1. PRODUCT NAME

Codeine Phosphate Tablets (PSM)

15 mg, 30 mg & 60 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name and strength of the active substance
Codeine Phosphate Hemihydrate BP 15 mg
Codeine Phosphate Hemihydrate BP 30 mg
Codeine Phosphate Hemihydrate BP 60 mg

Codeine phosphate hemihydrate is obtained from opium or made by methylating morphine. It occurs as odourless colourless crystals or white crystalline powder. The molecular formula of codeine phosphate is $C_{18}H_{21}NO_3,H_3PO_4.½H_2O$ and the molecular weight 406.4.

Excipient(s) with known effect
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral – tablet, uncoated

Presentation

Codeine Phosphate Tablets (PSM) are white, biconvex circular tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Codeine phosphate is indicated for:

- the relief of mild to moderate pain (including pain associated with terminal illness, post-operative pain, headache),
- the relief of symptoms of diarrhoea (except diarrhoea caused by poisoning).

4.2 Dose and method of administration

Adults

Codeine phosphate may be given orally in doses of 15 mg – 60 mg every 4 – 6 hours as needed.
If these doses fail to relieve pain, larger doses rarely succeed and may give rise to restlessness and excitement.

The maximum daily dose in adults should not exceed 300 mg.

Paediatric

Do not use in children aged less than 12 years (see sections 4.3 and 4.4).

The usual paediatric dose is 0.5 mg per kg of body weight, every 4 to 6 hours as needed. The total dose should not exceed 240 mg in 24 hours. The duration of treatment should not normally exceed 3 days.

4.3 Contraindications

Codeine phosphate is contraindicated in:

- Known hypersensitivity to codeine, other opioids, or any component of the tablets
- Acute respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion
- Obstructive airways disease
- Acute alcoholism
- Head injuries and conditions in which intracranial pressure is raised
- Patients at risk of paralytic ileus
- Hepatic failure
- Acute asthma attack
- Heart failure secondary to chronic lung disease
- Diarrhoea associated with pseudomembranous colitis or caused by poisoning
- Patients taking monoamine oxidase inhibitors or within fourteen days of stopping such treatment
- Children aged less than 12 years (see section 4.4)
- Adolescents aged less than 18 years for pain following surgery to remove tonsils or adenoids (see section 4.4)
- Adolescents aged less than 18 years in whom respiratory function might be compromised (see section 4.4)
- Adolescents aged less than 18 years for symptomatic relief of cough and cold (see section 4.4)
- Women who are breastfeeding (see section 4.4)

4.4 Special warnings and precautions for use

WARNINGS

Hazardous and harmful use

Codeine Phosphate Tablets (PSM) contain the opioid Codeine phosphate ingredient and is a potential drug of abuse, misuse and addiction. Addiction can occur in patients appropriately prescribed Codeine Phosphate Tablets (PSM) at recommended doses.

The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the drug is used and with higher doses.
Patients should be assessed for their risks for opioid abuse or addiction prior to being prescribed Codeine Phosphate Tablets (PSM).

All patients receiving opioids should be routinely monitored for signs of misuse and abuse. Opioids are sought by people with addiction and may be subject to diversion. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the safe storage and proper disposal of any unused drug (see *section 6.4 Special precautions for storage and section 6.6 Special precautions for disposal)*. Caution patients that abuse of oral or transdermal forms of opioids by parenteral administration can result in serious adverse events, which may be fatal.

Patients should be advised not to share Codeine Phosphate Tablets (PSM) with anyone else.

Respiratory depression

Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended. It can occur at any time during the use of Codeine Phosphate Tablets (PSM) but the risk is greatest during initiation of therapy or following an increase in dose. Patients should be monitored closely for respiratory depression at these times.

The risk of life-threatening respiratory depression is also higher in elderly, frail, or debilitated patients and in patients with existing impairment of respiratory function (e.g. chronic obstructive pulmonary disease; asthma). Opioids should be used with caution and with close monitoring in these patients (see *section 4.2 Dose and method of administration*). The use of opioids is contraindicated in patients with severe respiratory disease, acute respiratory disease and respiratory depression (see *section 4.3 Contraindications*).

The risk of respiratory depression is greater with the use of high doses of opioids, especially high potency and modified release formulations, and in opioid naïve patients. Initiation of opioid treatment should be at the lower end of the dosage recommendations with careful titration of doses to achieve effective pain relief. Careful calculation of equianalgesic doses is required when changing opioids or switching from immediate release to modified release formulations, (see *section 4.2 Dose and method of administration*).

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-

dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper.

Risks from concomitant use of benzodiazepines or other CNS depressants, including alcohol

Concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of Codeine Phosphate Tablets (PSM) with CNS depressant medicines, such as other opioid analgesics, benzodiazepines, gabapentinoids, cannabis, sedatives, hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, centrally active anti-emetics and other CNS depressants, should be reserved for patients for whom other treatment options are not possible. If a decision is made to prescribe Codeine Phosphate Tablets (PSM) concomitantly with any of the medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. Patients should be followed closely for signs and symptoms of respiratory depression and sedation. Patients and their caregivers should be made aware of these symptoms. Patients and their caregivers should also be informed of the potential harms of consuming alcohol while taking Codeine Phosphate Tablets (PSM).

Use of opioids in chronic (long-term) non-cancer pain (CNCP)

Opioid analgesics have an established role in the treatment of acute pain, cancer pain and palliative and end-of-life care. Current evidence does not generally support opioid analgesics in improving pain and function for most patients with chronic non-cancer pain. The development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, increase with the length of time a patient takes an opioid. The use of opioids for long-term treatment of CNCP is not recommended.

The use of an opioid to treat CNCP should only be considered after maximised non-pharmacological and non-opioid treatments have been tried and found ineffective, not tolerated or otherwise inadequate to provide sufficient management of pain. Opioids should only be prescribed as a component of comprehensive multidisciplinary and multimodal pain management.

Opioid therapy for CNCP should be initiated as a trial in accordance with clinical guidelines and after a comprehensive biopsychosocial assessment has established a cause for the pain and the appropriateness of opioid therapy for the patient (see *Hazardous and harmful use, above*). The expected outcome of therapy (pain reduction rather than complete abolition of pain, improved function and quality of life) should be discussed with the patient before commencing opioid treatment, with agreement to discontinue treatment if these objectives are not met.

Owing to the varied response to opioids between individuals, it is recommended that all patients be started at the lowest appropriate dose and titrated to achieve an adequate level of analgesia and functional improvement with minimum adverse reactions. Immediate-release products should not be used to treat chronic pain but may be used for a short period in opioid-naïve patients to develop a level of tolerance before switching to a modified-release formulation. Careful and regular assessment

and monitoring is required to establish the clinical need for ongoing treatment. Discontinue opioid therapy if there is no improvement of pain and/or function during the trial period or if there is any evidence of misuse or abuse.
Treatment should only continue if the trial has demonstrated that the pain is opioid responsive and there has been functional improvement. The patient's condition should be reviewed regularly, and the dose tapered off slowly if opioid treatment is no longer appropriate (see *Ceasing Opioids*).

Tolerance, dependence and withdrawal

Neuroadaptation of the opioid receptors to repeated administration of opioids can produce tolerance and physical dependence. Tolerance is the need for increasing doses to maintain analgesia. Tolerance may occur to both the desired and undesired effects of the opioid.

Physical dependence, which can occur after several days to weeks of continued opioid usage, results in withdrawal symptoms if the opioid is ceased abruptly or the dose is significantly reduced.

Withdrawal symptoms can also occur following the administration of an opioid antagonist (e.g. naloxone) or partial agonist (e.g. buprenorphine). Withdrawal can result in some or all of the following symptoms: dysphoria, restlessness/agitation, lacrimation, rhinorrhoea, yawning, sweating, chills, myalgia, mydriasis, irritability, anxiety, increasing pain, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, increased blood pressure, increased respiratory rate and increased heart rate.

When discontinuing Codeine Phosphate Tablets (PSM) in a person who may be physically dependent, the drug should not be ceased abruptly but withdrawn by tapering the dose gradually (see *Ceasing opioids and section 4.2 Dose and Method of Administration*).

Accidental ingestion/exposure

Accidental ingestion or exposure of Codeine Phosphate Tablets (PSM), especially by children, can result in a fatal overdose of [opioid]. Patients and their caregivers should be given information on safe storage and disposal of unused Codeine Phosphate Tablets (PSM) (see *section 6.4 Special precautions for storage and section 6.6 Special precautions for disposal*).

Hyperalgesia

Hyperalgesia may occur with the use of opioids, particularly at high doses. Hyperalgesia may manifest as an unexplained increase in pain, increased levels of pain with increasing opioid dosages or diffuse sensitivity not associated with the original pain. Hyperalgesia should not be confused with tolerance (see Tolerance, dependence and withdrawal). If opioid induced hyperalgesia is suspected, the dose should be reduced and tapered off if possible. A change to a different opioid may be required.

Ceasing opioids

Abrupt discontinuation or rapid decreasing of the dose in a person physically dependent on an opioid may result in serious withdrawal symptoms and uncontrolled pain (see *Tolerance, dependence and withdrawal*). Such symptoms may lead the patient to seek other sources of licit or illicit opioids. Opioids should not be ceased abruptly in a patient who is physically dependent but withdrawn by tapering the dose slowly. Factors to take into account when deciding how to discontinue or decrease therapy include the dose and duration of the opioid the patient has been taking, the type of pain being treated and the physical and psychological attributes of the patient. A multimodal approach to pain management should be in place before initiating an opioid analgesic taper. During tapering, patients require regular review and support to manage any increase in pain, psychological distress and withdrawal symptoms.

There are no standard tapering schedules suitable for all patients and an individualised plan is necessary. In general, tapering should involve a dose reduction of no more than 10 percent to 25 percent every 2 to 4 weeks (see *section 4.2 Dose and Method of Administration*). If the patient is experiencing increased pain or serious withdrawal symptoms, it may be necessary to go back to the previous dose until stable before proceeding with a more gradual taper.

When ceasing opioids in a patient who has a suspected opioid use disorder, the need for medication assisted treatment and/or referral to a specialist should be considered.

The following patients may be more susceptible to the effects of codeine. The lowest effective dose for the shortest period of time should be prescribed. Signs of toxicity or overdose may include nausea, vomiting, constipation, lack of appetite, somnolence, extreme sleepiness, confusion, shallow breathing and even coma. If symptoms of toxicity are present, codeine should be stopped immediately and medical advice sought.

- recent tonsillectomy, adenoidectomy or throat surgery
- hypothyroidism
- adrenocortical insufficiency e.g. Addison's disease
- impaired kidney or liver function
- prostatic hypertrophy
- shock/hypotension
- myasthenia gravis
- convulsions / convulsive disorders
- gall bladder disease or gall stones
- recent gastro-intestinal surgery
- urinary tract surgery
- reduced respiratory function or history of asthma
- obstructive bowel disorders – codeine reduces peristalsis, increases tone and segmentation in the bowel and can raise colonic pressure
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment

Hypersensitivity

Maculopapular rash, fever, splenomegaly and lymphadenopathy have been seen as part of a codeine hypersensitivity reaction.

Dependence

Taking codeine regularly for a long time can lead to addiction. Stopping treatment can result in withdrawal symptoms.
Prolonged use of high doses of codeine has produced dependence of the morphine type in a very small proportion of users. Codeine produces less euphoria and sedation than morphine and is not a completely satisfactory substitute for morphine in morphine addicts.
Regular use of analgesics for headache can result in an overuse syndrome.

Withdrawal

Abrupt withdrawal precipitates a withdrawal syndrome. Symptoms may include tremor, insomnia, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, mydriasis, weakness, pyrexia, muscle cramps, dehydration and increase in heart rate, respiratory rate and blood pressure. These effects can also occur in neonates exposed to codeine *in utero* (see use in pregnancy).
Tolerance diminishes rapidly after withdrawal so a previously tolerated dose may prove fatal.

Withdrawal symptoms develop more slowly than with morphine and are milder.

CYP2D6 Genetic polymorphism

Codeine may be partially metabolised by CYP2D6 to morphine. Patients who are deficient in or lacking this enzyme cannot convert codeine to morphine and therefore will not obtain adequate analgesic effects. Conversely, some patients are able to convert codeine to morphine more rapidly and completely. Patients who metabolise codeine very rapidly (ultra-rapid metabolisers) are at increased risk of developing adverse effects or opioid toxicity, even at low doses. Adverse effects range from less serious symptoms such as nausea, vomiting, constipation, 'pin-point' pupils and dizziness or drowsiness, through to life-threatening symptoms such as shallow breathing, slow heart rate, confusion, hallucinations, seizure and coma. Healthcare professionals should inform patients about these risks and the signs and symptoms of morphine toxicity and advise patients that if signs of toxicity are present, codeine should be stopped immediately and medical advice sought.

Estimates suggest that up to 10% of the Caucasian population may be poor metabolisers and up to 10% may be ultra-rapid metabolisers. The prevalence in Maori and Pacific people is not known.

Use in children

Children are more susceptible to the respiratory and circulatory depressant effects of opioid analgesics such as codeine. Parents and caregivers should be advised to seek medical advice immediately if signs of toxicity are present, such as excessive sleepiness, difficulty waking, difficulty breathing, confusion, slow heart rate or weak pulse. Paradoxical excitation or restlessness may also occur in paediatric patients receiving opioids (see section 4.9).

Use of codeine is contraindicated in:

- Children aged less than 12 years (see section 4.4)
- Adolescents aged less than 18 years for pain following surgery to remove tonsils or adenoids (see section 4.4)
- Adolescents aged less than18 years in whom respiratory function might be compromised (see section 4.4)
- Adolescents aged less than 18 years for symptomatic relief of cough and cold (see section 4.4)

Use in the elderly

Geriatric patients may be more susceptible to the effects, especially the respiratory depressant effects, of these medications. Also, geriatric patients are more likely to have prostatic hypertrophy or obstruction and age-related renal function impairment, and are therefore more likely to be adversely affected by opioid-induced urinary retention. The risk of constipation and faecal impaction is also greater in the elderly. Geriatric patients may metabolize or eliminate opioid analgesics more slowly than younger adults. Lower doses or longer dosing intervals than those usually recommended for adults may be required and are usually therapeutically effective for these patients.

4.5 Interaction with other medicines and other forms of interaction

The following interactions with codeine have been noted:

- Monoamine oxidase inhibitors – due to the possible risk of excitation or depression, avoid concomitant use and for 14 days after discontinuation of MAOI
- Benzodiazepines or other CNS depressants, including alcohol - concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death.
- Hypnotics and anxiolytics – enhanced sedative effect, increased risk of respiratory depression
- Anticholinergics – risk of severe constipation which may lead to paralytic ileus and/or urinary retention
- Metoclopramide and domperidone – antagonistic effect on GI activity

- Anti-diarrhoeal drugs – increased risk of severe constipation
- Anaesthetics – enhanced sedative and hypotensive effect
- Tricyclic antidepressants – enhanced sedative effect
- Antipsychotics, including phenothiazines – enhanced sedative and hypotensive effect
- Opioid antagonists – may precipitate withdrawal symptoms
- Quinidine – reduced analgesic effect
- Antihypertensive drugs – enhanced hypotensive effect
- Ciprofloxacin – avoid premedication with opioids as they reduce ciprofloxacin concentration
- Ritonavir – may increase plasma levels of opioid analgesics
- Mexiletine – delayed absorption of mexiletine
- Cimetidine – inhibits the metabolism of opioid analgesics causing increased plasma codeine concentrations

4.6 Fertility, pregnancy and lactation

Fertility

There is no fertility data available.

Use in Pregnancy

The risk-benefit balance must be carefully considered because opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the foetus, leading to withdrawal symptoms (convulsions, irritability, excessive crying, tremors, hyperactive reflexes, fever, vomiting, diarrhoea, sneezing and yawning) in the neonate. Prolonged high dose use of Codeine prior to delivery may produce Codeine withdrawal symptoms in the neonate.

Although studies for teratogenic effects in humans have not been done, studies in animals have not shown codeine to cause adverse effects on foetal development. Studies in animals have shown codeine (single dose of 100mg per kg) to cause delayed ossification in mice and (in doses of 120mg per kg) increased resorption in rats.

The administration of opioid analgesics during labour may cause respiratory depression in the new-born infant. Withdrawal symptoms in new-born infants have been reported with prolonged use of this class of drug.

Use in Lactation

Codeine is excreted into breast milk. However, with usual analgesic doses, concentrations are generally low.

However, infants of nursing mothers taking codeine may have an increased risk of morphine overdose if the mother is an ultra-rapid metaboliser of codeine. When codeine enters the body and is metabolized, it changes to morphine. Nursing mothers taking codeine, who are ultra-rapid metabolisers of codeine, may have higher morphine levels in their breast milk. These higher levels of morphine in breast milk may lead to life-threatening or fatal side effects in nursing babies.

Use of codeine is contraindicated in women who are breastfeeding (see section 4.4)

4.7 Effects on ability to drive and use machines

Codeine may cause drowsiness or a decrease in alertness in some patients. Patients should be cautioned about operating vehicles or machinery or engaging in activities which require them to be fully alert.

4.8 Undesirable effects

In normal doses the commonest side effects of codeine and other opioid analgesics are nausea, vomiting, constipation (especially during chronic therapy), drowsiness and confusion.
The following have been noted:

Immune system disorders

Rash, urticaria, pruritus, difficulty breathing, increased sweating, redness of flushed face, angioedema.

Nervous system disorders

Confusion, drowsiness, malaise, tiredness, vertigo, dizziness, changes in mood, hallucination, CNS excitation (restlessness/excitation), convulsions, mental depression, headache, nightmares, raised intracranial pressure, tolerance or dependence, dysphoria, hypothermia.

Eye disorders

Miosis, blurred or double vision.

Cardiac disorders

Bradycardia, palpitations, hypotension, orthostatic hypotension, tachycardia.

Respiratory, thoracic and mediastinal disorders

Respiratory depression.

Gastrointestinal Disorders

Constipation, biliary spasm, nausea, vomiting, dry mouth.

Musculoskeletal, connective tissue and bone disorders

Muscle rigidity.

Renal and urinary disorders

Ureteral spasm, anti-diuretic effect, urinary retention.

Reproductive system and breast disorders

Decrease in libido and potency.

Withdrawal effects

Abrupt withdrawal precipitates a withdrawal syndrome. Symptoms may include tremor, insomnia, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, mydriasis, weakness, pyrexia, muscle cramps, dehydration and increase in heart rate, respiratory rate and blood pressure.
Tolerance diminished rapidly after withdrawal so a previously tolerated dose may prove fatal.
Regular prolonged use of codeine is known to lead to addiction and tolerance.
Prolonged use of a painkiller for headaches can make them worse.
These effects occur more commonly in ambient patients than in those at rest in bed.
Codeine has a lower dependence liability than other opioid agonists because of its comparatively lower potency with usual doses.
Withdrawal symptoms are also less severe than those produced by stronger opioid agonist analgesics.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Symptoms

Signs of overdose may include nausea, vomiting, constipation, lack of appetite, somnolence, extreme sleepiness, confusion, shallow breathing, and coma.

Signs of overdose in children include excessive sleepiness, difficulty waking, difficulty breathing, confusion, slow heart rate, weak pulse, paradoxical excitation or restlessness, and coma.

Toxic doses vary considerably with the individual and regular users may tolerate larger doses.

Treatment

The stomach should be emptied by aspiration or lavage. A laxative may be given to aid peristalsis. Intensive supportive therapy may be required to correct respiratory failure and shocks. In addition, the specific antagonist naloxone hydrochloride is used to counteract very rapidly the severe respiratory depression and coma produced by excessive doses of opioid analgesics. A dose of 0.4mg to 2mg is given intravenously, intramuscularly or subcutaneously, repeated at intervals of 2 to 3 minutes if necessary, up to 10mg. The effect of naloxone may be of shorter duration than that of the opioid analgesic and additional doses may be required to prevent relapses.

The use of opioid antagonists such as naloxone, nalorphine and levallorphan in persons physically dependent on opioid agonists may induce withdrawal symptoms.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).}

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Codeine phosphate is an opioid analgesic with uses similar to those of morphine, but is much less potent as an analgesic and has only mild sedative effects. Its primary site of action is at the mu opioid receptors distributed throughout the central nervous system.

Codeine phosphate reduces intestinal motility through both a local and possibly central mechanism of action.

Codeine and its salts are absorbed from the gastro-intestinal tract and onset of analgesic action occurs 30 to 45 minutes after administration, when given orally.

Peak effect is reached within 1 to 2 hours and the duration of analgesic action is 4 hours.

5.2 Pharmacokinetic properties

Codeine is readily absorbed from the gastro-intestinal tract and metabolised by O- and N- demethylation in the liver to morphine and norcodeine which, with codeine, are

excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. Most of the excretion products appear in the urine within 6 hours and 40 to 60 percent of the codeine is excreted free or conjugated, approximately 5 to 15 percent as free and conjugated morphine and about 10 to 20 percent free and conjugated norcodeine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those included in other sections.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

For Codeine Phosphate Tablets (PSM) 15 mg
Maize starch, Lactose, Magnesium stearate

For Codeine Phosphate Tablets (PSM) 30 mg
Acacia Gum, Maize starch, Lactose, Talc Purified, Magnesium stearate

For Codeine Phosphate Tablets (PSM) 60 mg
Maize starch, Lactose, Magnesium stearate

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

36 months from date of manufacture when stored at 25^{o}C

6.4 Special precautions for storage

Protect from light and moisture. Store at or below 25°C. Keep out of reach of children.

6.5 Nature and contents of container

Codeine Phosphate Tablets (PSM) 15 mg: Bottle, glass. 100 tablets
Codeine Phosphate Tablets (PSM) 30 mg: Bottle, glass. 100 tablets
Codeine Phosphate Tablets 9PSM) 60 mg: Bottle glass. 100 tablets

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with

local requirements.

7. MEDICINE SCHEDULE

Controlled Drug C2.

8. SPONSOR

PSM Healthcare Limited, t/a API Consumer Brands
14-16 Norman Spencer Drive
PO Box 76 401
Manukau, AUCKLAND 2241
Telephone 0508 776746

9. DATE OF FIRST APPROVAL

30/12/1969

10. DATE OF REVISION OF THE TEXT

18th August 2021

SUMMARY TABLE OF CHANGES

Section changes	Summary of new information
4.4	Updated as per June 2021 MARC recommendations for Opioid products that the data sheet should align with the safety warnings in the Australian product information, plus additional warning 'Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper.'
4.5	Updated to include: 'Benzodiazepines or other CNS depressants, including alcohol - concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death.'
6.5	500 tablet pack size removed, as only 100 tablets are the Pharmac pack size.