

PRESCRIBING INFORMATION

^NMS•IR[®]

**Morphine Sulfate Immediate Release Tablets
5, 10, 20 and 30 mg**

**Purdue Pharma Std.
Opioid Analgesic
ATC: N02AA01**

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PRESCRIBING INFORMATION

NAME OF DRUG

^NMS•IR[®]

Morphine Sulfate Immediate Release Tablets
5, 10, 20 and 30 mg

PHARMACOLOGICAL CLASSIFICATION

Opioid Analgesic

ACTIONS

Morphine is an opioid analgesic which exerts an agonist effect at specific, saturable opioid receptors in the CNS and other tissues. In man, morphine produces a variety of effects including analgesia, constipation from decreased gastrointestinal motility, suppression of the cough reflex, respiratory depression from reduced responsiveness of the respiratory centre to CO₂, nausea and vomiting via stimulation of the CTZ, changes in mood including euphoria and dysphoria, sedation, mental clouding, and alterations of the endocrine and autonomic nervous systems.

Morphine is readily absorbed when given orally, rectally or by s.c. or i.m. injection. Due to first-pass metabolism in the liver, the effect of an oral dose is less than after parenteral administration. With repeated regular dosing, oral morphine is about 1/3 as potent as when given by i.m. injection. Morphine is primarily excreted in the urine as morphine-3-glucuronide. About 7 to 10% of a dose of morphine is excreted in the feces via the bile.

INDICATIONS

For the symptomatic relief of severe pain.

CONTRAINDICATIONS

MS•IR[®] (morphine sulfate tablets) should not be given to patients with: hypersensitivity to opioid analgesics morphine or any other component of the product; in acute asthma or other obstructive airway disease and acute respiratory depression; cor pulmonale; cardiac arrhythmias; acute alcoholism; delirium tremens; severe CNS depression; convulsive disorders; increased cerebrospinal or intracranial pressure; head injury; brain tumor; suspected surgical abdomen; concomitant MAO inhibitors (or within 14 days of such therapy).

WARNINGS

Abuse of Opioid Formulations: **MS•IR[®]** (morphine sulfate tablets) is intended for oral use only. Abuse can lead to overdose and death. This risk is increased if **MS•IR** is taken with alcohol or other CNS depressants. With parenteral abuse, the tablet excipients, can be expected to result in local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury.

Patients should be instructed not to give MS•IR to anyone other than for whom it was prescribed, as such, inappropriate use may have severe medical consequences, including death.

Patients should be cautioned not to consume alcohol while taking **MS•IR**, as it may increase the chance of experiencing dangerous side effects.

MS•IR should be used with caution preoperatively and within the first 24 hours postoperatively.

Drug Dependence: As with other opioids, 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. **MS•IR** 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 usually a problem in patients with severe pain in which morphine is appropriately indicated. However, in the absence of a clear indication for a strong opioid analgesic, drug-seeking behaviour must be suspected and resisted, particularly in individuals with a history of, or propensity for drug abuse. Withdrawal symptoms may occur following abrupt discontinuation of morphine therapy or upon administration of a opioid antagonist. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control.

CNS Depression: Morphine should be used only with caution and in reduced dosage during concomitant administration of other opioid analgesics, general anaesthetics, phenothiazines and other tranquilizers, sedative-hypnotics, tricyclic antidepressants and other CNS depressants (including alcohol). Respiratory depression, hypotension and profound sedation or coma may result.

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 **MS•IR** within 24 hours of the procedure.

Use in Pregnancy: Animal studies with morphine and other opioids have indicated the possibility of teratogenic effect. In humans, it is not known whether morphine can cause fetal harm when administered during pregnancy or can affect reproductive capacity. **MS•IR** should be given to pregnant patients only if clearly needed and when the anticipated benefits outweigh the risks to the fetus.

PRECAUTIONS

Respiratory Depression: Morphine should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia. Such patients are often less sensitive to the stimulatory effects of carbon dioxide on the respiratory center and the respiratory depressant effects of morphine may reduce respiratory drive to the point of apnea.

Head Injury: The respiratory depressant effects of morphine, and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of an already elevated intracranial pressure produced by trauma. 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 essential.

Hypotension: Morphine administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of such drugs as phenothiazines or certain anaesthetics.

Acute Abdominal Conditions: Morphine has been shown to decrease bowel motility. Morphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Special Risk Groups: Morphine should be administered with caution, and in reduced dosages, to elderly or debilitated patients, to patients with severely reduced hepatic or renal function, and to patients with adrenocortical insufficiency (e.g., Addison's disease), biliary tract disorders, hypothyroidism, pancreatitis, prostatic hypertrophy or urethral stricture.

Morphine should not be used where there is the possibility of paralytic ileus occurring.

Morphine may lower the seizure threshold in patients with a history of epilepsy.

Use during Labor/Delivery and in Nursing Mothers: Morphine crosses the placental barrier and its administration during labor can produce respiratory depression in the neonate. Morphine has

been detected in human breast milk. Caution should be exercised if morphine is administered to a nursing mother.

Driving and Operating Dangerous Machinery: Morphine may impair the mental and/or physical abilities needed for certain potentially hazardous activities such as driving a car or operating machinery. Patients should be cautioned accordingly.

Patients should also be cautioned about the combined effects of morphine with other CNS depressants, including other opioids, phenothiazines, sedative/hypnotics and alcohol.

Drug Interactions: Generally, the effects of morphine may be antagonized by acidifying agents and potentiated by alkalizing agents. The analgesic effect of morphine is potentiated by amphetamines, chlorpromazine and methocarbamol. CNS depressants, such as other opioids, anaesthetics, sedatives, hypnotics, barbiturates, phenothiazines, other tranquilizers, chloral hydrate and glutethimide may enhance the depressant effect of morphine and may result with respiratory depression, hypotension, profound sedation or coma. Monoamine oxidase inhibitors (including procarbazine hydrochloride) should not be taken within two weeks of use. Pyrazolidone antihistamines, beta-blockers and alcohol may also enhance the depressant effect of morphine. When combined therapy is contemplated, the dose of one or both agents should be reduced.

Mixed agonist/antagonist opioid analgesics (i.e., pentazocine, nalbuphine, butorphanol, and buprenorphine) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as morphine. In this situation, mixed agonist/antagonist analgesics may reduce the analgesic effect of morphine and/or may precipitate withdrawal symptoms in these patients.

Morphine may increase the anticoagulant activity of coumarin and other anticoagulants.

ADVERSE REACTIONS

The major hazards associated with morphine, as with other opioid analgesics, are 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, vomiting, constipation, lightheadedness, dizziness, and sweating.

Sedation: Some degree of sedation is experienced by most patients upon initiation of therapy. This may be at least partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Drowsiness usually clears in three to five days and is usually not a reason for concern providing that it is not excessive, or associated with unsteadiness or confusion. If excessive sedation persists, the reason for it must be sought. Some of these are: concomitant sedative medications, hepatic or renal failure, exacerbated respiratory failure, higher

doses than tolerated in an older patients, or the patient is actually more severely ill than realized. If it is necessary to reduce the dose, it can be carefully increased again after three or four days if it is obvious that the pain is not being well controlled. Dizziness and unsteadiness may be caused by postural hypotension particularly in elderly or debilitated patients. It can be alleviated if the patient lies down. Because of the slower clearance in patients over 50 years of age, an appropriate dose in this age group may be as low as half or less the usual dose in the younger age group.

Nausea and Vomiting: Nausea and vomiting occur frequently after single doses of opioids or as an early unwanted effect of regular opioid therapy. When instituting prolonged therapy for chronic pain, the routine prescription of an antiemetic should be considered. Patients taking a single dose of 20 mg or more of oral morphine every four hours usually require an antiemetic during early therapy. Small doses of prochlorperazine or haloperidol are the most frequently prescribed antiemetics. Nausea and vomiting tend to lessen in a week or so but may persist due to opioid-induced gastric stasis. In such patients, metoclopramide is often useful.

Constipation: Practically all patients become constipated while taking opioids on a persistent basis. In some instances, particularly the elderly or bedridden, fecal impaction may result. It is essential to caution the patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid therapy. Stool softeners, stimulant laxatives and other appropriate measures should be used as required.

Other Adverse Reactions Include:

Cardiovascular: faintness, palpitations, postural hypotension, supraventricular tachycardia and syncope

Central Nervous System: agitation, confusion, dizziness, dysphoria, euphoria, hallucinations, headache, insomnia, involuntary muscle contractions, malaise, mood changes, paresthesia, seizure, somnolence, thought abnormalities, vertigo, vision abnormalities, weakness and withdrawal syndrome

Dermatologic: edema, pruritus, other skin rashes and urticaria

Endocrine: a syndrome of inappropriate antidiuretic hormone secretion characterized by hyponatremia secondary to decreased free-water excretion may be prominent (monitoring of electrolytes may be necessary)

Gastrointestinal: abdominal pain, anorexia, biliary tract spasms, constipation, cramps, dry mouth, dyspepsia, elevated hepatic enzymes, gastrointestinal disorders, ileus, nausea, taste alterations and vomiting

General: allergic reaction, anaphylactic/anaphylactoid reactions, asthenia, chills, drug dependence, facial flushing, hypertonia, miosis, sweating and tolerance

Genitourinary: amenorrhea, reduced libido or potency, urinary retention or hesitance

Metabolic and Nutritional: peripheral edema and pulmonary edema

Respiratory: bronchospasm and cough decreased

Withdrawal (Abstinence) Syndrome: Physical dependence with or without psychological dependence tends to occur with chronic administration. An abstinence syndrome may be precipitated when opioid administration is discontinued or opioid antagonists administered. The following withdrawal symptoms may be observed after opioids are discontinued: body aches, diarrhea, gooseflesh, loss of appetite, nervousness or restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, nausea, trouble with sleeping, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate medical use of opioids and gradual withdrawal from the drug, these symptoms are usually mild.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms: Serious morphine overdosage is characterized by respiratory depression (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, and sometimes hypotension and bradycardia. Severe overdosage may result in apnea, circulatory collapse, cardiac arrest and death.

Treatment: Primary attention should be given to the establishment of adequate respiratory exchange through the provision of a patent airway and controlled or assisted ventilation. The opioid antagonist naloxone hydrochloride is a specific antidote against respiratory depression due to overdosage or as a result of unusual sensitivity to morphine. An appropriate dose should therefore be administered, preferably by the intravenous route. The usual initial i.v. adult dose of naloxone is 0.4 mg or higher. Concomitant efforts at respiratory resuscitation should be carried out. Since the duration of action of morphine may exceed that of the antagonist, the patient should be under continued surveillance and doses of the antagonist should be repeated as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated.

In an individual physically dependent on opioids, the administration of the usual dose of opioid antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of opioid antagonists in such individuals should be avoided if possible. If an opioid antagonist must be used to treat serious respiratory depression in the physically dependent patient, the antagonist should be administered with extreme care by using dosage titration, commencing with 10 to 20% of the usual recommended initial dose.

Evacuation of gastric contents may be useful in removing unabsorbed drug.

DOSAGE AND ADMINISTRATION

Administration and dosing of morphine should be individualized 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.

Adult Dose: Individual dosing requirements vary considerably based on each patient's age, weight, severity of pain, and medical and analgesic history.

The most frequent initial dose is 10 mg every 4 hours as needed for acute pain and every 4 hours around the clock for chronic pain, or as directed by a physician. The suppository may be used in situations where the patient cannot tolerate oral dosing, at the same dosage and frequency.

Patients over the age of 50 tend to require much lower doses of morphine than in the younger age group. In elderly and debilitated patients and those with impaired respiratory function or significantly decreased renal function, the initial dose should be one half the usual recommended dose.

Patients Currently Receiving Opioids: For patients who are receiving an alternate opioid, the "oral morphine sulfate 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 sulfate dosage that should provide equivalent analgesia.

Dose Titration: Dose titration is the key to success with morphine therapy. **Proper optimization of doses scaled to the relief of the individual's pain should aim at the regular administration of the lowest dose of morphine which will maintain the patient free of pain at all times.**

Dose adjustments should be based on the patient's clinical response. Higher doses may be justified in some patients to cover periods of physical activity.

Adjustment or Reduction of Dosage: Following successful relief of severe pain, periodic attempts to reduce the opioid dose should be made. Smaller doses or complete discontinuation may become feasible due to a change in the patient's condition or improved mental state. If treatment discontinuation is required, the dose of opioid may be decreased as follows: one-half of the previous daily dose given q4h for the first two days, followed thereafter by a 25% reduction every two days.

Opioid analgesics may only be partially effective in relieving dysesthetic pain, post-herpetic neuralgia, stabbing pains, activity-related pain, and some forms of headache. This is not to say that patients with advanced cancer suffering from some of these forms of pain should not be given an adequate trial of opiate analgesics, but it may be necessary to refer such patients at an early time for other forms of pain therapy.

TABLE 1
OPIOID ANALGESICS: APPROXIMATE ANALGESIC EQUIVALENCES¹

Drug	Equivalent Dose (mg) ² (compared to morphine 10 mg IM)		Duration of Action (hours)
	Parenteral	Oral	
Strong Opioid Agonists:			
Morphine	10	60 ³	3-4
Oxycodone ⁴	15	30	2-4
Hydromorphone	1.5	7.5	2-4
Anileridine	25	75	2-3
Levorphanol	2	4	4-8
Meperidine ⁶	75	300	1-3
Oxymorphone	1.5	5 (rectal)	3-4
Methadone ⁵	-	-	-
Heroin	5-8	10-15	3-4
Weak Opioid Agonists:			
Codeine	120	200	3-4
Propoxyphene	50	100	2-4
Mixed Agonist-Antagonists⁷:			
Pentazocine ⁶	60	180	3-4
Nalbuphine	10	-	3-6
Butorphanol	2	-	3-4

¹References:

Expert Advisory Committee on the Management of Severe Chronic Pain in Cancer Patients, Health and Welfare Canada. Cancer pain: A monograph on the management of cancer pain. Ministry of Supplies and Services Canada, 1987. Cat. No. H42-2/5-1984E.

Foley KM. The treatment of cancer pain. N Engl J Med 1985;313(2):84-95.

Aronoff GM, Evans WO. Pharmacological management of chronic pain: A review. In: Aronoff GM, editor. Evaluation and treatment of chronic pain. 2nd ed. Baltimore (MD): Williams and Wilkins; 1992. p. 359-68.

Cherny NI, Portenoy RK. Practical issues in the management of cancer pain. In: Wall PD, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1437-67.

² **Most of the data were derived from single-dose, acute pain studies and should be considered an approximation for selection of doses when treating chronic pain.**

³ **For acute pain, the oral or rectal dose of morphine is six times the injectable dose. However, for chronic dosing, clinical experience indicates that this ratio is 2 - 3: 1 (i.e., 20-30 mg of oral or rectal morphine is equivalent to 10 mg of parenteral morphine).**

⁴ Based on single entity oral oxycodone in acute pain.

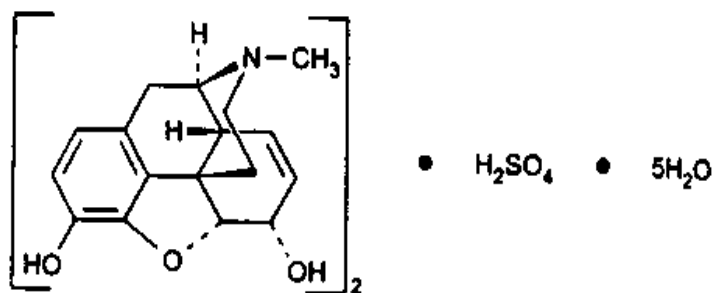
⁵ Extremely variable equianalgesic dose. Patients should undergo individualized titration starting at an equivalent to 1/10 of the morphine dose.

⁶ Not recommended for the management of chronic pain.

⁷ Mixed agonist-antagonists

PHARMACEUTICAL INFORMATION

The chemical name of morphine sulfate is 7,8-didehydro-4,5 α -epoxy-17-methyl-morphinan-3,6 α -diol sulfate (2:1) (salt) pentahydrate, and it has the following structure:



Molecular Formula: $(\text{C}_{17}\text{H}_{19}\text{NO}_3) \cdot \text{H}_2\text{SO}_4$

Molecular Weight: 758.8 (pentahydrate)

668.8 (anhydrous)

Description: Morphine sulfate is a white, odourless crystalline powder or needlelike crystals. Morphine sulfate is soluble 1:21 in water and 1:1000 in ethanol. It is practically insoluble in ether or chloroform.

Composition:

Active ingredient(s): Morphine Sulfate

Non-medicinal Ingredients (all strengths): croscarmellose sodium, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose and polyethylene glycol 400

AVAILABILITY

MS•IR[®] (morphine sulfate pentahydrate) is available as white film-coated immediate-release tablets in four strengths:

5 mg: Scored round tablets with "5" engraved on one side and "PF" on the other.

10 mg: Scored round tablets with "10" engraved on one side and "PF" on the other.

20 mg: Scored caplet-shaped tablets with "20" engraved on one side and "PF" on the other.

30 mg: Scored caplet-shaped tablets with "30" engraved on one side and "PF" on the other.

Supplied in opaque plastic bottles of 50 tablets.

Stability and Storage Recommendations:

Store tablets at room temperature (15 - 30° C).

INFORMATION FOR THE CONSUMER

Read this information carefully before you take MS•IR[®] tablets. Also read the information you get with your prescription refills, since there may be something new. This information does not take the place of talking with your doctor about your medical condition or your treatment. Only you and your doctor can decide if **MS•IR** is right for you. Share the information in this leaflet with members of your household.

What is morphine?

Morphine is a medicine used to treat severe pain and should help you live more comfortably and independently. Morphine belongs to a class of drugs which is commonly referred to as opiates, opioids or narcotics, and also includes codeine, fentanyl, hydromorphone and oxycodone.

Your pain may increase or decrease from time to time and your doctor may need to change the amount of morphine you take daily (daily dosage).

What is MS•IR?

MS•IR is an immediate release tablet containing the medicine morphine, to treat severe pain. **MS•IR** is made to release morphine promptly, usually requiring dosing every 4 hours to control pain.

MS•IR tablets are available as white film-coated immediate-release tablet in four strengths: 5 mg, 10 mg, 20 mg, and 30 mg. It may be necessary for you to take more than one tablet strength at the same time, in order to receive the total daily dosage prescribed by your doctor.

Before you take MS•IR:

Your doctor should know about all of your medical conditions before deciding if **MS•IR** is right for you and what daily dosage is best. Tell your doctor about all of your medical problems, especially the following ones: trouble breathing or lung problems; head injury; liver or kidney problems; gastrointestinal problems; low blood pressure; prostate problems; urethral stricture (unusual narrowing of the urethra); adrenal gland problems, such as Addison's disease; convulsions or seizures; alcoholism; hallucinations or other severe mental problems; past or present substance abuse or drug addiction.

You should also tell your doctor if you are pregnant, breast-feeding, or intend to become pregnant while receiving **MS•IR** as this drug may not be right for you in these circumstances.

MS•IR should not be used if:

- your doctor did not prescribe it for you;
- your pain is mild;
- you have experienced severe allergic reactions (e.g., severe rash, hives, breathing problems, swelling of the mouth, tongue, face, or other areas or dizziness) while taking any opioid, including morphine, or any of the non-medicinal ingredients, in the past;

- you have severe asthma or severe lung problems;
- you have an irregular heartbeat;
- you suffer from alcoholism;
- you have a head injury;
- you have a brain tumour;
- you suffer from seizures.

How to take MS•IR:

You should not consume alcohol while taking MS•IR, as it may increase the chance of experiencing dangerous side effects.

Follow your doctor's directions exactly. **MS•IR** tablets must be taken regularly, usually every 4 to 6 hours (with 4 to 6 oz. of water), as directed by your doctor. If your pain worsens, making you uncomfortable, contact your doctor immediately and she/he may decide that it is necessary to adjust your daily dosage of **MS•IR** tablets.

Your daily dosage of **MS•IR** will be clearly labelled on the medication bottle. Be sure to follow these directions exactly; this is very important. Do not increase or decrease your daily dosage without consulting your doctor. If your daily dosage is changed by your doctor, be sure to write it down at the time your doctor calls you or sees you and follow the new directions exactly. Regularly discuss your pain control and any side effects with your doctor, to determine if you still need **MS•IR**. Be sure to use **MS•IR** only for the condition for which it was prescribed.

Stopping MS•IR:

Consult your doctor for instructions on how to discontinue taking **MS•IR**. You should not stop taking **MS•IR** all at once if you have been taking it for more than a few days, since this may lead to uncomfortable symptoms.

After you stop taking **MS•IR**, you should take the unused tablets to your pharmacist to be destroyed.

Side effects you may have while taking MS•IR:

The most common side effects you may experience are constipation, nausea, drowsiness, dizziness, vomiting, itching, headache, dry mouth, weakness and sweating. Tell your doctor about these problems if they arise. Your doctor may prescribe a laxative and/or stool softener to help relieve constipation while you are taking **MS•IR**.

If you experience any symptoms related to difficulty in breathing, such as tight chest or wheezing, fainting, or rapid heartbeat, tell your doctor or pharmacist immediately.

Overdose:

The most important signs of overdose are suppressed breathing (abnormally slow or weak breathing), dizziness, confusion, or extreme drowsiness. In case of suspected overdose, or if any of these symptoms occur, call your doctor and/or your local emergency number immediately.

Taking MS•IR with other medications:

You should not take **MS•IR** if you are currently taking (or recently stopped taking) one of the medicines known as monoamine oxidase inhibitors (e.g. Nardil[®], Parnate[®]).

Tell your doctor about all medicines that you are taking. Your doctor should decide whether you can take **MS•IR** with other medicines. These include:

- other opioids, anaesthetics, sedatives, hypnotics, barbiturates, phenothiazines, amphetamines, chlorpromazine, methocarbamol, tranquilizers, some heart medications (e.g., beta-blockers), blood-thinners (coumarin or other anticoagulants), chloral hydrate and glutethimide (not available in Canada);
- antihistamines or sleep aids (these medicines could depress your breathing or your level of consciousness);
- medicines that you buy yourself without a prescription;
- any herbal remedies that you may be taking.

Driving/Other Activities:

Driving, operating hazardous machinery, or other tasks requiring full alertness should not be attempted for the first few days of taking **MS•IR**, or after your daily dosage is changed, since you may experience drowsiness or sedation. If drowsiness or sedation occurs, do not undertake such activities until you have talked with your doctor.

Abuse, Addiction and Physical Dependence:

There is a risk of abuse or addiction with all opioids. Some patients, particularly those who may have abused drugs in the past, may have a higher risk of abusing or developing an addiction while taking opioids, such as **MS•IR**.

Patients who have taken **MS•IR** for a period of time may develop physical dependence, and should not abruptly stop taking it. However, physical dependence is not the same as addiction.

If you have concerns about abuse, addiction or physical dependence, please tell your doctor.

Reordering MS•IR:

A new written prescription is required from your doctor each time you need more **MS•IR**. Therefore, it is important that you contact your doctor at least three working days before your current supply runs out.

It is very important that you do not miss any doses. If you miss one dose, take it as soon as possible, but if it is almost time for your next dose, then skip the missed dose. Do not take two doses at once, unless your doctor tells you to. If you miss several doses in succession, talk to your doctor before restarting.

Do not seek additional prescriptions for **MS•IR** from any other doctor - unless responsibility for your pain management has been transferred to another doctor.

Should your pain increase, or any other complaint develop as a result of taking **MS•IR**, tell your doctor immediately.

Storage of MS•IR:

MS•IR contains an opioid medicine and must be stored in a secure place to prevent theft and misuse. Do not give **MS•IR** to anyone other than the person for whom it was prescribed since it may seriously harm them. Keep **MS•IR** out of the reach of children. Accidental overdose by a child is dangerous and may result in death. Keep **MS•IR** in a cool, dry place, between 15 and 30°C.

This leaflet summarizes important information about **MS•IR**. If you would like more information, talk with your doctor and/or pharmacist or contact the manufacturer, Purdue Pharma, at 1-800-387-5349.