

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Presentation

Modified release capsules filled with off-white spherical microgranules.*

m-Eslon SR 10 mg

Size 4 capsules with natural transparent body and yellow cap, printed **10 mg** in black ink. Each capsule contains microgranules providing 10 mg of morphine sulphate.*

m-Eslon SR 30 mg

Size 4 capsules with natural transparent body and pink cap, printed **30 mg** in black ink. Each capsule contains microgranules providing 30 mg of morphine sulphate.*

m-Eslon SR 60 mg

Size 3 capsules with natural transparent body and orange cap, printed **60 mg** in black ink. Each capsule contains microgranules providing 60 mg of morphine sulphate.*

m-Eslon SR 100 mg

Size 2 capsules with natural transparent body and white cap, printed **100 mg** in black ink. Each capsule contains microgranules providing 100 mg of morphine sulphate.*

m-Eslon SR 200 mg

Size 0 capsules with natural transparent body and cap, printed **200 mg** in black ink. Each capsule contains microgranules providing 200 mg of morphine sulphate. Not currently marketed.*

Uses

Pharmacotherapeutic group

N02AA01: member of N02AA – natural opium alkaloids, a subset of N02A – opioids.*

Actions

Morphine is an opioid analgesic which exerts an agonist effect at specific, saturable opioid receptors in the central nervous system (CNS) and on smooth muscle. In man, morphine produces a variety of pharmacological effects including analgesia, constipation from decreased gastrointestinal motility, suppression of the cough reflex, respiratory depression from reduced responsiveness of the respiratory centre to carbon dioxide, nausea and vomiting via stimulation of the chemoreceptor trigger zone (CTZ), changes in mood including euphoria and dysphoria, sedation, mental clouding, and alterations of the endocrine and autonomic nervous systems.*

The psychological effects are of longer duration than that of analgesia. Morphine-induced analgesia is relatively selective in that other sensory modalities (touch, vision, hearing) are not affected. Moderate doses of morphine are effective in relieving clinical (pathological) pain and increasing pain threshold to tolerate pain. The capacity to perceive the sensation of pain may be relatively unaltered. The analgesic effects of morphine are due to its CNS action, i.e., limbic system, hypothalamus, and centrally induced endocrinological effect. At present, the exact mechanism by which the opiates exert their effects remains unknown.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Oral morphine is as efficacious as parenteral morphine when it is used at three times the parenteral dose.*

m-Eslon SR capsules release morphine from microgranules that are specially coated enabling twice daily administration to control pain when opiate medication is required. The capsules may be swallowed whole or separated and the contents mixed with soft foods and consumed immediately or given through a compatible feeding tube.*

Pharmacokinetics

m-Eslon SR capsules produce peak morphine levels at steady state in approximately 3 to 4 hours following administration. In human pharmacokinetic studies, they have been shown to have an extended release action, when compared to oral morphine sulphate syrup, as characterized by a flatter peak serum concentration curve which took longer to attain; the elimination half-life was significantly lengthened. Therapeutic levels are maintained over a period of 12 hours.*

Summary of pharmacokinetic parameters (mean \pm SD) in cancer patients presenting severe pain (n = 25) who received morphine sulphate 60 to 300 mg/day for 6 days as syrup or as modified release capsules from Gillette et al, Clin Drug Invest 14:suppl. 1 pp.22-27 (1997).*

Parameter	Morphine syrup	m-Eslon SR capsules
C _{max} (mcg/l)	49.52 \pm 28.38	48.13 \pm 30.67
AUC _{0-12h}	308.41 \pm 203.81	323.17 \pm 201.69
t _{max} (h)	1.18 \pm 0.93	3.60 \pm 1.95

m-Eslon SR has not been compared to any modified-release morphine preparation on the New Zealand market, and therefore it is not interchangeable with other formulations.*

Absorption

Morphine is readily absorbed from the gastrointestinal tract and after subcutaneous or intramuscular injection. Due to extensive first-pass metabolism in the liver and gut, the effect of an oral dose is less than after parenteral administration. With repeated regular dosing, orally administered morphine is about one-third as potent as when given by intramuscular injection. Enterohepatic circulation probably occurs.*

As the rate of morphine release from m-Eslon SR formulation is independent of pH over the range 1.5 to 7.2, it does not limit the absorption of morphine to any part of the gastrointestinal tract. Following oral administration of morphine, the extent of absorption is essentially the same for immediate or extended release formulations, whether the latter are given once or twice a day. This means that morphine can be absorbed all along the GI tract, including the colon. Diarrhoea may reduce morphine absorption.*

There is no clinical evidence of dose dumping in either the fed or fasting state. However, the consumption of fatty food with m-Eslon SR capsules may affect the morphine release properties resulting in a higher and delayed C_{max}.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Distribution

Morphine is widely distributed throughout the body but mainly in the kidneys, liver, lungs and spleen with lower concentrations in the brain and muscles. Volume of distribution is about 3 to 5 litres/kg and 20 to 35% is bound to plasma proteins.*

Morphine crosses the blood-brain barrier less readily than more lipid soluble opioids, but it has been detected in the cerebrospinal fluid as have its highly polar metabolites morphine-3-glucuronide and morphine-6-glucuronide. Morphine diffuses across the placenta and residual levels also appear in breast milk and sweat.*

Biotransformation

Morphine is mostly conjugated to morphine-3-glucuronide and morphine-6-glucuronide which then undergo renal excretion. These metabolites are also excreted in bile and may be subject to hydrolysis and subsequent reabsorption.*

Elimination

The elimination half-life of morphine is 2 to 3 hours with great interpatient variability. About 90% of total morphine is excreted in 24 hours with traces in urine for 48 hours or more.

Special patient groups

Because morphine-6-glucuronide has been observed to accumulate in patients with renal disease, caution should be exercised in patients with clinically significant impairment of the renal function.

Indications

For the prolonged relief of chronic, moderate to severe pain.*

Dosage and administration

Dosage

Administration and dosing of morphine should be individualised bearing in mind the properties of the drug. In addition, the nature and severity of the pain or pains experienced, and the total condition of the patient must be taken into account. Of special importance is other medication given previously or concurrently.*

As with other strong opioid analgesics, use of morphine for the management of persistent pain should be preceded by a thorough assessment of the patient and diagnosis of the specific pain or pains and their causes. Use of opioids for the relief of chronic pain, including cancer pain, all important as it may be, should be only one part of a comprehensive approach to pain control including other treatment modalities or drug therapy, non-drug measures and psychosocial support.*

m-Eslon SR capsules are not recommended for paediatric use.

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Initial dosing

All strengths: One capsule every 12 hours or as prescribed by a physician.*

The dosage is dependent upon the severity of the pain and the patient's previous history of analgesic requirements. The capsules should normally be administered twice daily at 12 hourly intervals. One or two 10 mg capsules twice daily is the recommended starting dosage for a patient presenting with severe pain. With increasing severity of pain it is recommended that the dosage of morphine be increased to achieve the desired relief. The dosage may be varied by choosing combinations of available strengths (10 mg, 30 mg, 60 mg, 100 mg and 200 mg) or by using higher strength capsules alone.*

When m-Eslon SR capsules are to be given for the relief of post-operative pain, it is not advisable to administer it during the first 24 hours. Following this initial period, the dosage should be at the physician's discretion.*

Some patients may require supplemental parenteral morphine which is perfectly acceptable. Careful attention should be paid to the total morphine dosage however, and the prolonged effects of morphine in the m-Eslon SR capsules should also be borne in mind.*

m-Eslon SR capsules should be used with caution post operatively (as with all morphine preparations) but especially in cases of 'acute abdomen' and following abdominal surgery. Gastric motility should have returned and be maintained before treatment with m-Eslon SR is initiated.*

Because of the high inter-patient variation in morphine pharmacokinetics, and in analgesic requirements, the daily dosage in individual patients must be titrated to achieve appropriate pain control. Reduced dosing is necessary in patients with renal or hepatic dysfunction, and also in the elderly due to increased sensitivity to its effect.*

Converting from immediate release morphine

It is recommended that a patient transferred from another oral morphine preparation, having a similar bioavailability to immediate release morphine tablets, should receive the same total morphine dose in one 24 hour period. This total dose should be divided between the morning and evening administration. Dosage titration and clinical assessment may be appropriate.*

Where a patient has previously received parenteral morphine prior to being transferred to m-Eslon SR capsules, a higher total dosage of morphine may be required. Individual dosage adjustment will be necessary to compensate for any reduction in analgesic effect associated with oral administration.*

Converting from other opioid analgesics

For patients who are receiving an alternate opioid, the oral morphine equivalent of the analgesic presently being used should be determined. Having determined the total daily dosage of the present analgesic, the following equivalence table can be used to calculate the approximate daily oral morphine dosage that should provide equivalent analgesia. This total

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

daily oral morphine dosage should then be divided equally in two to obtain the 12 hourly dose of m-Eslon SR capsules.*

Approximate potency factors to convert the total 24 hour dose of a opioid analgesic to the equivalent total 24 hour oral morphine dose (adapted from Pharmacological management of chronic pain, Best Practice Journal 16, September 2008, pp. 6-12)

WHO analgesic ladder for pain management	Opioid analgesic	Route	Oral morphine conversion factors
Step 2 – weak opioids	Codeine	oral	0.1
	Dihydrocodeine	oral	0.1
	Tramadol	oral	0.2
	Pethidine	oral	0.25
Step 3 – strong opioids	Oxycodone	oral	1.5 to 2
	Morphine	parenteral	3
	Methadone (1)	oral	5 to 20
	Fentanyl (2)	transdermal	100 to 150

(1) Although a single 5 mg dose of methadone is equivalent to morphine 7.5 mg, it has a prolonged plasma half life which on repetitive dosing, leads to accumulation. Therefore the potency of methadone, relative to morphine, increases with regular dosing.*

(2) Refer to the manufacturer's instructions for dose conversion specific to the transdermal system under consideration.*

Administration

m-Eslon is intended for oral administration only.*

The microgranules should not be chewed or crushed because of the risk of rapid release of morphine leading to toxic concentrations.

The capsules may be opened, and the microgranules given mixed with soft food or liquids. Alternatively, the contents of the capsules may be given by gastric tube or gastrostomy to dysphagic (e.g. E.N.T. cancer) patients who can benefit from the analgesia obtained from an extended release preparation. It is recommended that the internal diameter of the tube is at least 2.5 mm and the procedure for a tube with a dead volume must be strictly followed according to the instructions for each tube. In addition the tube's composition is important as the material needs to allow the microgranules to slide through and this property has to be determined for each tube. Some tubes are not suitable for use with this formulation and compatibility will need to be discerned from the manufacturer's data.*

Contraindications

- Co-ingestion with alcohol (in the presence of alcohol, dose-dumping of opioid to potentially fatal plasma levels may occur, even in opioid-tolerant patients)*
- Respiratory depression especially in the presence of cyanosis and excessive bronchial secretion, obstructive airways disease, known morphine sensitivity or acute hepatic disease.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

- Acute alcoholism, severe cirrhosis, delirium tremens.*
- Severe CNS depression.*
- Convulsive disorders (may lower the seizure threshold).*
- Head injuries, brain tumours and other conditions in which cerebrospinal or intracranial pressure is raised (may cause marked exaggeration of cerebrospinal fluid pressure and mask the clinical course).*
- Acute attacks of bronchial asthma*
- Heart failure secondary to chronic lung disease, cor pulmonale.*
- Cardiac arrhythmias.*
- Hypotension.*
- Surgical anastomosis (narcotics may cause increase in intraluminal pressure).*
- Concurrent administration with or within 2 weeks of discontinuation of monoamine oxidase inhibitors (MAOIs).
- Patients with paralytic ileus, acute abdomen, or delayed gastric emptying.*
- Patients with phaeochromocytoma as morphine appears to increase catecholamine levels.
- m-Eslon is not to be used as a pre-operative medication.
- Children under the age of 6 months.
- Patients with chronic pain of non-malignant origin who have a prior history of substance abuse.*

Warnings and precautions

Warnings

m-Eslon SR has not been compared to any modified-release morphine preparation on the New Zealand market, and therefore it is not interchangeable with other formulations.*

As with other opiates, tolerance and physical dependence tend to develop upon repeated administration of morphine and there is potential for abuse of the drug and for development of strong psychological dependence. m-Eslon SR capsules should therefore be prescribed and handled with the high degree of caution appropriate to the use of a drug with strong abuse potential. Drug abuse is not, however, a problem in patients with severe pain in which morphine is appropriately indicated. In these patients, an increase in the doses for pain management does not necessarily reflect a development of dependence. On the other hand, in the absence of a clear indication for a strong opioid analgesic, drug-seeking behaviour must be suspected and resisted, particularly in patients with a history of, or propensity for drug abuse. Withdrawal symptoms may occur following abrupt discontinuation of morphine therapy or upon administration of a narcotic antagonist. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control.*

Infants born to mothers who are physically dependent upon opioid analgesics may also be physically dependent and may exhibit withdrawal symptoms such as generalized tremors, hypertonicity, hyperalertness, sleeplessness, excessive crying, vomiting, diarrhoea, yawning, and occasional fever. These infants may have respiratory depression at birth.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Severe pain antagonizes the subjective and respiratory depressant actions of morphine. Should pain suddenly subside, these effects may rapidly become manifest. Patients who are scheduled for cordotomy or other interruption of pain transmission pathways should not receive m-Eslon SR within 24 hours of the procedure.*

Precautions

m-Eslon SR capsules should be given with caution or in reduced doses to elderly or debilitated patients and in patients presenting adrenocortical insufficiency, impaired kidney or liver function, prostatic hypertrophy or urethral stricture, hypopituitarism, anemia, severe malnutrition, fulminant ulcerative colitis, hypothyroidism or untreated myxedema, shock. Cautions should also be exercised in its administration to patients presenting CNS depression, toxic psychosis, severe kyphoscoliosis, myasthenia gravis, patients about to undergo biliary tract surgery and patients with acute pancreatitis secondary to biliary disease.*

m-Eslon SR should not be given to patients with gastrointestinal obstruction as there is a risk of the medication remaining in the stomach for an extended period and the subsequent bolus of morphine when normal gut motility is restored.

Morphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions.*

Respiratory depression is the major hazard of all morphine preparations. It occurs more frequently in the elderly or debilitated and those suffering from conditions accompanied by hypoxia or hypercapnia where even moderate therapeutic doses may significantly decrease pulmonary ventilation.

Morphine should be used with caution in patients presenting chronic pulmonary disease, substantially decreased respiratory reserve, hypoxia, hypercapnia or pre-existing respiratory depression. Such patients are often less sensitive to the stimulatory effects of carbon dioxide on the respiratory centre and therapeutic doses of morphine may increase airway resistance and decrease respiratory drive to the point of apnoea. Severe pain antagonizes the respiratory depressant effects of morphine.*

The respiratory depressant effects of morphine with carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure may be exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Also, morphine may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, morphine must be used with extreme caution and only if it is judged to be essential.*

It is important to reduce the doses of morphine when other analgesic treatments are prescribed simultaneously, as such combinations enhance the risk of sudden occurrence of respiratory failure.

Morphine may cause severe hypotension in patients whose blood pressure has already been compromised by reduced blood volume or concurrent administration of medicines such as

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

phenothiazines or certain anaesthetics. Morphine may cause a decrease in systemic vascular resistance in patients with myocardial infarction. A transient fall in systemic arterial pressure may result, leading to severe hypotension. Administered in large doses, morphine may cause severe hypotension even in the supine patient and may induce orthostatic hypotension in ambulatory patients. Morphine should be administered with caution to patients in circulatory shock as its vasodilatory effects may further reduce cardiac output and blood pressure.*

Morphine may also lead to acute retention of urine by causing spasm of the sphincter of the bladder especially in men with prostatism. Monitoring of patients at risk is recommended.

Prior to long term prescription, a trial of m-Eslon SR capsules or shorter acting opioid analgesics should be undertaken (e.g. for a period of four to six weeks). Long term administration of m-Eslon SR capsules should only occur if this trial demonstrates that the pain is opioid sensitive. Opioid naive patients who require rapid dose escalation with no concomitant pain relief within the trial period should generally be considered inappropriate for long term therapy. A single doctor should be responsible for the prescription and monitoring of the patient's opioid use.*

The use of morphine for managing chronic pain of non-malignant origin should be restricted to cases where: all other conservative methods of analgesia have been tried and failed; the pain is having a significant impact on the patient's quality of life; there is no psychological contraindication, drug-seeking behaviour or history of drug misuse. Therapy should only be initiated by a specialist with experience in chronic pain management and in accordance with guidelines approved by the New Zealand Medical Association.*

When the cause of pain is treated simultaneously e.g. post-operative pain, the doses of morphine should be adjusted according to the results of the treatment administered .

Competitive sports people should be made aware that morphine may produce a positive reaction to anti-doping tests.

Pregnancy and lactation

Pregnancy

m-Eslon SR is not recommended for use in pregnancy. Morphine is assigned Category C in the Australian Categorisation of risk system. Category C refers to medicines which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details. Opioid analgesics may cause respiratory depression in the newborn infant. Withdrawal symptoms in newborn infants have been reported with prolonged use of this class of drugs.*

Lactation

Although morphine is secreted in breast milk, it is usually considered safe due to the relatively low transfer into milk at about 0.4% of the maternal dose, and its subjection to high first-pass metabolism.

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Effects on ability to drive and use machinery

Morphine may impair the mental and/or physical abilities needed for driving a car or operating machinery. Patients should be cautioned accordingly.*

Adverse effects

The major hazards associated with morphine, as with other opioid analgesics, are dose-related respiratory depression and, to a lesser degree, circulatory depression. Respiratory arrest, shock and cardiac arrest have occurred following oral or parenteral use of morphine.*

The most frequently observed side effects of opioid analgesics such as morphine are sedation, nausea and vomiting, constipation and sweating.*

Incidence by body system

The adverse effects listed below are classified by body system according to their incidence: common (1 in 100 or more); uncommon (< 1 in 100).

Gastrointestinal

Common

Abdominal pain, anorexia, constipation, dry mouth, dyspepsia, nausea, vomiting.

Uncommon

biliary pain, gastrointestinal disorders, ileus, taste perversion.

Central nervous system

Common

Asthenia, confusion, headache, insomnia, involuntary muscle contractions, somnolence, thought abnormalities.

Uncommon

Agitation, dysphoria, euphoria, hallucinations, malaise, mood changes, respiratory depression, seizure, paresthesia, vertigo, vision abnormalities, withdrawal syndrome.

Genitourinary

Uncommon

Amenorrhoea, decreased libido, impotence, urinary retention.

Cardiovascular

Uncommon

Hypotension, syncope

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Metabolic and nutritional

Uncommon

Peripheral edema, pulmonary edema

Respiratory

Common

Bronchospasm, cough decreased, respiratory depression.

Dermatological

Common

Rash

Uncommon

Urticaria

General

Common

Chills, pruritus, sweating.

Uncommon

Allergic reaction, anaphylactic/anaphylactoid reactions, drug dependence, facial flushing, hypertonia, miosis, tolerance.

Withdrawal Syndrome

Chronic use of opioid analgesics may be associated with the development of physical dependence. Withdrawal symptoms may occur when opioid administration is abruptly discontinued or opioid antagonists administered. Withdrawal symptoms include body aches, diarrhoea, piloerection, anorexia, nervousness or restlessness, rhinorrhoea, sneezing, tremors or shivering, abdominal colic, nausea, sleep disturbances, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate dose adjustments and gradual withdrawal these symptoms are usually mild.

INTERACTIONS

General considerations

The depressant effects of morphine may be enhanced by other CNS depressants such as alcohol, anaesthetics, hypnotics and sedatives, tricyclic antidepressants, phenothiazines and antipsychotics. Concurrent use may result in potentiation of respiratory depression, hypotension, profound sedation or coma and death may occur. If used concurrently with CNS depressants, dosage adjustment may be required.*

Antihistamines, beta-blockers and skeletal muscle relaxants may also enhance the depressant effects of morphine.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

The action of morphine may in turn affect the activities of other compounds; for example its gastrointestinal effects may delay absorption as with mexilitine or may be counteractive as with cisapride, domperidone or metoclopramide.*

Agonist/antagonist analgesics e.g. buprenorphine should not be administered to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic. The analgesic effect may be reduced or withdrawal symptoms may occur.

Specific interactions

Other medicines and drugs

Alcohol

In vitro data have shown that in the presence of alcohol there is an increased rate of morphine release from the microgranules in the capsule. Co-ingestion with alcohol is contraindicated. Patients should be instructed against taking m-Eslon SR capsules with alcohol as this may lead to the rapid release and absorption of a potentially toxic dose of morphine.*

Amphetamines

Amphetamines potentiate the analgesic effect of morphine.*

Anticholinergics

The concomitant use of anticholinergics with opioid analgesics, including morphine, may result in an increased risk of severe constipation and urinary retention. For example, concomitant administration of morphine with tricyclic antidepressants may increase the likelihood of adverse effects such as confusion and constipation.*

Cimetidine

Cimetidine inhibits the metabolism of morphine. There is a report of confusion and severe respiratory depression when a patient receiving haemodialysis was administered morphine and cimetidine. Caution is therefore advised when administering morphine with cimetidine.*

Cyclizine

Cyclizine may counteract the haemodynamic benefits of opioid analgesics.*

Diuretics

Morphine reduces the efficacy of diuretics by inducing the release of anti-diuretic hormone.

MAO inhibitors

Morphine should not be given to patients receiving MAOIs or within 14 days of their discontinuation. Non-selective MAOIs intensify the effects of morphine and other opioids which can cause anxiety, confusion and significant depression of respiration sometimes leading to coma.

Narcotic antagonists

Concomitant use of narcotic antagonists may result in reversal of analgesia, and may precipitate withdrawal symptoms in patients who are physically dependent on opioids.*

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Oral anticoagulants

Morphine may increase the anti-coagulant activity of coumarin and other anti-coagulants.*

Skeletal muscle relaxants

Morphine may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.*

Zidovudine

Morphine may competitively inhibit the hepatic gluconuronidation of zidovudine thus reducing its clearance. Concurrent use of morphine and zidovudine should be avoided because the toxicity of either or both medicines may be potentiated.*

Food

The bioavailability of morphine is not significantly affected by food.

OVERDOSAGE

Signs and symptoms

Serious morphine overdosage is characterised by the following signs: pinpoint pupils; respiratory depression (manifested as reduced respiratory rate and/or tidal volume; Cheyne-Stokes respiration; cyanosis); extreme somnolence progressing to stupor or coma; flaccidity of skeletal muscle; cold or clammy skin; sometimes hypotension and bradycardia. Severe overdosage may result in apnoea, circulatory collapse, cardiac arrest and death. Convulsions may occur in young children. Dilation of pupils occurs as hypoxia develops.*

Treatment

In acute poisoning resulting from oral ingestion, the stomach should be emptied by aspiration and lavage. A laxative may be given to aid peristalsis.

Treatment of respiratory failure and shock may require intensive supportive therapy. In addition to this the specific antagonist naloxone hydrochloride should be administered at a dose of 0.4 to 2 mg IV. This dose should be repeated at intervals of 2 to 3 minutes if required, up to a total dose of 10 mg.*

The contents of m-Eslon SR capsules remaining in the intestinal tract will continue to release and add to the morphine load for up to 12 hours after ingestion and management of the morphine overdosage should be modified accordingly. Fluid and electrolyte levels must be maintained.*

PHARMACEUTICAL PRECAUTIONS

Incompatibilities

None

NEW ZEALAND DATA SHEET

m-Eslon SR

Morphine Sulphate Ph Eur, modified release capsules, 10 mg, 30 mg, 60 mg, 100 mg and 200 mg

Storage conditions

Unopened container

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

MEDICINE CLASSIFICATION

Controlled Drug B1

PACKAGE QUANTITIES

Cartoned blister strips of 10 capsules.*

FURTHER INFORMATION

List of inactive ingredients

Capsule shells

Gelatin, may also contain titanium dioxide [171], quinolone yellow [104], erythrosine [127] and sunset yellow [110] as colouring agents. Capsule shells are printed with a black ink composed of black iron oxide. The gelatin is derived from animal sources.*

Microgranules

Sugar, corn starch, polyethylene glycol 4000, polymeric dispersion of ethylcellulose, dibutyl sebecate, talc.*

Instructions for patients

m-Eslon SR capsules must NOT be taken with alcohol.*

NAME AND ADDRESS

Multichem NZ Limited
8 Apollo Drive,
Rosedale,
North Shore City 0632
Auckland

Telephone: (09) 488 0330

DATE OF PREPARATION

27 October 2011

Version 4. Revisions to the previous version are indicated by (*).