants. The effects of anticholinergics e.g. some psychotropic drugs and atropine may be potentiated by diphenhydramine giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. colic, urinary retention and headache.

4.6 Pregnancy and lactation.

Safety in pregnancy has not been established. Pregnant or lactating patients should not take this medication unless it is considered essential by a doctor.

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.

Diphenhydramine hydrochloride crosses the placenta and is excreted in breast milk.
4.7 Effects on ability to drive and operate machinery

May cause drowsiness, dizziness or blurred vision. If affected do not drive or operate machinery. Avoid alcoholic drink.

4.8 Undesirable effects.

Adverse effects of paracetamol are rare, but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Most reports of adverse reactions to paracetamol relate to overdosage with the drug.

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.

Nephrotoxicity following therapeutic doses of paracetamol is uncommon, but papillary necrosis has been reported after prolonged administration.

Diphenhydramine may cause drowsiness, dizziness, gastrointestinal disturbance, dry mouth, nose and throat, difficulty in urination or blurred vision. Less frequently it may cause palpitations, tremor, convulsions or paraesthesiae.

Hypersensitivity reactions to diphenhydramine have been reported, in particular, skin rashes, erythema, urticaria and angiodema.

4.9 Overdose.

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.

Symptoms of diphenhydramine overdose include drowsiness, hyperpyrexia and anticholinergic effects. In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

**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, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the National Poisons Information Service (NPIS) or a liver unit.

5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Paracetamol (ATC Code: NO2B E01) is an antipyretic analgesic with a mechanism of action that is not fully elucidated. Diphenhydramine hydrochloride (ATC Code: RO6A A02) is an antihistamine with anticholinergic, anti-emetic, anti-allergic and sedative effects.
5.2 Pharmacokinetic properties

Paracetamol and diphenhydramine hydrochloride are both readily absorbed from the gastrointestinal tract. Both are widely distributed throughout the body, metabolised in the liver and excreted in the urine. As Calpol Night is an oral solution, the active ingredients are absorbed rapidly following ingestion.

5.3 Preclinical safety data

Paracetamol and diphenhydramine hydrochloride are well established drug substances whose preclinical profiles have been investigated and are thoroughly established.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Propylene Glycol
- Polyethylene Glycol 4000
- Benzoic Acid (E210)
- Glycerol
- Liquid Sorbitol 70%
- Liquid Maltitol (Lycassin 80/55)
- Strawberry Flavour
- Base Sugar 555049E
- Sodium Cyclamate
- Saccharin Sodium
- Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 25°C. Keep bottle in the outer carton.

6.5 Nature and contents of container

Pharmaceutical grade III amber glass bottles with pilfer proof screw caps. Pack sizes: 100ml, 150ml, 200ml. All pack sizes may not 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.

No special requirements.

Administrative Data

7. MARKETING AUTHORIZATION HOLDER

Pfizer Consumer Healthcare

*Alternative Trading Style:*

Warner-Lambert Consumer Healthcare
Walton Oaks
Dorking Road
Walton-on-the-Hill
Surrey KT20 7NS
United Kingdom

8. MARKETING AUTHORIZATION NUMBER

PL 15513/0146

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION.

10. DATE OF REVISION OF THE TEXT.

December 2006
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

CalCold Sachets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CalCold Sachets contains Paracetamol 120mg and Diphenhydramine hydrochloride 12.5mg in each 5 ml.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solution.
Clear, alcohol-free, strawberry flavour solution.

4. CLINICAL INDICATIONS

4.1 Therapeutic indications
For the treatment of mild to moderate pain in infants and children, including
teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness, and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep.

4.2 Posology and method of administration

For Oral Administration

<table>
<thead>
<tr>
<th>Dosage:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months – under 1 year</td>
</tr>
<tr>
<td>2.5 ml to 5 ml three to four times daily</td>
</tr>
<tr>
<td>1 year – under 6 years</td>
</tr>
<tr>
<td>5 ml – 10 ml three to four times daily</td>
</tr>
<tr>
<td>6 years – 12 years</td>
</tr>
<tr>
<td>10 ml - 20 ml three times daily</td>
</tr>
</tbody>
</table>

4.3 Contraindications

Hypersensitivity to paracetamol, diphenhydramine hydrochloride or any of the other constituents.

Large doses of anti-histamines may precipitate seizures in epileptics.
CalCold Sachets is contraindicated in individuals with chronic or persistent cough, such as that which occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a doctor.

CalCold Sachets should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or those patients who have received treatment with MAOIs within the last two weeks.
4.4 Special warnings and precautions for use

Do not give this medication to babies under 3 months unless under the direction of a doctor.

Do not give with any other paracetamol-containing products.

Dose should not be repeated more frequently than four hour intervals.
Not more than 4 doses should be taken in 24 hours. Dosage should not be continued for more than three days without consulting a doctor.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with (non-cirrhotic) alcoholic liver disease. Patients with moderate to severe renal or hepatic dysfunction or urinary retention should exercise caution when using this product (see Section 5.2 - Renal/Hepatic Dysfunction).

Immediate medical advice should be sought in the event of overdose, even if the child seems well, because of the risk of delayed serious liver disease.

Diphenhydramine should not be taken by patients with narrow-angle glaucoma or symptomatic prostatic hypertrophy unless directed by a doctor.

Alcohol or other potential sedating medicines should not be used concurrently with CalCold Sachets.

Patients with rare hereditary problems of fructose intolerance should not take this medicine. CalCold Sachets contains Maltitol and Sorbitol which may have a mild laxative effect at high doses.

This product contains propylene glycol and may cause alcohol-like symptoms. Children should be supervised while on this medication.

Do not exceed the recommended dose.

If symptoms persist consult your doctor.

Keep out of the reach and sight of children.

Special label warnings
Do not give with any other paracetamol-containing products.
Immediate medical advice should be sought in the event of an overdose, even if the child seems well.

Special leaflet warnings
Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage.
If you have been told by your doctor that your child has an intolerance to some sugars, contact your doctor before giving this medicinal product.

4.5 **Interactions 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 colestyramine.

The anti-coagulant 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.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual’s ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

Diphenhydramine may potentiate the effect of alcohol, codeine, antihistamines and other CNS depressants. The effects of anticholinergics e.g. some psychotropic drugs and atropine may be potentiated by diphenhydramine giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. colic, urinary retention and headache.

4.6 **Pregnancy and lactation.**

Safety in pregnancy has not been established. Pregnant or lactating patients should not take this medication unless it is considered essential by a doctor.

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.

Diphenhydramine hydrochloride crosses the placenta and is excreted in breast milk.

4.7 **Effects on ability to drive and operate machinery**

May cause drowsiness, dizziness or blurred vision. If affected do not drive or operate machinery. Avoid alcoholic drink.
4.8 Undesirable effects.

Adverse effects of paracetamol are rare, but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Most reports of adverse reactions to paracetamol relate to overdosage with the drug.

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.

Nephrotoxicity following therapeutic doses of paracetamol is uncommon, but papillary necrosis has been reported after prolonged administration.

Diphenhydramine may cause drowsiness, dizziness, gastrointestinal disturbance, dry mouth, nose and throat, difficulty in urination or blurred vision. Less frequently it may cause palpitations, tremor, convulsions or paraesthesiae.

Hypersensitivity reactions to diphenhydramine have been reported, in particular, skin rashes, erythema, urticaria and angiodema.

4.9 Overdose.

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, phenytion, 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.

Symptoms of diphenhydramine overdose include drowsiness, hyperpyrexia and anticholinergic effects. In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

**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, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the National Poisons Information Service (NPIS) or a liver unit.

5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Paracetamol (ATC Code: NO2B E01) is an antipyretic analgesic with a mechanism of action that is not fully elucidated. Diphenhydramine hydrochloride (ATC Code: RO6A A02) is an antihistamine with anti-cholinergic, anti-emetic, anti-allergic and sedative effects.

5.2 **Pharmacokinetic properties**

Paracetamol and diphenhydramine hydrochloride are both readily absorbed from the gastrointestinal tract. Both are widely distributed throughout the body, metabolised in the liver and excreted in the urine. As CalCold is an oral solution, the active ingredients are absorbed rapidly following ingestion.
5.3 **Preclinical safety data**

Paracetamol and diphenhydramine hydrochloride are well established drug substances whose preclinical profiles have been investigated and are thoroughly established.

6. **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

Propylene Glycol  
Polyethylene Glycol 4000  
Benzoic Acid (E210)  
Glycerol  
Liquid Sorbitol 70%  
Liquid Maltitol (Lycassin 80/55)  
Strawberry Flavour  
Base Sugar 555049E  
Sodium Cyclamate  
Saccharin Sodium  
Purified water

6.2 **Incompatibilities**

None known.

6.3 **Shelf life**

36 months

6.4 **Special precautions for storage**

Do not store above 25°C. Keep container in the outer carton.

6.5 **Nature and contents of container**

Pharmaceutical grade III amber glass bottles with pilfer proof screw caps.  
Pack sizes: 100ml, 150ml, 200ml.  
All pack sizes may not 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.**

No special requirements.
Administrative Data

7. MARKETING AUTHORISATION HOLDER

McNeil Products Limited
Foundation Park
Roxborough Way
Maidenhead
Berkshire
SL6 3UG
UK

8. MARKETING AUTHORISATION NUMBER

PL 15513/0151

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION.

12/12/2006

10. DATE OF REVISION OF THE TEXT.

19/10/2007
2 Before giving the medicine to your child

This medicine is suitable for most people, but a few people should not use it. If you are in any doubt, talk to your doctor or pharmacist.

Do not give your child this medicine...

If you have ever had a bad reaction to any of these ingredients.

If it is likely to be unsuitable alongside certain medicines

If it is likely to be more effective alongside certain medicines

If it is likely to be unsuitable alongside certain medicines

If it is likely to be more effective alongside certain medicines

Talk to your doctor or pharmacist...

If your child has sudden breathing problems

If you are at all unsure about the medicine

If you are at all unsure about the medicine

3 How to use this medicine

Check the table below to see how much medicine to use.

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
</table>
| 3 years and under    | 1 to 2 years old: 2 ml (65 mg)  
| 3 years to 12 years  | 1 to 2 years old: 2 ml (65 mg)  

If anyone has too much

Immediate medical advice should be sought in the event of an overdose, even if the child seems well.

If you forget to give the medicine

Give the last dose that you normally would have given for that dose missed plus 4 hours later. Do not give a double dose.

4 Possible side-effects

Calcold can have side-effects, like all medicines, although there aren’t too many and they usually mild.

Tell your doctor as soon as possible if you notice any of these:

- Diarrhoea or other signs of an infection
- Becoming unusually tired, drowsy or listless
- Sudden swelling in the mouth, face or lips
- Swelling of the mouth, face or lips
- Difficulty in breathing or wheezing
- Difficulty in swallowing or tightness in the throat
- Allergic reaction (including itching, swelling of the mouth, face or lips, or a rash)
- Seizures or fits

What the medicine looks like

Calcold is a clear liquid, available in 100 ml, 150 ml or 200 ml bottles.

5 Storing this medicine

Keep the medicine out of reach of children.

Do not store above 25°C.

Keep the bottle in the outer carton.

Do not use after the end of the month shown on the packaging.

6 Further information

What’s in this medicine?

The active ingredients are 150 mg Paracetamol and 12.5 mg Diphenhydramine hydrochloride per 5 ml of medicine.

Other ingredients are Propylene glycol, polyethylene glycol, benzyl alcohol and E216, dyes, sodium chloride, citric acid monohydrate, sodium citrate, saccharin sodium and purified water. The flavourings are Pomegranate and watermelon.

What the medicine looks like

Calcold is a clear liquid, available in 100 ml, 150 ml or 200 ml bottles.

The Prescriber’s Healthcare, Waverley Road, Surry KT12 5ND.

The manufacturer is Perrigo Laboratories Limited, Bridgehampton, Chichester, West Sussex, England.

This booklet was revised August 2006.

Calcold is a registered trademark of Pfizer Consumer Healthcare.
2 Before giving the medicine to your child

This medicine is suitable for most children, but if your child is under 1 month old or has any of the conditions listed above, speak to your doctor or pharmacist.

Do not give your child this medicine...
- If he/she has ever had a bad reaction to any of the ingredients.
- If it is given to children under 3 months old.
- If your child has previously had a reaction to Calpol Night.
- If your child has previously had a reaction to any other medicines.
- If your child is suffering from a rash or other skin problems.

If any of these apply, get advice from a pharmacist or doctor without using Calpol Night.

Tell your doctor or pharmacist...
- If your child has any serious kidney or liver problems.
- If your child is suffering from a rash or other skin problems.
- If your child is pregnant or breastfeeding.
- If your child has any allergies.
- If your child is under 1 year old.
- If your child is over 10 years old.
- If your child has any other medical problems.

Now read this leaflet carefully before you use this medicine. Keep the leaflet, you might need it again.

1 What the medicine is for

PL 15513/0145/46/51

UKPAR McNeil Products Ltd, Calcold, Calcold Sachets and Calpol Night

This medicine is for the symptoms of the common cold and flu. It helps to ease breathing and removes mucus from deeper parts of the throat.

Neat products of McNeil Products Ltd, Calcold Sachets and Calpol Night

3 How to use this medicine

Check the table below to see how much medicine to give:

<table>
<thead>
<tr>
<th>Age</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Babies</td>
<td>2 to 5 months</td>
</tr>
<tr>
<td>6 to 12 months</td>
<td>2 to 3 drops</td>
</tr>
<tr>
<td>1 to 2 years</td>
<td>3 to 4 drops</td>
</tr>
<tr>
<td>2 to 5 years</td>
<td>4 to 5 drops</td>
</tr>
<tr>
<td>5 to 10 years</td>
<td>5 to 6 drops</td>
</tr>
<tr>
<td>10 years and over</td>
<td>6 to 8 drops</td>
</tr>
</tbody>
</table>

Speak to your doctor:
- If your child needs more than is shown in the table, or if he/she doesn’t seem to be getting better.
- If your child is under 3 months old or over 10 years old.
- If your child is pregnant or breastfeeding.
- If your child has any other medical problems.
- If your child has any allergies.
- If your child has any other conditions.

4 Possible side-effects

Calpol Night can have side-effects. All medicines, although these don’t affect everyone, can usually be treated.

How to use this medicine

UKPAR McNeil Products Ltd, Calcold Sachets and Calpol Night
CalcCold

Sachets
Contains 100 mg ibuprofen and 12.5 mg Ephedrine hydrochloride per sachet

1 What the medicine is for

This medicine is for the temporary relief of coughs and cold. It helps to ease breathing, reduce fever and provide relief from a runny nose, sore throat and hoarsening.

2 Before giving the medicine to your child

This medicine is suitable for most people, but a few people should not use it. If you are in any doubt, talk to your doctor or pharmacist.

3 How to use this medicine

Check the table below to see how much medicine to use.

Always shake the bottle thoroughly before use.

Do not use more medicine than shown in the table.

Children under 3 months

Babies under 3 months

Do not give babies under 3 months unless your doctor tells you to.

Children from 3 months to 12 years

Age

Dosage

6-12 months

One to two small (15 ml) spoons to 3-6 months a day

One to two large (30 ml) spoons to 3-6 months a day

Children 6-12 years

Two to four large (30 ml) spoons a day

4 Possible side-effects

CalcCold Sachets can have side-effects, like all medicines, although they don’t affect everyone and are usually mild.

If you forget to give the medicine

Give the next dose when needed. If the last dose was given after 4 hours ago, give a double dose.

5 Storing this medicine

Keep in a cool dry place.

Larger term people who can practice continuous asepsis every day for a long time, do not have to wash their hands, because they are not likely to develop infections that can be passed on to others.

Other Information

What’s in this medicine?

The active ingredients are 100 mg ibuprofen and 12.5 mg Ephedrine hydrochloride per sachet in a clear liquid.

Other ingredients are Propylene glycol, glycerol, benzyl alcohol, water, and a preservative.

Contains: ibuprofen, senna, and cornstarch.

What is CalcCold Sachets a treatment for?

CalcCold Sachets are a treatment for colds.

What is CalcCold Sachets used for?

CalcCold Sachets are used to relieve the symptoms of colds and flu.

UKPAR McNeil Products Ltd, Calcold, Calcold Sachets and Calpol Night

34
CalCold®

Paracetamol
Diphenhydramine Hydrochloride

USES: for the symptomatic relief of nasal and throat colds. Helps to ease sneezing and provides active relief of coughing and breathing difficulties, some drowsiness and soothing of nasal passages. For use in children aged 3 years and over.

DOSAGE AND INSTRUCTIONS: To be taken when needed or as directed. Store below 25°C. If symptoms persist consult your pharmacist.

DO NOT EXCEED THE STATED DOSE. May cause drowsiness. If affected, do not drive or operate machinery. Avoid alcoholic drinks. Children should be supervised while on this medication.

B/N: 100 ml

UKPAR McNeil Products Ltd, Calcold, Calcold Sachets and Calpol Night 37