

New Zealand Datasheet

1. NAME OF MEDICINE

PANAFEN® PLUS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredients:

Ibuprofen 200 mg, codeine phosphate 12.8 mg

3. PHARMACEUTICAL FORM

Ibuprofen

Chemical name: 2-(4-isobutylphenyl) propionic acid

Molecular formula: C₁₃H₁₈O₂

MW: 206.3

CAS: 15687-27-1

Ibuprofen is a white or almost white powder or crystals with a characteristic odour. Practically insoluble in water, soluble 1 in 1.5 of alcohol, 1 in 1 of chloroform, 1 in 2 of ether and 1 in 1.5 of acetone; soluble in aqueous solutions of alkali hydroxides and carbonates.

Codeine phosphate.

Chemical name: (5R,6S)-7, 8-didehydro-4,5- epoxy-3-methoxy-N- methylmorphinan-6-ol dihydrogen orthophosphate hemihydrate

Molecular formula: C₁₈H₂₁NO₃H₃PO₄·½H₂O MW: 406.4

CAS: 41444-62-6

Codeine phosphate is a small, colourless, odourless crystal or a white, odourless crystalline powder. It is soluble in four parts water, slightly soluble in ethanol (96%), practically insoluble in chloroform and ether.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The temporary relief of strong pain and discomfort associated with migraine headache, tension headache, period pain, toothache, cold & flu symptoms, back or muscular pain,

arthritis and neuralgia. Reduces fever.

4.2 Dosage and Method of Administration

18 years - Adults

Initial dose: 2 caplets taken with fluid, then 1 or 2 caplets every four hours when necessary. Maximum: 6 caplets in a 24 hour period.

Children (under 18 years)

Must not be used in patients under 18 years.

Do not exceed the stated dose.

Should not be used with other ibuprofen, NSAID or codeine-containing products.

Minimum dosing interval: 4 hours

Maximum duration of continued use without medical advice: 3 days

If symptoms persist or worsen, medical advice must be sought.

Panafen Plus should not be used for more than 3 days at a time unless on medical advice, in which case the patient should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

4.3 Contraindications

Known hypersensitivity to ibuprofen, codeine or other opioid analgesics or any of the excipients in the product.

Children under the age of 18 years because of the risk of opioid toxicity due to the variable and unpredictable metabolism of codeine to morphine (see Pharmacology)

Known hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs).

Patients with gastrointestinal bleeding or with an active or previous peptic ulcer.

Patients with a history of upper gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Patients who are taking concomitant NSAIDs including cyclo-oxygenase-2 (Cox-2) specific inhibitors (see Drug Interactions).

Panafen Plus should not be used in heart failure.

Panafen Plus should not be used in renal impairment or severe liver impairment.

Respiratory depression, chronic constipation and active alcoholism.

Diarrhoea caused by pseudomembranous colitis or poisoning (until the causative organism or toxin has been eliminated from the gastrointestinal tract, since codeine may slow down the elimination and thereby prolonging the diarrhoea).

Patients who are pregnant [see Use in Pregnancy].

Patients who are breastfeeding. [see Use in Lactation].

Patients who are known to be CYP2D6 ultra-rapid metabolisers. If the patient is an extensive or ultra-rapid CYP2D6 metaboliser, there is an increased risk of developing symptoms of opioid toxicity, even at commonly prescribed doses [see Pharmacology]. General symptoms of opioid toxicity, include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression which may be life-threatening and very rarely fatal.

Patients undergoing treatment of perioperative pain in setting of coronary artery bypass surgery (CABG).

4.4 Special Warnings and Precautions for Use

If symptoms persist, medical advice must be sought.

Do not take for more than 3 days unless told to do so by your doctor.

Prolonged or excessive consumption of codeine can result in dependence [see Adverse Effects].

Panafen Plus should be used with caution in patients who have a history of drug abuse.

Use with caution in elderly patients who are more prone to adverse events.

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.

Panafen Plus should be administered with caution to patients with asthma or allergic disease, and especially those patients who have not taken an NSAID before.

Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this product. The use of NSAIDs may result in deterioration of renal function.

Patients with a history of hypertension and/or heart failure should seek medical advice before use, as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

Use with caution in patients with chronic inflammatory intestinal disease (ulcerative

colitis. Crohn's disease), obstructive bowel disorders or acute abdominal conditions, as these conditions may be exacerbated.

Use with caution in patients with a history of cholecystectomy as NSAIDs may cause acute pancreatitis in some patients.

Use with caution in patients with Systemic Lupus Erythematosus (SLE) and mixed connective tissue disease due to increase risk of aseptic meningitis.

Gastrointestinal (GI) bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. When GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn and patients should consult a doctor (see Adverse Reactions)

Discontinue at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity, as serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs

Cardiovascular and cerebrovascular effects:

Observational studies have indicated that NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use. Patients with cardiovascular disease, history of atherosclerotic disease or cardiovascular risk factors may also be at greater risk.

Patients should be advised to remain alert for such cardiovascular events, even in the absence of previous cardiovascular symptoms. Patients should be informed about signs and / or symptoms of serious cardiovascular toxicity and the steps to take if they occur.

Fluid retention, hypertension and oedema have been reported in association with NSAID therapy. Patients taking antihypertensives with NSAIDs may have an impaired antihypertensive response. Therefore, Panafen Plus should only be used under medical advice in patients with hypertension (see also *Contraindications* – heart failure).

Hepatic:

As with other NSAIDs elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may resolve with continued therapy. Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled clinical trials in less than 1 % of patients.

Patients should be advised to remain alert for hepatotoxicity and be informed about the signs and / or symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritis, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms).

As with other drugs of this class, ibuprofen may mask the usual signs of infection.

Codeine may also obscure the diagnosis or the course of gastrointestinal diseases. Panafen Plus should therefore be administered with caution in such situations.

Panafen Plus should be administered with caution to patients who have recently had gastrointestinal surgery, as codeine may reduce gastrointestinal motility.

The use of non-steroidal anti-inflammatory drugs (NSAIDs) may result in deterioration of renal function.

Panafen Plus should be administered with caution to those with hypotension and/or hypothyroidism. The caplets should be used with caution in patients with CNS depression, raised intracranial pressure or head injury, since codeine may increase the risk of respiratory depression and further elevate intracranial pressure.

Panafen Plus should be administered with caution to patients with prostatic hypertrophy since codeine may cause urinary retention.

Patients taking other medications should consult a physician prior to taking this product.

Keep out of sight and reach of children.

Panafen Plus contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

Use in the elderly

NSAIDs should be used with particular caution in elderly patients who are more prone to adverse events. The elderly may also be more susceptible to the CNS depressant effects of opioids.

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Panafen Plus with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anaesthetics, medicines with antihistamine-sedating actions such as antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of medicine-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics [see Section 4.5 Interactions with other medicines and other forms of interaction].

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Advise both patients and caregivers about the risks of respiratory depression and sedation when Panafen Plus is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs [see Section 4.5 Interactions with other medicines and other forms of interaction].

4.5 Interactions with Other Medicines and Other Forms of Interactions

Ibuprofen-containing products should not be used in combination with other NSAIDs including aspirin and cyclo-oxygenase-2 (COX-2) specific inhibitors as these may increase the risk of adverse effects [see Contraindications].

Ibuprofen-containing products may inhibit the anti-platelet effect of low dose aspirin. Patients on low dose aspirin (not above 75 mg) should be instructed to consult their doctor or pharmacist before taking ibuprofen [see PRECAUTIONS].

Ibuprofen-containing products should be used with caution in combination with the following drugs as interactions have been reported:

ACE inhibitors, beta-blockers and diuretics: Ibuprofen, like other NSAIDs, can reduce the antihypertensive effect with possible loss of blood pressure control and can attenuate the natriuretic effects of diuretics.

ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics: The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time, increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drugs. Concomitant use of all three classes of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the treatment. The combination of drugs from these three classes should be used with caution.

Aminoglycosides: Reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentration.

Anticoagulants: Concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage. The mechanism of this interaction is not known but may involve increased bleeding from NSAID-induced gastrointestinal ulceration or an additive effect of NSAID inhibition of platelet function with the anticoagulant effect of warfarin. Panafen Plus should only be used in patients taking warfarin if absolutely necessary. Patients taking this combination must be closely monitored.

Benzodiazepines and other Central Nervous System (CNS) Depressants: Concomitant use of benzodiazepines or other CNS depressants including alcohol, increases the risk of respiratory depression, profound sedation, coma and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation [see Section 4.4 Warnings and Precautions]. Examples of medicines which interact are: benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anaesthetics, drugs with antihistamine-sedating actions such as antipsychotics, other opioids, alcohol.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels. Care should therefore be taken in patients treated with cardiac glycosides.

Corticosteroids: An increased risk of gastrointestinal bleeding may occur with corticosteroids.

Lithium: Ibuprofen has been shown to decrease the renal clearance and increase plasma concentrations of lithium. Lithium plasma concentrations should be monitored in patients on concurrent ibuprofen therapy.

Methotrexate: NSAIDs inhibit tubular secretion of methotrexate in animals. As a result, reduction in the clearance of methotrexate may occur. Use of high doses of methotrexate concomitantly with NSAIDs should be avoided. At low doses of methotrexate, caution should be used if ibuprofen is administered concomitantly.

Cyclosporin: Increased risk of nephrotoxicity.

Hypoglycaemic agents (oral): Inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

Quinolones: NSAIDs can increase the risk of convulsions associated with quinolone antibiotics.

Zidovudine: Increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs.

Selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.

Diuretics - reduced diuretic effect.

Codeine-containing products should be used with caution in combination with the following drugs as interactions have been reported.

Anticholinergics: Concurrent use of codeine and anticholinergic agents may increase the risk of severe constipation and/or urinary retention.

Antihypertensives: Hypotensive effects of antihypertensive agents may be potentiated when used concurrently with codeine and lead to orthostatic hypotension.

Antiperistaltic antidiarrhoeals (including kaolin, pectin, loperamide): Concurrent use of these agents with codeine may increase the risk of severe constipation.

Central nervous system depressants: Codeine may potentiate the effects of CNS depressants including alcohol, anaesthetics, anxiolytics, hypnotics, sedatives, tricyclic antidepressants, phenothiazines, muscle relaxants, other opioids and drugs with antihistamine-sedating actions such as antipsychotics

Metoclopramide & domperidone: Codeine may antagonise the effects of these antiemetics on gastrointestinal motility.

Monoamine oxidase inhibitors (MAOIs): Concurrent administration or use within 14 days of ceasing monoamine oxidase inhibitors may enhance the potential respiratory depressant effects of codeine.

Opioid analgesics: Concurrent use of codeine and other opioid receptor agonists is usually inappropriate as additive CNS depression, respiratory depression and hypotensive effects may occur.

Probenecid and phenytoin: Interactions may also occur with probenecid, antidiabetic medications and phenytoin.

Quinidine: Interferes with the metabolism of codeine to morphine, lowering the analgesic effect of codeine.

It is possible that interactions could occur between drugs that can inhibit CYP2D6 (such as quinidine, phenothiazines and antipsychotic agents) and codeine.

4.6 Fertility, Pregnancy and Lactation

Effect on female fertility

There is some evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment. Therefore, Panafen Plus is not recommended

in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs should be considered.

Use in pregnancy (Category C)

This product should not be used during pregnancy. The safety of codeine during pregnancy has not been established relative to the possible adverse effect on foetal development. Maternal use of codeine during labour may cause respiratory depression in the child. There is an ibuprofen-related risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension during the third trimester of pregnancy. The onset of labour may be delayed and its duration increased, with an increased risk of bleeding tendency in both mother and child.

Use in lactation

This product should not be used while breastfeeding.

In nursing mothers, who are ultra-rapid metabolisers of codeine, higher than expected serum and breast milk morphine levels can occur. Morphine toxicity in babies can cause excessive somnolence, hypotonia and difficulty breastfeeding or breathing. In severe cases respiratory depression and death can occur.

4.7 Effects on ability to drive and use machinery

Codeine may cause dizziness or drowsiness. Those affected should not drive or operate machinery.

Following treatment with ibuprofen, the reaction time of patients may be affected. NSAIDs may cause dizziness, drowsiness, fatigue and visual disturbances. If affected patients should not drive or operate machinery

4.8 Undesirable Effects

Adverse reactions reported from extensive post-marketing experience are listed below by System Organ Class and frequency. The following convention has been utilised for the classification of undesirable effects: very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ and $< 1/1000$), very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Ibuprofen

The following list of adverse effects related to those experienced with ibuprofen at OTC doses, for short term use. The treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Body System	Undesirable Effect	Frequency
Gastrointestinal disorders	Abdominal pain, nausea, dyspepsia	Uncommon
	Diarrhoea, flatulence, constipation and vomiting	Rare
	Peptic ulcer, perforation or	Very rare

	gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly. Exacerbation of ulcerative colitis and Crohn's disease (see Precautions)	
Nervous system disorders	Headache, drowsiness, dizziness, hearing disturbance (tinnitus)	Common
Skin and subcutaneous tissue disorders	Skin rashes, itching	Uncommon
	Severe forms of skin reactions, exfoliative and bullous dermatitoses such as erythema multiforme and epidermal necrolysis	Very rare
Renal and urinary disorders	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema	Very rare
Hepatobiliary disorders	Liver disorders	Very rare
Blood and lymphatic disorders	Haematopoietic disorders (anaemia, leucopaenia, thrombocytopaenia, pancytopenia, agranulocytosis). First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising	Very rare
Immune system disorders	Hypersensitivity reactions including: urticaria and pruritus	Uncommon
	Severe hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock), exacerbation of asthma and bronchospasm	Very rare
Other	Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment (see Precautions). In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen,	Unknown

	single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see Precautions)	
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Codeine

Body system	Undesirable Effect	Frequency
Psychiatric disorders	Drug dependency can occur after prolonged use of codeine at higher doses (see Precautions)	Not known
Gastrointestinal disorders	Constipation, nausea, vomiting, dyspepsia, dry mouth, acute pancreatitis in patients with a history of cholecystectomy (see Precautions)	Not known
Nervous system disorders	Dizziness, worsening of headache with prolonged use and drowsiness	Not known
Skin and subcutaneous tissue disorders	Pruritus, sweating	Not known

4.9 Overdose

The National Poisons Centre can also be contacted (telephone 0800 764 766) for current information on the treatment of oral overdoses.

Ibuprofen

In children ingestion of more than 400mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 – 3 hours.

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more severe poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Treatment should be symptomatic and supportive including the maintenance of a

clear airway and monitoring of cardiac and vital signs until stable. Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

Codeine

An overdose of codeine is characterised, in the first phase, by nausea and vomiting. An acute depression of the respiratory centre can cause cyanosis, slower breathing, drowsiness, ataxia and, more rarely, pulmonary oedema. Respiratory pauses, miosis, convulsion, collapse and urine retention as well as signs of histamine release have been observed as well. In severe cases, this may include symptoms of circulatory and respiratory depression which may be life-threatening and very rarely fatal.

Treatment should include general symptomatic and supportive measures including a clear airway and monitoring of vital signs until stable. Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected. Give naloxone if coma or respiratory depression is present. Observe for at least four hours after ingestion.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

It is thought that ibuprofen produces an anti-inflammatory effect at least in part by inhibiting prostaglandin synthetase. Ibuprofen has shown anti-inflammatory, analgesic and antipyretic activity in both animal and human studies.

Codeine phosphate is a narcotic analgesic acting on central opiate receptors, although its pharmacological effects are thought to be largely due to its biotransformation to morphine.

5.2 Pharmacokinetic Properties

Ibuprofen

Absorption

Ibuprofen is well absorbed after oral administration with peak serum levels occurring after one to two hours.

Distribution

The apparent volume of distribution for ibuprofen is 0.14 L/kg. Ibuprofen and its metabolites readily cross the placental barrier in pregnant rabbits and rats. It is not known if the drug enters the cerebrospinal fluid. 99% of ibuprofen is protein bound. The high protein binding of the drug should

be borne in mind when prescribing ibuprofen together with other protein bound drugs that bind to the same site on human serum albumin.

Metabolism and Elimination

90% of ibuprofen is metabolised in the liver to produce two major metabolites, a hydroxylated and carboxylated compound.

Both the inactive metabolites of ibuprofen and a small amount of unchanged ibuprofen are excreted rapidly and completely by the kidney with 95% of the administered dose eliminated in the urine within four hours of ingestion. The elimination half-life of ibuprofen is in the range of 1.9 to 2.2 hours.

Codeine

Absorption

Codeine is well absorbed from the gastrointestinal tract and peak plasma concentrations are reached one hour after oral administration. Onset of action occurs in 15 to 30 minutes and analgesia is maintained for four to six hours.

Distribution

Codeine is rapidly distributed to skeletal muscles, kidneys, liver, gastrointestinal tract, lungs, spleen and brain. It crosses the placenta and is distributed in low levels in breast milk.

Metabolism and Excretion

Codeine is metabolised mainly in the liver. The major metabolic pathway involves glucuronidation of codeine to codeine-6-glucuronide. Codeine can also undergo O- and N-demethylation catalysed by CYP2D6 and CYP3A4 respectively. About 10% of an administered dose of codeine is converted by O-demethylation to morphine, which subsequently undergoes glucuronidation to morphine-3 or morphine-6 glucuronide, or N-demethylation to normorphine. Approximately 5 to 10% of the Caucasian population cannot convert codeine to morphine as they are deficient in the CYP2D6 enzyme. These patients are likely to obtain reduced pain relief from codeine. Codeine is also converted by N-demethylation to norcodeine, which subsequently undergoes glucuronidation to norcodeine glucuronide or O-demethylation to normorphine. Codeine is excreted mainly by the kidneys. Of the excreted material in the urine, 40 to 70% is free or conjugated codeine, 5 to 15% is free or conjugated morphine and 10 to 20% is free or conjugated norcodeine. The plasma half-life of codeine is two to four hours. Only traces of codeine and its metabolites are found in the faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

cellulose-microcrystalline, vegetable oil-hydrogenated, sodium starch glycollate, silica-colloidal anhydrous, lactose, cellulose-powdered, hypromellose, macrogol 400.

6.2 Incompatibilities

No known incompatibilities

6.3 Shelf life

36 months from date of manufacture

6.4 Special Precautions for storage

Store below 25 degrees Celsius. Keep out of reach of children.

6.5 Nature and contents of container

Blister packs of 15 and 30 caplets.

Not all pack size may be marketed.

7 MEDICINE SCHEDULE

Restricted Medicine

8 SPONSOR

GlaxoSmithKline Consumer Healthcare
Level 11, Zurich House
21 Queen Street
Auckland 1010
New Zealand
FREECALL NZ: 0800 540 144

9 DATE OF FIRST APPROVAL

8 January 2004

10 DATE OF REVISION OF THE TEXT

15 May 2018

Summary table of changes

Section changes	Summary of new changes
All	Transferred to new data sheet template

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