FEDRIL NIGHT COLD AND FLU ORAL SOLUTION
(PL 04917/0053)
UKPAR

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Fedril Night Cold and Flu Oral Solution

(PL 04917/0053)

LAY SUMMARY

On 5th November 2009, the MHRA granted PINEWOOD Laboratories Limited a Marketing Authorisation (licence) for the medicinal product Fedril Night Cold and Flu, Oral Solution (PL 04917/0053). This is a pharmacy only medicine (P) for the symptomatic night time relief of colds, chills and influenza consisting of headache, shivers, sore throat pain, tickly cough, runny nose, aches and pains.

This product contains paracetamol to reduce fever, promethazine to dry up a runny nose, ease breathing and dextromethorphan which relieves a tickly cough.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Fedril Night Cold and Flu, Oral Solution outweigh the risks, hence a Marketing Authorisation has been granted.
Fedril Night Cold and Flu Oral Solution

(PL 04917/0053)

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Fedril Night Cold and Flu, Oral Solution (PL 04917/0053) to Pinewood Laboratories on 5th November 2009. The product is Pharmacy only medicine for the symptomatic night time relief of colds, chills and influenza consisting of headache, shivers, sore throat pain, tickly cough, runny nose, aches and pains.

This standard abridged application for Fedril Night Cold and Flu, Oral Solution is submitted under Article 10.1 of Directive 2001/83/EC as amended. The application claims to be a generic medicinal product of Night Nurse, PL 00079/0187 granted 23rd January 1978 to the Beecham Group PLC (trading as GlaxoSmithKline Beecham Consumer Healthcare).

This product contains 1000mg/20ml dose paracetamol (analgesic and antipyretic), 20mg/20ml promethazine hydrochloride (antihistamine with anticholinergic activity) and 15mg/20ml dextromethorphan hydrobromide (antitussive).
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE – PARACETAMOL

Chemical Name: N-(4-hydroxyphenyl)acetamide
Molecular Formula: C₈H₉NO₂

Chemical Structure:

Molecular Weight: 151.2
Appearance: A white crystalline powder
Properties: Sparingly soluble in water, freely soluble in alcohol

Paracetamol is the subject of a European Pharmacopoeia monograph.

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.

ACTIVE SUBSTANCE – PROMETHAZINE HYDROCHLORIDE

Chemical Name: (RS)-N,N-dimethyl-1-(10H-phenothiazin-10-yl)propan-2-amine hydrochloride
Molecular Formula: C₁₇H₂₀N₂S Hcl

Chemical Structure:

Molecular Weight: 320.9
Appearance: Almost White, crystalline powder.

Properties: sparingly soluble in water, freely soluble in alcohol

Promethazine hydrochloride is the subject of a European Pharmacopoeia monograph.

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

**ACTIVE SUBSTANCE – DEXTROMETHORPHAN HYDROBROMIDE**

Chemical Name: Ent-3-methoxy-17-methylmorphinan hydrobromide monohydrate.

Molecular Formula: \( \text{C}_{18}\text{H}_{25}\text{NOH}_2\text{O} \)

Chemical Structure:

![Chemical Structure of Dextromethorphan Hydrobromide](image)

Molecular Weight: 370.3

Dextromethorphan hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance dextromethorphan hydrochloride 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, namely ethanol, propylene glycol, maltitol liquid (hydrogenated glucose syrup), sodium citrate, ascorbic acid, acesulfame K, citric acid monohydrate, mint flavour, patent blue V (E131), quinoline Yellow (E104) and purified water.

All excipients are controlled to their respective European Pharmacopoeia specifications, with the exception of mint flavour, patent blue V, quinoline yellow which are controlled to suitable in-house specification.

Satisfactory certificates of analysis have been provided for all excipients.

None of the excipients used contain materials of animal or human origin.
Pharmaceutical development
The objective of the product development programme was to produce oral solution that could be considered a generic medicinal product of Night Nurse (PL 00079/0187).

The pharmaceutical development data submitted are satisfactory.

Manufacture
A description and flow-chart of the manufacturing method has 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 product. The results appear satisfactory.

Finished product specification
The finished product specification is satisfactory. 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 finished product is packaged in 200ml Type III clear glass bottles fitted with polypropylene child resistant closures. This is supplied with a 20ml measuring cup.

Specifications and Certificates of Analysis for all packaging have been provided. These are satisfactory. The primary packaging has been shown to comply with guidelines concerning materials in contact with parenteral products.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years has been set with storage conditions are “Do not store above 25°C”, “Store in the original container” and “Keep the bottle in the outer carton”.

ADMINISTRATIVE
Expert Report
A pharmaceutical expert report has been written by a suitably qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Summary of Product Characteristics (SPC)
This is consistent with the SPC for the reference product and is satisfactory.

Labelling
These are satisfactory.

Patient Information Leaflet (PIL)
This is consistent with the PIL for the reference product and is satisfactory.

MAA Form
This is satisfactory.
Conclusion
It is recommended that a Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

This application for generic product claims essential similarity to Night Nurse (PL 04917/0053), granted 23 January 1978 to the Beecham Group PLC (trading as GlaxoSmithKline Beecham Consumer Healthcare).

No new preclinical data have been supplied with this application and none are required for applications of this type.
CLINICAL ASSESSMENT

1. INTRODUCTION
This is a standard abridged application for Marketing Authorisation submitted under Article 10.1 of Directive 2001/83/EEC for Fedril Night Cold and Flu oral solution.

The application cross-refers to Night Nurse marketed by GlaxoSmithKline Beecham Consumer Healthcare (PL 00079/0187). The reference medicinal product was first authorised in the UK on 23rd January 1978.

2. BACKGROUND
Paracetamol is a paraminophenol derivative possessing analgesic and antipyretic effects that do not differ significantly from those of aspirin. The effects are thought related to a selective inhibition of prostaglandin synthesis. The incomplete inhibition of COX may account for the lack of anti-inflammatory activity and the absence of many of the adverse effects associated with the use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). The major risk attached to paracetamol use is that of severe liver damage following an overdose.

Promethazine is a classical phenothiazine histamine H₁-receptor antagonist and its major action is to diminish or abolish the major action of histamine in the body by reversible blockade of histamine H₁-receptor sites in tissues. In addition promethazine also has sedating properties and some antimuscarinic and local anaesthetic effects. The mechanism of action in coughs and colds probably involves reduction in cholinergic nerve transmission.

More recently first generation antihistamines including promethazine have been shown to have some antiallergic and anti-inflammatory properties independent of their H₁ blockade activity (1).

Dextromethorphan is the methylated dextro-rotatory analogue of levorphanol. It acts on the cough centre in the medulla oblongata, raising the threshold for the cough reflex. It is also an antagonist of N-methyl-D-aspartate receptors. Although structurally related to morphine, dextromethorphan lacks the pharmacological characteristics of opiate alkaloids. In normal individuals at therapeutic doses dextromethorphan is devoid of analgesic, euphoriant and physical dependence-producing properties.

3. INDICATIONS
The proposed indications are the same as those of Night Nurse, namely:

For the symptomatic night time relief of colds, chills and influenza consisting of headaches, shivers, sore throat pain, tickly cough, runny nose, aches and pains.

4. DOSE AND DOSAGE SCHEDULE
The proposed posology is identical to that authorised for Night Nurse:
Route of Administration: Oral

Adults and children aged 12 years and over:
One measured 20ml dose (or four 5ml spoonfuls) to be taken just before going to bed.

Not to be given to children under 12 years.

Elderly:
The normal adult dose can be used.

5. TOXICOLOGY
No new data is presented and none is required for this application.

6. CLINICAL PHARMACOLOGY
No new data is presented and none is required for this application. The sections on the pharmacodynamic and pharmacokinetic properties of the three active ingredients in the Summary of Product Characteristics contain largely the same information as do most similar preparations. All the information included is factually correct.

7. EFFICACY
No new data is presented and none is required for this application. The clinical expert refers in the report to wide-ranging studies on all three compounds.

8. SAFETY
No new data is presented and none is required for this application. The sections in the Summary of Product Characteristics under Clinical Particulars contain largely the same information as do most similar preparations.

The clinical expert provides a succinct overview of the safety issues of all three compounds including a separate section on Pregnancy and Lactation.

9. EXPERT REPORT
The Clinical Expert Report has been written by an appropriately qualified person and is a suitable summary of the clinical aspects of the dossier.

10. SUMMARY OF PRODUCT CHARACTERISTICS
This is consistent with the SPC for the reference product and satisfactory.

11. PATIENT INFORMATION LEAFLET
The Patient Information Leaflet is satisfactory.

12. LABELLING
The labelling is satisfactory.

13. MAA
The Marketing Authorisation Application form is satisfactory.

14. DISCUSSION
This national, standard, abridged application by Pinewood Laboratories cross-refers to Night Nurse marketed by GlaxoSmithKline Beecham Consumer Healthcare. The clinical expert refers to the Pharmaceutical Expert Report in support of the statement that Fedril Cold and Flu oral solution is of equal strength and the same form as the reference product. It has thus been concluded that a bioequivalence study is not required.

15. CONCLUSION
The grant of a marketing authorisation is recommended.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Fedril Cold and Flu oral solution (PL 04917/0053) 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 were submitted and none are required for application of this type.

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

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with Fedril is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is considered to be positive.
**Fedril Night Cold and Flu Oral Solution**

*(PL 04917/0053)*

**STEPS TAKEN FOR ASSESSMENT**

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<tr>
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<th>Description</th>
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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 28(^{th}) January 2003</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 15(^{th}) April 2003</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 9(^{th}) February 2006, 9(^{th}) October 2007, 4(^{th}) December 2008, 24(^{th}) July 2009, 21(^{st}) August 2009 and on the clinical dossier on 28 March 2007</td>
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<tr>
<td>5</td>
<td>The application was determined on 5(^{th}) November 2009</td>
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Fedril Night Cold and Flu Oral Solution

(PL 04917/0053)

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME OF THE MEDICINAL PRODUCT
Fedril Night Cold and Flu, Oral Solution

2  QUALITATIVE AND QUANTITATIVE COMPOSITION
Active Constituents  mg/20 ml
Paracetamol  1000.0
Promethazine Hydrochloride  20.0
Dextromethorphan Hydrobromide  15.0

For excipients, see 6.1.

3  PHARMACEUTICAL FORM
Oral Solution
Clear green, mint flavoured, sugar free oral solution.

4  CLINICAL PARTICULARS
4.1 Therapeutic indications
For the symptomatic night time relief of colds, chills and influenza consisting of headache, shivers, sore throat pain, tickly cough, runny nose, aches and pains.

4.2 Posology and method of administration
Route of administration

For oral use.

Adults and children aged 12 years and over:
One measured 20 ml dose (or four 5 ml spoonfuls) to be taken just before going to bed.

Not to be given to children under 12 years.

Elderly:
The normal adult dose can be used.

4.3 Contraindications
Hypersensitivity to paracetamol or any of the other constituents. Hepatic or renal impairment.

4.4 Special warnings and precautions for use
Patients suffering from asthma or other respiratory disorders, epilepsy, glaucoma, urinary retention, prostatic hypertrophy, or cardiovascular problems, should only take the product after consulting a doctor.
Patients with rare hereditary problems of fructose intolerance should not take this medicine.

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

Do not exceed the stated dose.
Patients should be advised not to take other paracetamol-containing products or decongestant-containing medicines concurrently.

If symptoms persist consult your doctor.
Keep all medicines out of reach and sight of children.

Warning: May cause drowsiness. If affected, do not drive or operate machinery. Avoid alcoholic drink.

Special label warnings
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.

Special leaflet warnings
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.

This medicinal product contains ethanol (alcohol), i.e. up to 3.5ml per 20ml dose, equivalent to 70 ml of beer, 29 ml of wine per dose.

Harmful for those suffering from alcoholism.

To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with epilepsy.

Each 20ml dose contains up to 23.52mg of sodium. This should be taken into account by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction
The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
The hepatotoxicity of paracetamol may be potentiated by excessive intake of alcohol. Promethazine may potentiate the action of alcohol and other centrally acting depressants, hypnotics and anxiolytics. MAOIs may enhance the antimuscarinic effects of antihistamines. Antihistamines have an added antimuscarinic effect with other antimuscarinic drugs including tricyclic antidepressants. Promethazine may interfere with immunologic urine pregnancy test to produce false results.

Use of dextromethorphan in patients taking monoamine oxidase inhibitors should be avoided as severe reactions have been reported.

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 does not contraindicate breast feeding.

There are also no known contraindications to the use of Promethazine or Dextromethorphan during pregnancy and lactation. Hence, as with all medicines, the advice of a doctor should be sought before use of the product in pregnancy and lactation, and it should only be used when considered essential by the doctor.

4.7 Effects on ability to drive and use machines
This product may cause drowsiness. If affected do not drive or operate machinery.

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

Drowsiness, psychomotor impairment, antimuscarinic effects (such as urinary retention, dry mouth, and blurred vision), disorientation, restlessness and gastrointestinal disturbances may occasionally occur with promethazine. Hypersensitivity reactions including rash and photosensitivity reactions have been reported.

Adverse effects with dextromethorphan are rare, but gastrointestinal disturbances and dizziness have been reported occasionally.

4.9 Overdose
Immediate treatment is essential in the management of paracetamol overdosage. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who had ingested around 7.5g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have a beneficial effect up to at least 48 hours after the overdose may be required. General supportive measures must be available.
Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12-48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Liver damage is possible in adults who have taken 10 g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested); become irreversibly bound to liver tissue.

In children, Promethazine overdose can cause CNS stimulation and antimuscarinic effects. In severe cases in both adults and children, CNS depression with coma and convulsions may occur. Cardiorespiratory depression is uncommon. If the patient is seen soon enough after ingestion, it should be possible to induce vomiting with ipecacuanha despite the antiemetic effect of promethazine; alternatively gastric lavage may be used. Treatment otherwise supportive with attention to maintenance of adequate respiratory and circulatory status. Convulsions should be treated with diazepam or other suitable anticonvulsants.

Symptoms of Dextromethorphan overdose would be dizziness, excitation, mental confusion and gastrointestinal disturbances, and at very high doses, respiratory depression. Intravenous Naloxone is a specific antidote.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol: other analgesics and antipyretics, anilides.
Pharmacotherapeutic Group: Analgesics and Antipyretics, Anilides
ATC Code: N02B E01

Promethazine Hydrochloride: an antihistamine with anticholinergic activity.
Pharmacotherapeutic Group: Antihistamines for Systemic Use, Phenothiazine derivatives
ATC Code: R06A D02

Dextromethorphan Hydrobromide: an antitussive
Pharmacotherapeutic Group: Cough and Cold Preparations, Opium Alkaloids and derivatives
ATC Code: R05D A09

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the upper gastrointestinal tract. It is metabolised predominantly in the liver and excreted in the urine, mainly as glucuronide and sulphate conjugates.
Promethazine Hydrochloride is readily absorbed from the gastrointestinal tract, but undergoes extensive first pass metabolism in the liver, with only 25% of the oral dose reaching the systemic circulation unchanged. After oral therapy, therapeutic effects are identifiable at 15-30 minutes and peak plasma concentrations at 2 to 3 hours. Estimates of terminal half life in blood plasma are in the range of 4-6 hours. It is extensively plasma protein bound. It is eliminated mainly as metabolites, predominantly by the faecal (via biliary) route, with < 1% of the patient compound and ca. 10% as the sulphoxide metabolite being excreted in the urine over a 72 hour period.

Dextromethorphan Hydrobromide is well absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted as demethylated metabolites including dextrorphan, and as a minor proportion of unchanged dextromethorphan. In a small proportion of individuals, metabolism proceeds more slowly and dextromethorphan predominates in blood and urine.

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 of the product and which have not already been mentioned elsewhere in this summary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
- ethanol
- propylene glycol
- liquid maltitol (hydrogenated glucose syrup)
- sodium citrate
- ascorbic acid
- acesulfame k
- citric acid monohydrate
- natural mint flavour
- patent blue v (E131)
- quinoline yellow (E104)
- purified water

6.2 Incompatibilities
None known.

6.3 Shelf life
36 months
Shelf life after first opening: 1 month

6.4 Special precautions for storage
Do not store above 25°C. Store in the original container. Keep the bottle in the outer carton.

6.5 Nature and contents of container
Clear glass bottles – 200 ml with polypropylene child resistant closures.

6.6 Special precautions for disposal
Not applicable.

7 MARKETING AUTHORISATION HOLDER
Pinewood Laboratories Limited
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER(S)
PL 04917/0053

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
05/11/2009

10 DATE OF REVISION OF THE TEXT
05/11/2009
PATIENT INFORMATION LEAFLET

FEDRIL NIGHT COLD AND FLU ORAL SOLUTION
Paracetamol 1000mg/20ml,
Promethazine Hydrochloride 20mg/20ml,
Dextromethorphan Hydrobromide 15mg/20ml

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription, however, you still need to take Fedrill Night Cold and Flu Oral Solution 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.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Fedrill Night Cold and Flu is and what it is used for
2. Before you take Fedrill Night Cold and Flu
3. How to take Fedrill Night Cold and Flu
4. Possible side effects
5. How to store Fedrill Night Cold and Flu
6. Further information

1. WHAT FEDRILL NIGHT COLD AND FLU IS AND WHAT IT IS USED FOR
Fedrill Night Cold and Flu Oral Solution provides night time relief from the symptoms of colds, chills and ‘flu’. These include
headache, shivers, sore throat pain, runny nose, tickly cough, aches and pains. It contains paracetamol to reduce fever,
promethazine to dry up a runny nose, ease breathing and dextromethorphan which relieves a tickly cough.

2. BEFORE YOU TAKE FEDRILL NIGHT COLD AND FLU
Do not take Fedrill Night Cold and Flu if you
- are allergic (hypersensitive) to paracetamol, promethazine hydrochloride, dextromethorphan hydrobromide or any of the other ingredients of Fedrill Night Cold and Flu (see Section 6 and end of Section 2).
- have kidney or liver problems.

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

Take special care with Fedrill Night Cold and Flu
Tell your doctor if you:
- have asthma or other breathing problems
- have glaucoma
- have heart problems
- have alcohol problems
- have difficulty in passing urine (urinary retention)
- have prostate problems
- have epilepsy

If symptoms persist, consult your doctor.

Taking other medicines
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, even medicines obtained without
a prescription.
In particular, tell your doctor if you are taking medicines which:
- thin the blood (e.g. warfarin).
- control nausea or vomiting (e.g. domperidone or metoclopramide).
- reduce levels of cholesterol and other fats in the blood (e.g. cholestyramine).
- have been prescribed by your doctor to improve sleep, for anxiety or depression (including monoamine oxidase inhibitors (MAOIs) and antimuscarinic drugs).

Do not consume alcoholic drinks while you are taking Fedrill Night Cold and Flu.
Promethazine may interfere with pregnancy tests to produce false results.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicines during pregnancy.
If you are, or are likely to become pregnant, or are breast-feeding, Fedrill Night Cold and Flu should only be taken when
advised by your doctor.

Driving and using machines
This product may cause drowsiness. If affected, do not drive or operate machinery.

Important information about some of the ingredients of Fedrill Night Cold and Flu
The product contains:
Ethanol: up to 3.5% per measured dose, equivalent to 70ml of beer, or 29ml of wine. Harmful for those suffering from alcoholicism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients
with epilepsy.

Liquid maltol (hydrogenated glucose syrup): 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: This medicine contains up to 23.52mg of sodium per 20ml dose. To be taken into consideration by patients on a
controlled sodium diet.
3. HOW TO TAKE FEDRIL NIGHT COLD AND FLU

Always take the product exactly as directed. You should check with your doctor or pharmacist if you are not sure.

The usual dose is:

<table>
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<th>Age Group</th>
<th>Dosage</th>
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<tr>
<td>Adults and children aged 12 years and over</td>
<td>One 20ml dose (or four 5ml spoonfuls) to be taken just before going to bed.</td>
</tr>
<tr>
<td>Children under 12:</td>
<td>Do not give to children under 12 years of age.</td>
</tr>
<tr>
<td>Elderly:</td>
<td>Dose as for 'Adults' above.</td>
</tr>
</tbody>
</table>

DO NOT EXCEED THE STATED DOSE.

If you take more Fedril Night Cold and Flu than you should:
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.
Also seek immediate medical advice if you take other paracetamol-containing medicines by mistake.

If you forget to take Fedril Night Cold and Flu:
If you miss a dose, take it as soon as you remember. Do not take a double dose to make up for the forgotten dose.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Fedril Night Cold and Flu can cause side effects, although not everybody gets them.

You may notice the following:
- rash, itchy skin, swelling of the lips, eyes, tongue, or difficulty in breathing may be signs of an allergic reaction. Stop taking Fedril Night Cold and Flu immediately.
- mental and physical slowness
- inability to pass urine, dry mouth, blurred vision
- disorientation or dizziness
- restlessness
- upset stomach
- sensitivity to light
- feeling sleepy (drowsiness)

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

5. HOW TO STORE FEDRIL NIGHT COLD AND FLU

Do not store above 25°C.
Keep out of the reach and sight of children.
Store in the original container and keep the bottle in the outer carton (in order to protect from light).
Do not use after one month from first opening.
Do not use Fedril Night Cold and Flu after the expiry date which is stated on the label or carton. The expiry date refers to the last day of the month.
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

Each 20 ml of Fedril Night Cold and Flu Oral Solution contains:
- The active substances: 1000mg paracetamol, 20mg promethazine hydrochloride, 15mg dextromethorphan hydrobromide.
- The other ingredients are: ethanol, propylene glycol, liquid maltitol (E965), sodium citrate, ascorbic acid, acesulfame K, citric acid monohydrate, natural mint flavour, patent blue V (E131), quinoline yellow (E104), purified water.

What Fedril Night Cold and Flu looks like and contents of the pack:
Fedril Night Cold and Flu is a clear green, mint flavoured sugar-free solution, available in 200ml clear glass bottles with child resistant caps.

Marketing Authorisation Holder and Manufacturer:
Pinewood Laboratories Ltd., Ballymacarthy, Clonmel, Co. Tipperary, Ireland.
PL 04917/0053

This leaflet was last updated in: November 2009.
LABELLING

For symptomatic relief of colds, chills and flu symptoms.

INGREDIENTS

Each 20 ml of oral solution contains the active ingredients: Paracetamol 1000 mg, Promethazine Hydrochloride 20 mg and Scopolamine Hydrobromide 15 mg. It also includes the following inactive ingredients: Ethanol, Propylene Glycol, Sodium Citrate, Liquid Maltitol (E965), Patent Blue V (E131), Citric Acid Monohydrate and Carmine Liquid Yellow E104. See leaflet for further information.

DIRECTIONS FOR USE

For Oral Administration.

Dosage: Adults and children aged 12 years and over: One 20 ml dose (or four 5 ml spoonfuls) to be taken just before going to bed. Do not give to children under 12 years of age.

Do not exceed the stated dose.

CONTAINS PARACETAMOL

WARNINGS

Do not take if you:
• are allergic to any of the ingredients.
• have kidney or liver problems.

If symptoms persist consult your doctor.

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

Do not use with other paracetamol-containing products.

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

Please read patient information leaflet before use.

STORAGE

Keep all medicines out of the reach and sight of children. Do not store above 25°C. Store in the original container. The bottle should be stored in the outer carton in order to protect from light. Do not use after one month from first opening.