NEW ZEALAND DATA SHEET

1 PRODUCT NAME

MOVAPO ® PEN 10 mg/mL injection solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 3 mL pen contains 30 mg of apomorphine hydrochloride hemihydrate (equivalent to 10 mg/mL apomorphine hydrochloride hemihydrate).

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

MOVAPO PEN is a clear, colourless and practically particle free sterile solution for injection with a pH of 3.0 to 4.0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

MOVAPO PEN is indicated to reduce the number and severity of 'off' phases in patients with Parkinson's disease severely disabled by motor fluctuations refractory to conventional therapy. Initiation of therapy with apomorphine should be undertaken in a specialist unit in a hospital setting. Conventional therapy should be continued during 'on' phases.

4.2 Dosage and method of administration

The optimal dosage of MOVAPO PEN has to be determined on an individual patient basis. Hospital admission under appropriate specialist supervision is advised when establishing a patient's therapeutic regime.

It is essential that the patient is established on the antiemetic domperidone for at least 48 - 72 hours prior to initiation of therapy.

If incremental dose adjustments smaller than 1 mg are required another product containing apomorphine should be used.

Patient selection

For patients in whom conventional therapy has failed, MOVAPO PEN is only considered to be suitable for Parkinson's disease patients capable of recognising and anticipating 'off' phases in motor performance. Patients must be capable and motivated for MOVAPO PEN to be used effectively. Adult patients through all age ranges have been successfully managed with apomorphine injections. MOVAPO PEN is contraindicated in children and adolescents up to 18 years of age (see **section 4.3**).

The elderly are well represented in the population of patients with Parkinson's disease and constitute a high proportion of those studied in clinical trials of apomorphine. The management of elderly patients treated with apomorphine has not differed from that of younger patients, except for the extra caution on commencing therapy, because of the risk of postural hypotension.

Patients who have shown a good 'on' period response during the initiation stage of apomorphine therapy, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections, may be commenced on or transferred to continuous subcutaneous infusion by minipump and / or syringe driver.

The practical steps described below should be followed when commencing a patient on treatment:

- pre-treat with domperidone
- discontinue all existing antiparkinsonian medication to provoke an 'off' phase in motor performance
- determine the threshold dose response to MOVAPO PEN that produces an unequivocal motor response
- re-establish other antiparkinsonian agents
- determine effective treatment regimen for MOVAPO PEN
- teach patient and/or carer how and when to administer
- discharge from hospital
- monitor frequently and adjust dosage regimen as appropriate
- full instructions are given below.

Pre-treatment

Domperidone is a peripherally acting dopamine receptor antagonist given by mouth to prevent nausea and vomiting. Domperidone is commenced 48 - 72 hours prior to the first dose of MOVAPO PEN. When patients are stabilised with respect to dosage of apomorphine, the dose of domperidone is reduced by 10 mg per day every week until mild nausea appears. The maintenance dose of domperidone is the lowest level which completely prevents nausea. Domperidone can usually be withdrawn after several weeks. Before the decision to initiate domperidone and apomorphine treatment, risk factors for QT interval prolongation in the individual patient should be carefully assessed to ensure that the benefit outweighs the risk (see **section 4.4**). The cardiovascular assessment should include an ECG and QT measurement. Patients with severe renal insufficiency will require the dosing interval of domperidone to be changed from three times a day to once or twice a day. For further information regarding domperidone refer to the Product Information.

Provoking and assessing an 'off' phase

After at least 3 days of hospitalisation, all antiparkinsonian therapy is withheld overnight to provoke an 'off' phase in motor performance and to undertake a baseline motor assessment as follows:

(a) Alternate, unilateral hand tapping for 30 seconds on mounted digital counters (preferably 20 cm apart).
(b) Time taken to walk 12 metres.
(c) Clinical assessment of tremor and dyskinesia according to a four-point scale (0 = nil, 1 = mild, 2 = moderate, 3 = severe).
(d) Scoring on a modified Webster disability scale to assess 12 features of parkinsonism (maximum disability score of 36).

Determination of the threshold dose

Following baseline motor assessment, the patient is challenged for MOVAPO PEN responsiveness according to the following schedule:

- 1.0 mg MOVAPO PEN (0.1 mL) is injected subcutaneously and the patient is observed over 30 minutes for motor responsiveness.
- If no or poor response is obtained, a second dose of 3 mg MOVAPO PEN (0.3 mL) is given 40 minutes after the first dose, and the patient observed for a further 30 minutes.
- The dosage is increased in an incremental fashion every 40 minutes and the patient observed carefully for an unequivocal motor response. The third dose is 5 mg SC, and the fourth dose is 7 mg SC. If the patient shows no response to the 7 mg dose then the patient must be classified as a non- responder to MOVAPO PEN and no further attempts to provoke a motor response should be made. If the patient shows only a mild response to the 7 mg dose, a maximum dose of 10 mg can be used to see if an unequivocal motor response is possible.
- The lowest dose producing an unequivocal motor response is called the threshold dose. For the majority of patients the threshold dose is less than 7 mg MOVAPO PEN (0.7 mL), although very occasionally it can be up to 10 mg MOVAPO PEN (1.0 mL).

Motor responsiveness is judged to be positive if 2 or more of the following are seen:

(a) More than 15% increase in tapping score.
(b) More than 25% improvement in walking time.
(c) An improvement of at least 2 points of tremor score.
(d) An improvement of Webster's score of 3 or more.

Initiation of treatment

Following establishment of an acceptable threshold dose of MOVAPO PEN, the patient should be restarted on conventional antiparkinsonian therapy.

A subcutaneous injection of the established threshold dose may then be given into the lower abdomen or outer thigh at the first signs of an 'off' phase. The patient should then be observed over the following hour and the quality of their 'on' phase noted. It may be appropriate to modify the dose of MOVAPO PEN according to the patient's response.

Close monitoring of therapeutic benefits and adverse reactions under specialist supervision is required after initiation of treatment.

MOVAPO PEN is administered by the subcutaneous route by intermittent bolus injection. Intermittent injection is either into the anterior abdominal wall or anterolateral thigh. The usual dosage range is 2.0 to 4.0 mg per injection; the maximum single dose being 6 mg and the maximum total daily dose being 50 mg.

The intermittent injection is given in an undiluted form. For microbiological reasons, the pen injector used for intermittent injections should be used within 48 hours of first use. The unused or injector pen in use should be stored below 25ºC.

Patients who have shown a good 'on' phase response during the initiation stage, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections (e.g. 8-10 injections per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump.

Monitoring treatment

Long term specialist supervision of patients is advised.

There is a high probability of adverse effects to MOVAPO PEN therapy. The frequency and severity of adverse events should be monitored carefully at regular intervals and a

reassessment of the patient carried out if appropriate. Adjustments to the dosage or discontinuation may be necessary.

Instructions for use and handling

For instructions on use and handling of the medicine, see section 6.6.

4.3 Contraindications

MOVAPO PEN is contraindicated in patients with a known hypersensitivity or allergy to apomorphine, morphine or chemically related products.

MOVAPO PEN should not be administered to patients with pre-existing neuropsychiatric problems or dementias due to either pathological processes, e.g. Alzheimer's disease, or to patients whose 'on' response to L-dopa is marred by severe dyskinesia, hypotonia or psychotoxicity.

MOVAPO PEN is also contraindicated in patients with inadequate renal or liver function, unstable coronary vascular disease, cerebrovascular disease, respiratory depression or CNS depression.

MOVAPO PEN is contraindicated for children and adolescents under 18 years of age.

MOVAPO PEN is contraindicated in patients with a known hypersensitivity to sodium metabisulfite.

4.4 Special warnings and precautions for use

For Subcutaneous Use Only (see **section 4.8**).

Patients sensitive to morphine or its derivatives may be sensitive to MOVAPO PEN. MOVAPO PEN should therefore not be administered to patients with a known hypersensitivity or allergy to apomorphine, morphine or chemically related compounds (see **section 4.3**).

MOVAPO PEN contains sodium metabisulfite which may cause allergic type reactions, including anaphylactic symptoms and life threatening or less severe asthmatic episodes in susceptible people (see **section 4.3**).

In patients with cardiac decompensation or cerebrovascular disease, vomiting may cause an increase in blood pressure that may lead to haemorrhage and vascular accidents. Apomorphine is therefore contraindicated in these patients (see **section 4.3**).

Caution should be used in administering MOVAPO PEN to patients with a predisposition to nausea and vomiting. Apomorphine may cause an increased risk of persistent vomiting. A risk-benefit assessment should be considered in these patients.

Since apomorphine may produce hypotension, even when given with domperidone pre-treatment, care should be exercised in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as anti-hypertensives, and especially in patients with pre-existing postural hypotension.

Since apomorphine, especially at high doses, may have the potential for QT prolongation, caution should be exercised when treating patients at risk for Torsades de pointes arrhythmia.

When used in combination with domperidone, risk factors in the individual patient should be carefully assessed. This should be done before treatment initiation, and during treatment. Important risk factors include serious underlying heart conditions such as congestive cardiac failure, severe hepatic impairment or significant electrolyte disturbance. Also medication possibly affecting electrolyte balance, CYP3A4 metabolism or QT interval should be assessed. Monitoring for an effect on the QTc interval is advisable. An ECG should be performed:

- prior to treatment with domperidone
- during the treatment initiation phase
- as clinically indicated thereafter

The patient should be instructed to report possible cardiac symptoms including palpitations, syncope, or near-syncope. They should also report clinical changes that could lead to hypokalaemia, such as gastroenteritis or the initiation of diuretic therapy. At each medical visit, risk factors should be revisited.

Apomorphine is associated with local subcutaneous effects. These can sometimes be reduced by the rotation of injection sites or possibly by the use of ultrasound (if available) in order to avoid to areas of nodularity and induration (see **section 4.8**).

Haemolytic anaemia and thrombocytopenia have been reported in patients treated with apomorphine. Haematology tests should be undertaken at regular intervals as with levodopa, when given concomitantly with apomorphine.

Caution is advised when combining apomorphine with other medicinal products, especially those with a narrow therapeutic range (see **section 4.5**).

Neuropsychiatric problems co-exist in many patients with advanced Parkinson's disease. There is evidence that for some patients neuropsychiatric disturbances may be exacerbated by apomorphine. Special care should be exercised when apomorphine is used in these patients.

Apomorphine has been associated with somnolence and episodes of sudden sleep onset, particularly in patients with Parkinson's disease. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with apomorphine. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore, a reduction of dosage or termination of therapy may be considered.

The use of apomorphine in conjunction with levodopa treatment may cause Coombs' positive haemolytic anaemia. An initial screen prior to commencement of treatment and at 6 monthly intervals is recommended. In the event of the development of a haemolytic anaemia, a haematological specialist should be consulted. The dose of apomorphine and/or levodopa should be reduced, with careful monitoring of the patient's motor state. It may be necessary to discontinue treatment with levodopa and/or apomorphine in the event that it is not possible to control the anaemia satisfactorily.

Apomorphine should be used with caution in patients with endocrine, renal, pulmonary or cardiovascular disease.

Periodic evaluation of hepatic, haemopoietic, renal and cardiovascular function is advised.

Patients with severe renal insufficiency may require the dosing interval for domperidone to be less frequent (see **section 4.2, Pre-treatment**).

Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including apomorphine. Dose reduction/tapered discontinuation should be considered if such symptoms develop.

Dopamine Dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of MOVAPO PEN seen in some patients treated with apomorphine. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS.

Use in debilitated patients

Extra caution is also recommended in debilitated patients, since they may show an increased susceptibility or be more sensitive to the respiratory depressant effects of apomorphine.

Use in the elderly

Extra caution is also recommended in geriatric patients, since they may show an increased susceptibility or be more sensitive to the respiratory depressant effects of apomorphine. Extra caution is recommended during initiation of therapy in elderly patients because of the risk of postural hypotension.

Paediatric use

MOVAPO PEN is contraindicated for children and adolescents under 18 years of age.

Effect on laboratory tests

Positive Coombs' tests have been reported for patients receiving apomorphine.

4.5 Interaction with other medicines and other forms of interaction

Patients selected for treatment with apomorphine are almost certain to be taking concomitant medications for their Parkinson’s disease. In the initial stages of apomorphine therapy the patient should be monitored for unusual side-effects or signs of potentiation of effect.

Drugs which interfere with central amine mechanisms such as tetrabenazine, metoclopramide, antipsychotic dopamine blocking agents (such as phenothiazines, thioxanthines and butyrophenones), amphetamines and papaverine should be avoided. If their administration is considered essential, extreme care should be taken and the patient monitored for signs of potentiation, antagonism or other interactions and for any unusual adverse effects.

Neuroleptic medicinal products may have an antagonistic effect if used with apomorphine. There is a potential interaction between clozapine and apomorphine.

The possible side effects of apomorphine on the plasma concentrations of other medicinal products have not yet been studied. Therefore caution is advised when combining apomorphine with other medicinal products, especially those with a narrow therapeutic range.

Antihypertensive and Cardiac Active Medicinal Drugs

Even when co-administered with domperidone, apomorphine may potentiate the antihypertensive effects of antihypertensive and cardiac active medicinal products.

It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval.

4.6 Fertility, Pregnancy and lactation

Use in pregnancy (Category B3)

The safety of using apomorphine during pregnancy has not been established in either human or animal studies. MOVAPO PEN should therefore not be used in pregnant women, or those likely to become pregnant.

Use in lactation

It is not known whether apomorphine is excreted in breast milk although problems in humans have not been documented. Nevertheless, because many drugs are excreted in human milk and because of the potential for serious adverse drug reactions due to apomorphine in breastfed infants, a decision should be made either to discontinue breastfeeding or the drug, taking into account the importance of the drug to the mother.

Effects on fertility

In a fertility study in male rats, fertility was decreased at 2 mg/kg/day SC, one tenth that of the maximum recommended human dose (based on body surface area). Effects on female fertility have not been determined.

4.7 Effects on ability to drive and use machines

Apomorphine has varying degrees of impairment which influences the ability to drive and use machines.

Patients being treated with apomorphine and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities (e.g. operating machines) where impaired alertness may put themselves or others at risk of serious injury or death until such recurrent episodes and somnolence have resolved (see also **section 4.4**).

4.8 Undesirable effects

Very common (>10%)

Most patients experience injection site reactions, particularly with continuous use. These may include subcutaneous nodules, induration (see **section 4.4**), erythema, tenderness and panniculitis. Various other local reactions (such as irritation, itching, bruising, fibrosis and pain) may also occur (see **section 4.4)**. Care should be taken to ensure that areas of ulceration do not become infected.

Hallucinations have been reported.

Common (1-10%)

Gastrointestinal side effects including nausea and vomiting appear to be the most prevalent adverse effects, however tolerance to these effects develops rapidly. Pre-treatment with domperidone may reduce or prevent these effects (see **section 4.2**).

Apomorphine is associated with somnolence. Drowsiness and sedation occur in most patients on initial treatment but these effects largely subside with repeated dosing, although in some patients these effects may persist. Tachyphylaxis to postural related faintness or syncope also occurs rapidly.

Neuropsychiatric disturbances (including confusion and visual hallucinations) have occurred during apomorphine therapy.

Yawning has been reported during apomorphine therapy.

Uncommon (0.1- 1%)

Apomorphine may induce dyskinesias during 'on' periods, which can be severe in some cases, and in a few patients may result in cessation of therapy. Apomorphine has been associated with sudden sleep onset episodes (see **section 4.4**).

Postural hypotension is seen infrequently and is usually transient (see **section 4.4**).

Breathing difficulties have been reported.

Local and generalised rashes have been reported. Injection site necrosis and ulceration have been reported.

Haemolytic anaemia and thrombocytopenia have been reported in patients treated with apomorphine.

Rare (0.01 – 0.1%)

Eosinophilia has rarely occurred during treatment with apomorphine.

Due to the presence of sodium metabisulfite, allergic reactions (including anaphylaxis and bronchospasm) may occur.

Not known (cannot be estimated from available data)

Impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including apomorphine (see **section 4.4**).

Aggression and agitation have also been reported.

Headache has been reported.

Peripheral oedema has been reported.

Other adverse reactions to apomorphine that have been reported infrequently include transient rises in serum prolactin, stomatitis, transient metallic taste, rhinorrhoea, increased lacrimation, reduced facial hair growth, loss of libido and spontaneous penile erection.

Reporting of suspected adverse reactions

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

4.9 Overdose

Symptoms

The clinical features of overdose of MOVAPO PEN are an extension of the pharmacological effects of the drug. They include nausea and persistent vomiting, dyskinesias, hypotension and acute circulatory failure, cardiac arrest, respiratory depression, drowsiness and central nervous system depression or stimulation, euphoria, restlessness and hallucinations and possibly coma and death.

Concomitant use of domperidone may exacerbate the clinical features of overdose.

Treatment

An opioid antagonist such as naloxone may be given to treat excessive vomiting, central nervous system depression and respiratory depression due to MOVAPO PEN overdose. Excessive vomiting may also be treated with domperidone. Atropine may be also used to treat bradycardia. To treat hypotension, appropriate measures should be taken e.g. raising the foot of the bed.

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

Pharmatherapeutic group: Dopamine agonists

ATC Classification: N04B C07

Pharmacology

Apomorphine is a directly acting dopamine receptor agonist, structurally related to dopamine. Apomorphine has high *in vitro* binding affinity for the dopamine D_4 and D_5 receptor (K_i:4 and 14 nM respectively), moderate affinity (K_i: 26 to 130 nM) for the dopamine D_2 and D_3, adrenergic α_{1D}, α_{2B}, α_{2C} receptors, serotonin $5HT_{1A}$, $5HT_{2A}$, $5HT_{2B}$, and $5HT_{2C}$ receptors and low affinity for the dopamine D_1 receptor (K_i: 370 nM). Apomorphine exhibits no affinity for the adrenergic β_1 and β_2 or histamine H_1 receptors.

Pharmacological Actions

The effect of apomorphine as an antiparkinsonian agent is believed to be the result of direct stimulation of postsynaptic D_2 dopamine receptors, but stimulation of presynaptic D_2 dopamine receptors and antagonism of α_2 adrenergic receptors may also be important. Apomorphine reduces the tremor, rigidity and bradykinesia in patients receiving levodopa. Apomorphine induces vomiting by direct stimulation of the medullary chemoreceptor trigger zone.

5.2 Pharmacokinetic properties

The peripheral pharmacokinetics of apomorphine have been studied following subcutaneous injection, subcutaneous infusion and intravenous infusion.

Absorption

Following intramuscular or subcutaneous administration, apomorphine is reported to be well absorbed. Peak plasma concentration occurs as early as three minutes following subcutaneous bolus injection. The rapid and complete absorption from subcutaneous tissues and rapid clearance is believed to correlate with the rapid onset and brief duration of action respectively. Antiparkinsonian effects are observed within five minutes following subcutaneous bolus administration.

Distribution

The distribution half-life of apomorphine was found to be five minutes. The volume of distribution, plasma clearance and half-life were similar for subcutaneous injection, subcutaneous infusion and intravenous infusion.

Apomorphine reaches a concentration in the brain up to eight times higher than that in plasma, due to high lipid solubility which allows rapid equilibration between blood and tissue compartments.

Metabolism

Apomorphine is metabolised in the liver. Routes of metabolism in humans include sulfation, *N*-demethylation, glucuronidation and oxidation to norapomorphine by CYP 2B6, CYP 2C8 and CYP 3A4. The major metabolite in humans after sublingual administration was apomorphine sulfate.

Excretion

Apomorphine is cleared rapidly. The elimination half-life (t½) is about 33 minutes.

5.3 Preclinical safety data

Genotoxicity

In vitro genotoxicity studies demonstrated mutagenic and clastogenic effects, most likely due to products formed by oxidation of apomorphine. However, apomorphine was not genotoxic in the *in vivo* studies performed.

Carcinogenicity

No carcinogenicity studies have been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulphite (E223)

Hydrochloric acid, concentrated (for pH adjustment)

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

12 months. Once opened the pen should be used within 48 hours.

6.4 Special precautions for storage

Store below 25 °C. Do not freeze. Protect from light. (Keep the container in the outer carton).

6.5 Nature and contents of container

MOVAPO PEN, apomorphine hydrochloride hemihydrate 30 mg/3 mL is a disposable multiple dose pen injector system incorporating a clear glass (type I) cartridge containing a clear solution for injection. The glass cartridge is sealed at one end with a bromobutyl rubber piston, and at the other end with a bromobutyl rubber/aluminium membrane.

Each cartridge contains 3 mL of solution for injection.

Packs contain 5 x 3 mL pens in a moulded plastic tray in an outer cardboard carton.

6.6 Special precautions for disposal and other handling

Do not use if solution has turned green.

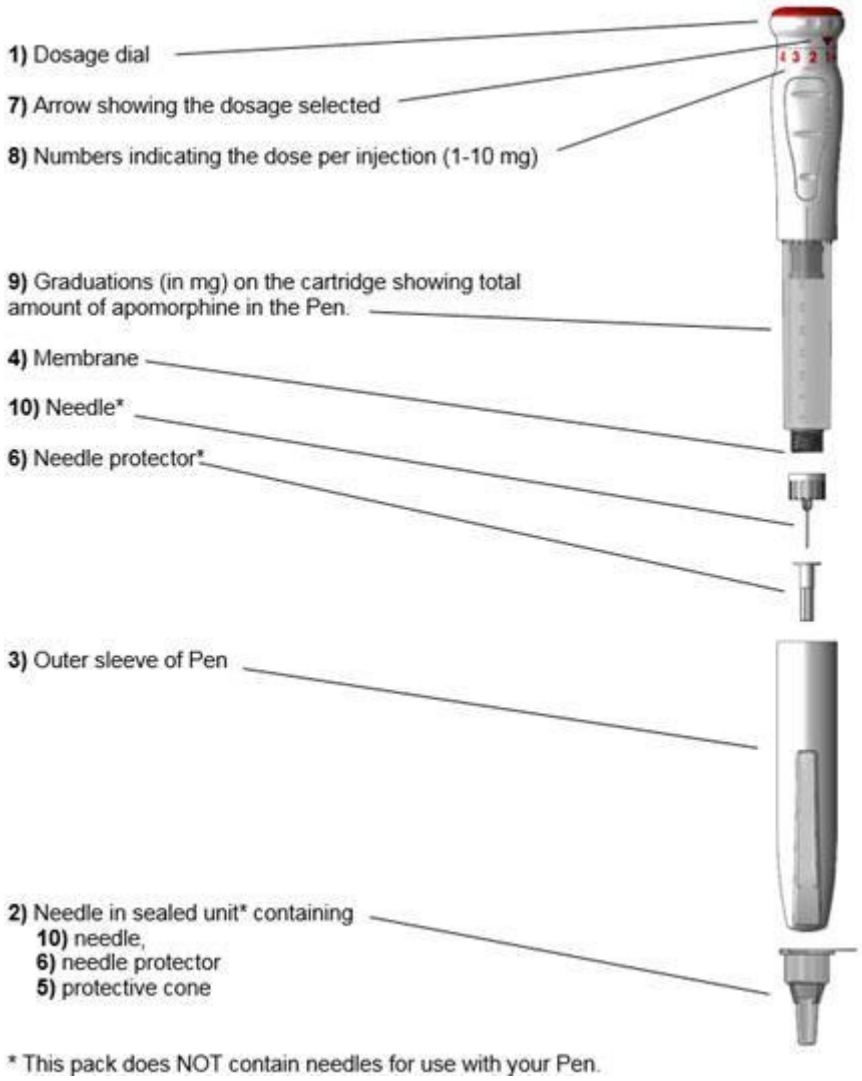
Discard each pen no later than 48 hours from first use.

Instructions for use and handling

The product is for individual patient use only.

Do not use if the solution has turned green.

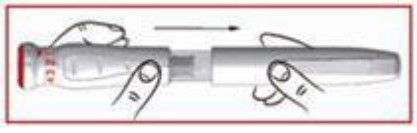
Discard each pen no later than 48 hours from first use.



IMPORTANT: Do not pull the red capped dial (see 1) before you have set the dosage (see 'Selecting the correct dosage').

Attaching the needle

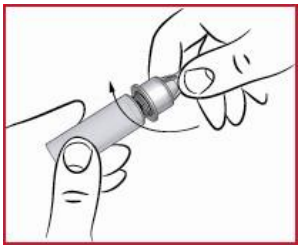
(a) Before using MOVAPO PEN you will need some surgical wipes and one needle in its protective cone (**see 2**).
(b) Take the Pen out of its box and remove the outer sleeve (**see 3**).

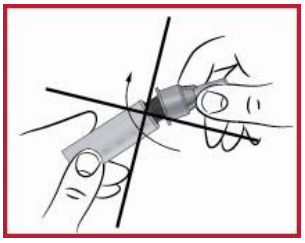


(c) Wipe the membrane of the Pen (**see 4**) with a surgical wipe.

(d) Peel off the paper from the needle cone (**see 2**).

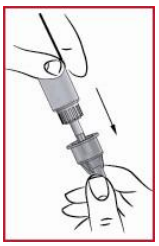
(e) It is important to bring the needle to the Pen in a straight line, as shown below. If the needle is presented at an angle it may cause the Pen to leak.





(f) Screw the cone (see 2) clockwise onto the membrane until it is tight. This securely attaches the needle.

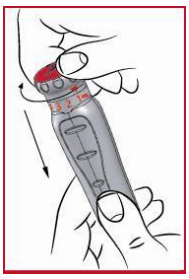
(g) Remove the protective cone (**see 5**), but do not throw it away. Do not remove the needle protector (**see 6**) at this stage.



(h) Replace the Pen's outer sleeve (**see 3**).

Selecting the correct dose

(i) Press the red capped dosage dial (**see 1**) and whilst holding it down, turn the dial clockwise until the arrow points to the dose your doctor chose for you (**see 7**&**8**). Release the downward pressure on the red capped dial. The dose is now set and you do not need to redial for subsequent injections.

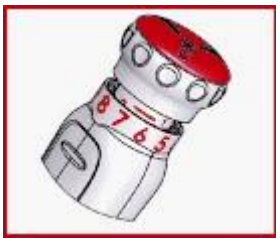


Important: If you pass your prescribed dose while turning the dial, just continue pressing and turning in the same direction until the arrow points to the dose your doctor chose for you. Never pull and turn the red capped dosage dial at the same time.

If your dose is 1 mg, start by emptying a 1 mg dose onto a paper tissue and discarding it. This is called 'priming' and is important because it ensures you get a full dose the first time you use your Pen. Then, set the dose you require for injection and inject it in the usual way (**see "Injecting"**). If the first dose required is more than 1 mg, you do not need to prime the Pen.

Injecting

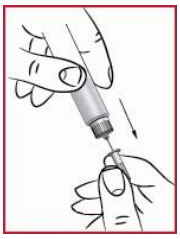
(j) Once you have set the dose, gently pull out the red capped dosage dial as far as it will go. Check the red scale on the plunger (**see 9**) and inject only if the line that is just visible matches the intended dose.



(k) Using a surgical wipe, clean the area of skin where you plan to inject the medicine and around it.

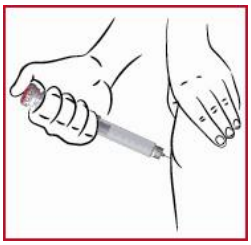
(l) Remove the Pen's outer sleeve (**see 3**).

(m) Remove the needle protector (**see 6**).

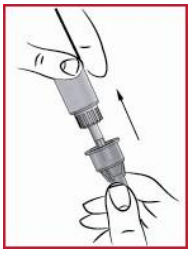


(n) Insert the needle (**see 10**) into the skin as shown by your doctor.

(o) To inject, press the red capped dosage dial (**see 1**) down as far as it will go, using your thumb if possible. Once the red capped dosage dial is fully depressed, count to three before withdrawing the needle.



(p) Replace the protective cone (**see 5**) onto the used needle and push gently into place. Once secure, turn the needle anti-clockwise to unscrew it. Keep the needle in its protective cone and discard it in a “Sharps” container.



Preparing for the next injection

(q) Remove the outer sleeve of the Pen and check there is enough apomorphine left in the cartridge for your next injection. If the amount is below 5 mg, it is recommended to have another Pen available for the next injection. If there is enough apomorphine, put a new needle in place in the same way as before.

(r) If there is not enough apomorphine left for another injection, prepare another pen.

(s) Finally, replace the outer sleeve of your Pen.

7 MEDICINE SCHEDULE

Prescription medicine

8 SPONSOR

CARSL Consulting
Clinical and Regulatory Services
24 Side Road
Parkhill Farm, RD10, Hastings
PO Box 766, Hastings
New Zealand
Phone: 0800 581 531

For Australia:

STADA Pharmaceuticals Australia Pty Ltd
Suite 2.04, 26 Rodborough Road,
Frenchs Forest NSW 2086,
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