MITIGO™ CII
(Morphine Sulfate Injection USP)

HOW ARE YOU CURRENTLY MANAGING CHRONIC-PAIN IN YOUR PATIENTS?

The only FDA-approved morphine sulfate for intrathecal and epidural pain management for use in continuous microinfusion devices, packaged in convenient, **easy-to-use vials!**

IMPORTANT RISK INFORMATION

WARNING: RISKS WITH NEURAXIAL ADMINISTRATION; LIFE-THREATENING RESPIRATORY DEPRESSION; RISK OF ADDICTION, ABUSE, AND MISUSE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

See full prescribing information for complete boxed warning.

Single-dose neuraxial administration may result in acute or delayed respiratory depression up to 24 hours. Because of the risk of severe adverse reactions when MITIGO is administered by the epidural or intrathecal route of administration, patients must be observed in a fully equipped and staffed environment for at least 24 hours after the initial dose.

Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Patients must be observed in a fully equipped and staffed environment for at least 24 hours after each test dose and, as indicated, for the first several days after surgery.

MITIGO exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions.

Prolonged use of MITIGO during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

For additional Important Risk Information, including boxed warning, see enclosed Full Prescribing Information.

CHANGING THE COURSE OF CHRONIC PAIN MANAGEMENT STARTS WITH YOU

Approximately 20 percent of adults in the United States have experienced chronic pain.[6]

In 2018, nearly 6 out of 10 Americans were prescribed an opioid for chronic pain.[9] The International Association for the Study of Pain, however, recommends caution when prescribing opioids, and there has been increased emphasis on the use of nonopioid pain management.[12]

If chronic pain persists and opioids are necessary, intrathecal pain management will offer a traceable method of opioid delivery, unlike oral opioids, which have been associated with abuse, addiction and overdose.[7]

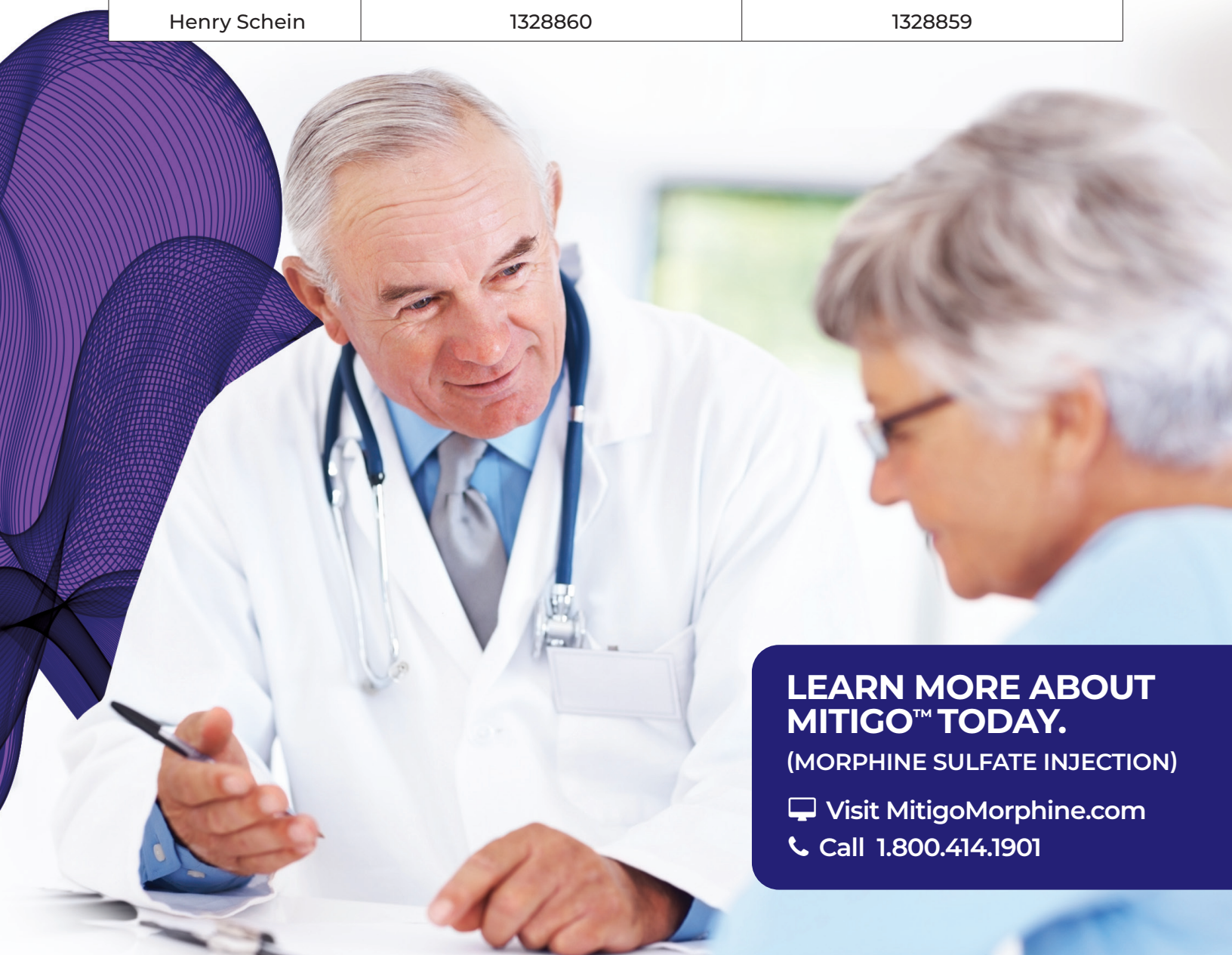
Approximate equianalgesic dosing of morphine by route of administration[10, 11]:

ROUTE OF ADMINISTRATION	RELATIVE POTENCY (MG)	RATIO
Oral	30	3:1 to intravenous
Intravenous	10	10:1 to epidural
Epidural	1	30:1 from oral to epidural
Intrathecal	0.1	300:1 from oral to intrathecal

REIMBURSEMENT COVERAGE

Reimbursement coverage for MITIGO™ is available using the following J-Code: J2274. The reimbursement hotline is +1-833-570-2159. MITIGO™ has been awarded multiple GPO contracts, and can be ordered through the major national wholesalers listed below.

VENDOR	MITIGO™ 10MG/ML 20ML CII NDC: 66794-160-02	MITIGO™ 25MG/ML 20ML CII NDC: 66794-162-02
AmerisourceBergen	10189461	10189462
Cardinal	5471388	5471396
McKesson	2450930	2450914
Morris & Dickson	410357	410555
Henry Schein	1328860	1328859



LEARN MORE ABOUT MITIGO™ TODAY.

(MORPHINE SULFATE INJECTION)

Visit MitigoMorphine.com

Call 1.800.414.1901

WHAT IS MITIGO™?
(MORPHINE SULFATE INJECTION)

MITIGO™ (morphine sulfate injection) is a USP and preservative-free injectable solution for intrathecal or epidural infusion for use in a continuous microinfusion device.[1] MITIGO™ is an opioid agonist, indicated only for management of intractable chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

INJECTION DOSAGE STRENGTHS

10 mg/mL (200 mg/20mL)[2]

25 mg/mL (500 mg/20mL)[2]

WHY CHOOSE MITIGO™?

FDA-APPROVED AND RECOMMENDED PRIOR TO USING COMPOUNDED DRUGS

- Off-label drug monotherapy or combination therapy, including using compounded morphine sulfate, is not recommended until FDA-approved drugs, like MITIGO™, are tried and failed or contraindicated.[2]
- If dilution of MITIGO™ is required, 0.9% Sodium Chloride Injection is recommended.[3] This does not make MITIGO™ a compounded drug, nor does it pose the same safety risks as compounding.

TRACEABLE METHOD OF OPIOID DISPENSING AND CONSUMPTION

- The administration of MITIGO™ provides a traceable and accountable method for dispensing and consumption of morphine sulfate. Individualized dosing is calculated by the clinician.
- This approach may help reduce the risk of deviating from an appropriate dosing regimen.

PACKAGED IN CONVENIENT, EASY-TO-USE VIALS, NOT GLASS AMPULES

- MITIGO™ is available in convenient, easy-to-use and preservative-free amber vials.[1]
- Glass particulates and bacterial contamination have long been recognized as potential hazards associated with the cracking of ampules,[4] and an estimated 62%-88% of sharps injuries can be prevented by using safer medical devices.[5]

1. Piramal Critical Care, Inc. MITIGO™ (morphine sulphate injection, USP-Preservative Free) [USPI]. 2017 [Cited 2018 Aug 15].
2. Medtronic, Inc. Intrathecal Drug Delivery for Chronic Pain Literature Review [Internet]. 2016 [Cited 2018 Aug 22]; Available from: https://www.medtronic.com/content/dam/medtronic-com/professional/documents/uc200805143d-tdd-chronic-pain-lit-review.pdf
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6. Defining the Prevalence of Chronic Pain in the United States [Internet]. 2018 [Cited 2019 June 18]; Available from: https://nccih.nih.gov/research/results/spotlight/Prevalence-of-Chronic-Pain
7. Opioids and the Treatment of Chronic Pain: Controversies, Current Status, and Future Directions [Internet]. 2008 [Cited 2019 June 18] Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2711509/
8. Prescription Opioid Data [Internet]. 2018 [Cited 2019 June 2019] Available from: https://www.cdc.gov/drugoverdose/data/prescribing.html
9. Pain Management and Opioid Misuse [Internet]. [Cited 2019 June 18] Available from: https://www.aafp.org/patient-care/public-health/pain-opioids.html
10. Paice JA. Intraspinal morphine for chronic pain: a retrospective, multicenter study. J Pain Symptom Manage. 1996;11:71-80
11. Medtronic Synchromed II Programmable Infusion System Clinical Reference Guide: Intrathecal Morphine for Pain Management. Minneapolis, MN: Medtronic, Inc.; May 2007
12. Nanna B. Finnerup, M.D. Nonnarcotic Methods of Pain Management. N Engl J Med 2019;380:2440-8. DOI: 10.1056/NEJMra1807061.

INDICATIONS AND USAGE

MITIGO (Morphine Sulfate Injection, USP – Preservative-free) is an opioid agonist for use in continuous microinfusion devices and indicated only for intrathecal or epidural infusion in the management of intractable chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Important Risk Information

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- **MITIGO exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions.**
- **Prolonged use of MITIGO during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.**
- **Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.**

CONTRAINDICATIONS

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting in absence of resuscitative equipment
- Concurrent use of monoamine oxidase inhibitors (MAOIs) or use of MAOIs within the last 14 days
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Hypersensitivity or intolerance to morphine

Neuraxial administration of MITIGO is contraindicated in patients with:

- Infection at the injection microinfusion site
- Concomitant anticoagulant therapy
- Uncontrolled bleeding diathesis

The presence of any other concomitant therapy or medical condition which would render epidural or intrathecal administration of medication especially hazardous

WARNINGS AND PRECAUTIONS

- Risk of Inflammatory Masses: Monitor patients receiving continuous infusion of MITIGO via indwelling intrathecal catheter for new signs or symptoms of neurologic impairment.
- Risk of Tolerance and Myoclonic Activity: Monitor patients for unusual acceleration of neuraxial morphine, which may cause myoclonic-like spasm of lower extremities. Detoxification may be required.
- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Monitor closely, particularly during initiation and titration.
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.
- Severe Hypotension: Monitor during dosage initiation and titration. Avoid use of MITIGO in patients with circulatory shock.
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of MITIGO in patients with impaired consciousness or coma.

ADVERSE REACTIONS

Most serious adverse reactions were respiratory depression, apnea, circulatory depression, respiratory arrest, shock, and cardiac arrest. Other common frequently observed adverse reactions include: sedation, lightheadedness, dizziness, nausea, vomiting, and constipation.

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm.
- Hepatic and Renal Impairment: May affect the metabolism and excretion of MITIGO.

For questions regarding Adverse Events, Product Monitoring, and Medical Inquiries for MITIGO™ (morphine sulfate injection, USP-Preservative-free), please call 888.525.8114 or email Global Medical Information at medical.information@piramal.com. You may also report this information to the FDA's MedWatch Reporting System by phone at 1.800.FDA.1088, by facsimile at 1.800.FDA.0178, or by mail using Form 3500 available at www.fda.gov/medwatch.

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Piramal Critical Care