

PRESCRIBING INFORMATION

NMS CONTIN[®]

Morphine Sulfate Sustained Release Tablets
15, 30, 60, 100 and 200 mg

NMS-IR[®]

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

Therapeutic Classification

Narcotic Analgesic

Indications: NMS CONTIN[®], for the relief of severe, chronic pain requiring prolonged use of an oral narcotic.

NMS-IR[®], for the symptomatic relief of severe pain.

Narcotic agents do not effectively relieve dyspeptic pain, post-operative neuralgia, radiating pain, activity-related pain, and some forms of headache. Although pain without nociception is usually not narcotic-responsive, this is not to say that patients with advanced cancer suffering from these forms of pain should not be given an adequate trial of a narcotic analgesic, but it may be necessary to re-evaluate the need for other forms of pain therapy.

Contraindications: Hypersensitivity to opioids, acute asthma, other obstructive airway disease and acute respiratory depression, acute pulmonary edema, acute myocardial infarction, severe CNS depression, convulsive disorders, increased intracranial or intraspinal pressure, head injury, brain tumor, suspected or proven alcoholism, airway tract surgery, surgical anesthesia; MAO inhibitors when given, 14 days.

Warnings: Tolerance and physical dependence tend to develop upon repeated administration of morphine and it should be used with the highest degree of caution necessary to elicit the desired analgesic effect. Drug abuse is not a problem in patients with severe pain provided morphine is appropriately indicated. When therapy is no longer needed, after prolonged use, pain should be withdrawn gradually to avoid the withdrawal symptoms which may occur on abrupt discontinuation.

Use only with caution and in reduced dosage with other narcotics, general anesthetics, phenothiazines and other narcotics, sedative-hypnotics, tranquilizers and other CNS depressants (including alcohol). Respiratory depression, hypotension and profound sedation or coma may result.

Use in pregnancy only if clearly needed and the anticipated benefits outweigh the risks to the fetus. Morphine crosses the placental barrier and use during labor can produce respiratory depression in the neonate. Morphine is excreted in breast milk.

Precautions: Use only with extreme caution and if judged essential in patients with head injury as morphines respiratory depressant effects and ability to raise cerebrospinal fluid pressure may be enhanced in the presence of elevated intracranial pressure. Side effects of morphine may obscure the clinical course of patients with head injury. Use with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia.

Morphine may produce severe hypotension when adequate blood pressure is already compromised by reduced blood volume or concomitant drugs (e.g., phenothiazines, certain anesthetics), and may produce orthostatic hypotension in ambulatory patients.

Use with caution in patients with acute myocardial infarction and severe myocardial infarction.

Use with caution and in reduced doses in elderly or debilitated patients, and in those with severely malnourished or liver function. Adverse effects, hypotension, probable hypotension or cerebral edema.

Patients should be cautioned that morphine may impair the mental/physical activities needed to driving or operating potentially hazardous machinery, and about the cumulative effects of morphine with other CNS depressants.

The effects of morphine are generally enhanced by smoking agents and potentiated by alcohol. Morphine's analgesic effects are potentiated by anticholinergics, antispasmodics and sedatives, and to depressant effects are enhanced by other opioids, anesthetics, hypnotics, barbiturates, phenothiazines, ethanol, hydrocortisone, glaucoma drugs, MAO inhibitors, sympathomimetics, beta-blockers and alcohol. The anticholinergic activity of anticholinergics may be increased.

Adverse Reactions: The major hazards are respiratory and circulatory depression. Respiratory arrest, shock and cardiac arrest have occurred following oral or parenteral use of morphine. The most common side effects are sedation, nausea and vomiting, constipation and sweating. When instituting prolonged therapy, the routine prescription of an antitardilic (morphine) antagonist (naltrexone) should be considered and an appropriate bowel management regimen instituted (laxatives, bulkers and other appropriate measures as required). Other effects of morphine include supraventricular tachycardia, orthostatic hypotension, palpitations, syncope, tachypnea, hypotonia, weakness, dizziness, confusion, hallucinations, dry mouth, anorexia, chills and flu-like prodromal symptoms, both alterations, urinary retention, resistance, reduced blood pressure, pruritus, urticaria, skin rashes, edema and a syndrome of intractable anticholinergic-like symptoms. Physical dependence tends to occur in chronic administration. Withdrawal symptoms may include body aches, diarrhea, posttussive, loss of appetite, nervousness/irritability, turns/nausea, sweating, shivering, tremor, cramps, nasal, nasal, trouble sleeping, sweating, yawning, weakness, tachycardia and fever.

Dosage and Administration: Administration and dosing of morphine should be individualized bearing in mind the severity of pain, the nature and severity of the pain, the total condition of the patient, and other medication given previously or concurrently. Individual dosing requirements vary considerably based on each patient's age, weight, sensitivity of pain, and medical and analgesic history.

Usual Initial Adult Dose: NMS CONTIN[®] (morphine sulfate sustained release) - 30 mg orally every 12 hours. NMS CONTIN[®] TABLETS SHOULD BE SWALLOWED INTACT, NOT CHEWED OR CRUSHED. THE 200 MG STRENGTH (ONLY) IS SCORED AND MAY BE BROKEN IN HALF. THE HALF TABLET SHOULD BE SWALLOWED INTACT.

NMS-IR[®] (morphine sulfate immediate release) - 10 mg orally (tablet) or rectally (suppositories) every 4 hours as needed for acute pain and every 4 hours around the clock for chronic pain. 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.

Dose Titration: In patients with chronic pain, dosage should be titrated with the aim of regular administration of the lowest dose of morphine which will maintain the patient free of pain at all times. Because of the sustained release properties of NMS CONTIN[®], dosage adjustments should generally be separated by 48 hours; the usual recommended dose (up to 200 mg) increments are 15, 30, 45, 60, 90, 120, 150, 180, 240 mg. Above 200 mg/dose (400 mg/day), the increments should be by 30-60 mg/dose. If "breakthrough" pain occurs repeatedly at the end of the NMS CONTIN[®] dose interval, the dosage should be increased, not given more frequently, however, where judged necessary for optimization of drug effect.

NMS CONTIN[®] may be administered (PRN) but should not be given more frequently.

During the first few days of effective pain relief, the patient with chronic pain may exhibit tiredness or sleep for prolonged periods. This can be misinterpreted as the effect of excessive analgesic dosing rather than the first sign of pain in a pain-tolerant patient. The dose therefore should be maintained for at least three days before reduction, provided the analgesia is not excessive or associated with undesirable and confounding symptoms, and respiratory activity and other vital signs are adequate. Following successful pain relief, periodic attempts to reduce the narcotic dose should be made.

Patients receiving other use morphine formulations may be transferred to NMS CONTIN[®] at the same total daily morphine dosage divided into ten 12 hourly NMS CONTIN[®] doses. For patients who are receiving an alternate narcotic, the following analgesic equivalence table can be used to calculate the approximately oral morphine sulfate dosage.

Supplies: NMS CONTIN[®] (Morphine Sulfate Sustained Release) are available as 15 mg (round, green), 30 mg (round, white), 60 mg (round, orange), 100 mg (round, grey) and 200 mg (tablets—scored, red/orange, film-coated tablets) strengths with PRN and the strength. The 200 mg strength (only) is scored and may be broken in half. Available in Control Packs of 20 tablets (all strengths) and in opaque plastic bottles of 50 tablets (200 mg strength).

NMS-IR[®] (Morphine Sulfate Immediate Release) is available as scored white film-coated 5, 10, 20 and 30 mg tablets imprinted with "K" and the strength and as smooth white round suppositories in 10, 20 and 30 mg strengths. The tablets are available in blister packs of 50 tablets and in Control Packs of 25 tablets. The suppositories are available in boxes containing 4 strips of 6 suppositories.

Store NMS CONTIN[®] and NMS-IR[®] at room temperature. PRODUCT MANAGEMENT INFORMATION AVAILABLE FOR NMS CONTIN[®] AND FULL PRESCRIBING INFORMATION AVAILABLE FOR NMS-IR[®]. December 5, 1990 NMS-IR[®], September 17, 1990

Warning: This product has the potential for being abused.

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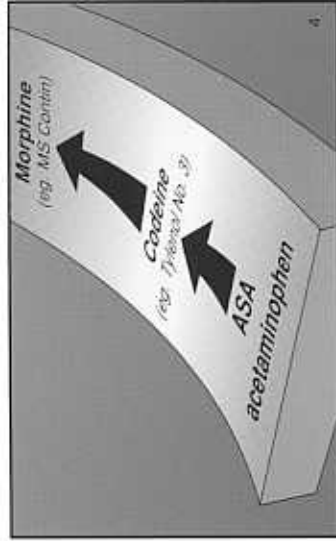
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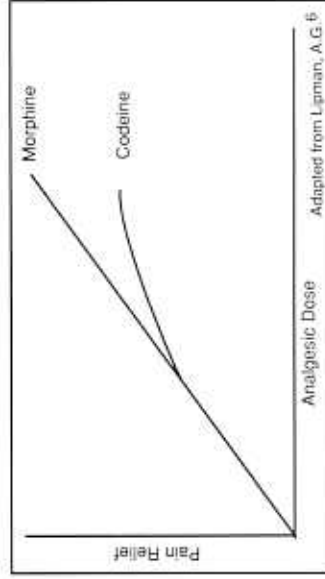
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2 ¹Tylenol No. 3¹ q4h = 360 mg codeine + 3600 mg acetaminophen ≈ ²MS Contin[®] 15 - 30 mg q12h.^{2,3}



- approximately 10% of an oral codeine dose is metabolized to morphine³
- patients taking more than 12-16 tablets per day of a combination product may need to be monitored for adverse effects of ASA or acetaminophen¹



Codeine does not appear to have a linear dose-response curve...[it] provides smaller analgesic increments with dose increments at doses above average.⁶

MS Contin[®] q12h

Sustained release morphine sulfate tablets

for continuous pain relief.



- small, easy-to-swallow tablets are colour-coded to ensure correct dosing

- reliable and trusted drug release - the Contin system is not adversely affected by food⁹

MS•IR[®] q4h

Immediate release morphine sulfate tablets and suppositories

for initial dosing, titration and breakthrough pain.



Start with oral morphine earlier,
stay with oral morphine longer.
To help keep patients pain free.

References: 1. MacDougal N. (Eds) *Essentials of Pain Management*. Philadelphia: JB Lippincott, 1990. 2. *Current pain management on the management of cancer pain*. Health & Welfare Canada, Ottawa, 1984. 3. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. Third Edition. American Pain Society, Illinois, 1992. 4. *Medical Uses of Morphine*. Guidelines Handbook on Use of Cancer Pain. World Health Organization, Geneva, 1981. 5. *Tylenol No. 3*. Monograph. *Concise Clinical Pharmacology and Therapeutics*. C.P. A. Ottawa, 1982. 6. *Adapted from Lerman A.C. Pain Management*. From *Herbst AL, Lurie DL, eds. Clinical Pharmacy and Therapeutics*. Fourth Edition, Williams & Wilkins, Baltimore, 1988, 945-962. 7. *Janzch S. The Oral Morphine Principle and Issues in Cancer Pain Management*. *Pain Practice*. 2001; 1: 8. *Fremel B, Weppert C, Weid C, Boman J. Effects of extended-release morphine on quality of life for cancer pain*. *Qual Man Pain* 1992; 16(52): 26. 9. *Kelly BE, Lazarus H, Green C, Grady R, Thomas S, Colquhoun P. Controlled-release morphine (Kadian[®]) tablets in the presence and absence of food*. *Resp J* 1990; 5(4): 17-20.



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