MORPHINE SULFATE - morphine sulfate tablet, extended release
Novel Laboratories, Inc.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
These highlights do not include all the information needed to use MORPHINE SULFATE EXTENDED-RELEASE TABLETS safely and effectively. See full prescribing information for MORPHINE SULFATE EXTENDED-RELEASE TABLETS.

**INDICATIONS AND USAGE**
Morphine sulfate extended-release tablets are an opioid analgesic indicated for the management of moderate to severe acute and chronic pain in patients for whom an extended-release opioid is appropriate. See 17 for patient counseling information and Medication Guide.

**DOSAGE FORMS AND STRENGTHS**
Morphine sulfate extended-release tablets, for oral use, are available in the following strengths:
- 10 mg extended-release tablets
- 20 mg extended-release tablets
- 30 mg extended-release tablets
- 40 mg extended-release tablets
- 50 mg extended-release tablets
- 60 mg extended-release tablets
- 75 mg extended-release tablets
- 100 mg extended-release tablets

For opioid-naive and opioid non-tolerant patients, use the lowest effective dosage for the shortest duration possible. (2.1)

**CONTRAINDICATIONS**
Morphine sulfate extended-release tablets are contraindicated in patients who are hypersensitive to morphine sulfate or any of its ingredients, in patients with known or suspected gastrointestinal obstruction, in patients with known or suspected paralytic ileus, and in patients with known or suspected obstruction of the nasopharynx or the upper alimentary tract. (5.1)

**WARNINGS AND PRECAUTIONS**
- **Allergic Reactions:** Morphine sulfate extended-release tablets may cause hypersensitivity reactions, including anaphylaxis, in patients who are hypersensitive to morphine sulfate or any of its ingredients. (5.2)
- **Respiratory Depression:** The risk of respiratory depression is greater for elderly, cachectic, or debilitated patients; these patients should be monitored closely during initiation and titration. Avoid use in patients with circulatory shock, because of the risk of profound sedation, respiratory depression, coma, and death. (5.2)
- **Addiction, Abuse, and Misuse:** Morphine sulfate extended-release tablets may be abused or diverted for non-medical use. (5.4)
- **Opioid Tapering:** Patients dependent on opioids should be tapered off their opioid in a controlled and monitored setting. See 17 for a complete description of the tapering process and also additional information on tapering in patients with chronic pain and in patients dependent on opioids for pain. (5.4)
- **Withdrawal:** A withdrawal syndrome, which may be life-threatening, may occur in opioid-dependent patients following abrupt discontinuation. (5.5)
- **Central Nervous System Depression:** Patients with asthma, chronic obstructive pulmonary disease, or other chronic respiratory conditions should be monitored closely during initiation and titration. (5.11)
- **Children:** The safety and efficacy of morphine sulfate extended-release tablets in children less than 12 years of age have not been established. (8.6)
- **Geriatric Use:** Elderly patients are at greater risk of adverse reactions from opioids due to age-related changes in pharmacokinetics and pharmacodynamics. (8.7)
- **Hepatic Impairment:** In patients with renal impairment, hepatic impairment, and in patients with altered consciousness levels, use lower initial doses of morphine sulfate extended-release tablets. (8.8)
- **Pregnancy:** Morphine sulfate extended-release tablets may cause fetal harm when administered to pregnant women; (5.13)
- **Lactation:** Morphine is excreted into breast milk; use caution when breastfeeding. (8.9)
- **Children:** The safety and efficacy of morphine sulfate extended-release tablets in children less than 12 years of age have not been established. (8.9)

**ADVERSE REACTIONS**
The most common adverse reactions (>10%) are constipation, nausea, and sedation. See 17 for a complete list of adverse reactions. (6)

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Revised: 12/2019
Morphine sulfate extended-release tablets are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations [see Warnings and Precautions (5.12)], observe morphine sulfate extended-release tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

Morphine sulfate extended-release tablets are not indicated in an as-needed (prn) fashion.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

Morphine sulfate extended-release tablets should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.

Morphine sulfate extended-release tablets100 mg and 200 mg capsules, a single dose greater than 60 mg, or a total daily dose greater than 120 mg, are only for use in patients in whom tolerance to an opioid of comparable potency has been established.

Patients considered opioid tolerant are those taking, for one week or longer, at least 60 mg morphine per day, 25 mg extended-release fentanyl per day, 25 mg oral hydromorphone daily, 25 mg oral oxymorphone per day, 20 mg oral oxycodone per day, or an equivalent dose of another opioid.

Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals [see Warnings and Precautions (5)].

Initiate the dosing regimen for each patient individually, taking into account the patient's severity of pain, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse [see Warnings and Precautions (5)].

Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy and following dosage increases with morphine sulfate extended-release tablets and adjust the dosage accordingly [see Warnings and Precautions (5)].

Instruct patients to swallow morphine sulfate extended-release tablets whole (see Warnings and Precautions (5.1)). Crushing, chewing, or dissolving morphine sulfate extended-release tablets will result in controlled delivery of morphine and can lead to overdose or death [see Warnings and Precautions (5.1)].

Morphine sulfate extended-release tablets are administered orally once every 8 or 12 hours.

2.2 Initial Dosage

Use of morphine sulfate extended-release tablets as the First Opioid Analgesic (unprecedented patients)

Initiate treatment with morphine sulfate extended-release tablets with 15 mg tablets orally every 8 or 12 hours.

Use of morphine sulfate extended-release tablets in Patients who are Not Opioid Tolerant (optical non-tolerant patients)

The starting dose for patients who are not opioid tolerant is morphine sulfate extended-release tablets 15 mg orally every 12 hours.

Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression.

Conversion from Other Oral Morphine to Morphine Sulfate Extended-Release Tablets

Patients receiving other oral morphine formulations may be converted to morphine sulfate extended-release tablets by administering one-half of the patient's required dose of morphine sulfate extended-release tablets on an every-12-hour schedule or by administering one-third of the patient's daily requirement as morphine sulfate extended-release tablets on an every-8-hour schedule.

Conversion from Other Opioids to Morphine Sulfate Extended-Release Tablets

Discontinue all other around-the-clock opioids when morphine sulfate extended-release tablets therapy is initiated.

There are no established conversion ratios for conversion from other opioids to morphine sulfate extended-release tablets defined by clinical trials. Initial dosing using morphine sulfate extended-release tablets 5 mg orally every 6 to 12 hours is more suitable for switching from other opioids.

It is safer to underestimate a patient's 24-hour oral morphine dosage and provide a rescue medication (e.g., immediate-release opioid) than to overestimate the 24-hour oral morphine dosage and manage an overdose with naloxone. While useful tables of opioid equivalents are readily available, there is inter-patient variability in the potency of opioid drugs and opioid formulations. Close observation and frequent titration are warranted until pain management is stable under new opioid treatment.

Pharmacological cross-tolerance exists among opioids. Naloxone administration should be performed after converting patients to morphine sulfate extended-release tablets.

Conversion from Parenteral Morphine or Other Opioids (Parenteral or Oral) to Morphine Sulfate Extended-Release Tablets

When converting from parenteral morphine or other non-morphine opioids (parenteral or oral) to morphine sulfate extended-release tablets, consider the following general points:

Parenteral oral morphine ratio: Between 2 to 6 mg of oral morphine may be required to provide...
anesthesia equivalent to 1 mg of morphine. Typically, a dose of morphine that is approximately three times the previous daily parenteral morphine requirement is sufficient.

Opioids are not to be used in patients without prior exposure to opioids. Specific recommendations are not available because of a lack of systematic evidence for these types of analgesic substitutions. Published relative potency data are available, but such ratios are approximations. In general, begin with half of the estimated daily morphine requirement at the initial dose, managing moderate analgesia by supplementation with immediate-release morphine.

Conversion from Fentanyl to Morphine Sulfate Extended-Release Tablets

Close monitoring is of particular importance when converting methadone to other opioid agonists. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. Methadone has a long half-life and can accumulate in the plasma.

2.3 Titration and Maintenance of Therapy

Initially dose morphine sulfate extended-release tablets to achieve adequate analgesia and minimize adverse reactions. Continually evaluate patients receiving morphine sulfate extended-release tablets to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse, or misuse (see Warnings and Precautions (5.2)). Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initiation, titration, and discontinuation. During chronic therapy periodically reassess the continued need for the use of opioids.

Patients who experience breakthrough pain may require a dosage adjustment of morphine sulfate extended-release tablets, or may need concomitant medication with an appropriate dose of an analgesic that provides supplemental pain relief. If the patient develops signs or symptoms of withdrawal, the dose may be increased as necessary to manage withdrawal symptoms (see section 5.2, Withdrawal). If the patient is converted directly from another opioid to morphine sulfate extended-release tablets, start with the lowest possible dose, 15 mg every 12 hours, and gradually increase the dose as needed (see section 2.3, Titration and Maintenance of Therapy). If the patient is currently taking a central nervous system (CNS) depressant and the decision is made to convert from another opioid to morphine sulfate extended-release tablets, start with the lowest possible dose, 15 mg every 12 hours, and gradually increase the dose as needed (see section 2.3, Titration and Maintenance of Therapy).

2.4 Dosage Modifications with Concomitant Use of Central Nervous System Depressants

If the patient is currently taking a central nervous system (CNS) depressant and the decision is made to begin morphine sulfate extended-release tablets, start with the lowest possible dose, 15 mg every 12 hours, and increase as needed to manage breakthrough pain (see section 2.3, Titration and Maintenance of Therapy). If the patient is currently taking a central nervous system (CNS) depressant and the decision is made to convert from another opioid to morphine sulfate extended-release tablets, start with the lowest possible dose, 15 mg every 12 hours, and gradually increase the dose as needed (see section 2.3, Titration and Maintenance of Therapy).

2.5 Discontinuation of Morphine Sulfate Extended-Release Tablets

When a patient no longer requires therapy with morphine sulfate extended-release tablets, taper the dose gradually, by 25% to 33% every 2 to 4 days, while monitoring carefully for signs and symptoms of withdrawal. If the patient develops these signs or symptoms, raise the dose to the previous level and taper again by 25% to 33% every 2 to 4 days, if necessary. If the patient appears to be withdrawing, adjust the dose by raising it to the previous level and continue to taper (see section 5.2, Withdrawal).

3 DOSAGE FORMS AND STRENGTHS

Morphine Sulfate Extended-Release Tablets 15 mg
- Round, blue-colored, film-coated tablets, debossed “n 15” on one side and plain on the other side.
- Morphine Sulfate Extended-Release Tablets 30 mg
- Round, lavender-colored, film-coated tablets, debossed “n 30” on one side and plain on the other side.
- Morphine Sulfate Extended-Release Tablets 60 mg
- Round, orange-colored, film-coated tablets, debossed “n 60” on one side and plain on the other side.
- Morphine Sulfate Extended-Release Tablets 105 mg
- Round, green-colored, film-coated tablets, debossed “n 105” on one side and plain on the other side.
- Morphine Sulfate Extended-Release Tablets 200 mg
- Capsule-shaped, green-colored, film-coated tablets, debossed “n 200” on one side and plain on the other side.

3 CONTRAINDICATIONS

Morphine sulfate extended-release tablets are contraindicated in patients with:
- Significant respiratory depression (see Warnings and Precautions (5.2))
- Acute or severe bronchial asthma or uncontrolled status asthmaticus (see Warnings and Precautions (5.3))
- Concurrent use of monoamine oxidase inhibitors (MAOIs) or use of MAOIs within the last 14 days (see Warnings and Precautions (5.4, Drug Interactions (7)).
- Known sensitivity to morphine (see Warnings and Precautions (5.5), Hypersensitivity (5.6), and Precautions (5.2)).
- Patients with an opioid abuse or addiction (see Drug Abuse and Dependence (9)).

3 WARNINGS AND PRECAUTIONS

3.1 Addiction, Abuse, and Misuse

Morphine sulfate extended-release tablets contain morphine, a Schedule II controlled substance. As an opioid, morphine sulfate extended-release tablets produce effects in users similar to the effects of addiction, abuse, and misuse. Because extended-release products such as morphine sulfate extended-release tablets deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of morphine present (see Drug Abuse and Dependence (9)).

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed morphine sulfate extended-release tablets. Addiction can occur at recommended doses and if the drug is misused or abused. Patients who have a history of drug or alcohol addiction are at increased risk of misuse and abuse of these products (see Drug Abuse and Dependence (9)).

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing morphine sulfate extended-release tablets, and monitor all patients receiving morphine sulfate extended-release tablets for development of these behaviors and conditions. Risk is increased with a personal or family history of substance abuse (e.g., drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in patients with pain that requires opioid therapy. Patients at increased risk may be prescribed opioids such as morphine sulfate extended-release tablets, but use in such patients requires intensive counseling about the risks of proper use of morphine sulfate extended-release tablets along with intensive monitoring for signs of addiction, abuse, and misuse. Abuse or misuse of morphine sulfate extended-release tablets by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of morphine and can result in overdose and death (see Overdosage (10)).

3.2 Drug Interactions

Morphine sulfate extended-release tablets are contraindicated in patients with:
- Significant respiratory depression (see Warnings and Precautions (5.2))
- Acute or severe bronchial asthma or uncontrolled status asthmaticus (see Warnings and Precautions (5.3))
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Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing morphine sulfate extended-release tablets. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and pursuing the patient on the proper disposal of unused drug (see Patient Counseling Information (17)).

Commit local state professional licensing board or state controlled substances authority for information on controls to prevent and detect abuse or diversion of this product.
Morphine sulfate extended-release tablets may increase the risk of serious adverse reactions such as arrest, circulatory depression, hypotension, or shock. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Observational studies have demonstrated that concurrent use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs (e.g., non-benzodiazepine sedative/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, phenothiazines, or alcohol).

If the decision is made to prescribe a benzodiazepine or other CNS depressant concurrently with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant when morphine sulfate extended-release tablets is given concomitantly with other drugs that depress respiration (see Warnings and Precautions (5.1)). Alternatively, consider the use of non-opioids for these patients.

5.4 Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

- **Interaction with Monoamine Oxidase Inhibitors**: The morphine in morphine sulfate extended-release tablets may cause vasodilation that can further reduce cardiac output and blood pressure. These effects may be more pronounced in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics or altered drug response to vasodilators.

- **5.6 Interaction with Monoamine Oxidase Inhibitors**: Monitor patients closely, particularly when initiating and titrating morphine sulfate extended-release tablets in patients with impaired consciousness or coma. Monitor such patients for signs of hypotension after initiating or titrating the dose of morphine sulfate extended-release tablets. When administered with other drugs that depress respiration, the resultant CO2 retention can further increase intracranial pressure. Patients at greatest risk include those with head injuries, brain tumors, or other conditions that may be associated with increased intracranial pressure.

5.8 Severe Hypersensitivity

If a patient experiences an anaphylactic reaction or severe allergic reaction, discontinue morphine sulfate extended-release tablets and administer standard supportive care. If anaphylaxis persists, administer epinephrine. Make the patient supine and assist ventilation if necessary. Give oxygen and intravenous fluids. Carefully observe the patient for at least 5-7 days as symptoms may occur up to 14 days post-discharge.

5.9 Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

- **5.9.1 Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness**: If a patient develops or worsens acute or chronic obstructive pulmonary disease, discontinue morphine sulfate extended-release tablets and administer standard supportive care. Consider the use of opioid analgesics that do not cause respiratory depression.

5.10 Risks of Use in Patients with Gastrointestinal Conditions

- **5.10.1 Increased Risk of Gastrointestinal Obstruction**: Monitor patients for signs of hypotension after initiating or titrating the dose of morphine sulfate extended-release tablets. If a patient has a history of bowel obstruction, do not administer morphine sulfate extended-release tablets. In patients with paralytic ileus, the morphine in morphine sulfate extended-release tablets may cause spasm of the sphincter of Oddi. Monitor patients with biliary tract disease, including acute pancreatitis, or other gastrointestinal conditions for increased risk of decreased respiratory drive, and the resultant CO2 retention can further increase intracranial pressure.

6.1 Clinical Trial Experience

- **6.1 Clinical Trial Experience**: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Morphine sulfate extended-release tablets may increase the risk of serious adverse reaction such as those observed with other opioid analgesics, including respiratory depression, coma, respiratory arrest, circulatory depression, hypotension, or shock. See Overdose (10).

7.6 Full Prescribing Information

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Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly. The severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for signs, symptoms, and physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth. Consider altered placentation, increased risk of congenital anomalies, low birth weight, and other adverse outcomes. In the U.S. general population, the estimated background risk of congenital anomalies is 2.5%. Based on animal data, advise pregnant women of the potential risk in a fetus. The estimated background risk of major birth defects in unexposed pregnancies is approximately 2-4%. Some of these defects may be more prominent in ambulatory patients and in those not experiencing severe pain.

Table 1: Clinically Significant Drug Interactions with Morphine sulfate extended-release tablets

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Monoamine</td>
<td>Examples</td>
</tr>
<tr>
<td>Agonist</td>
<td>Example</td>
</tr>
<tr>
<td>Antagonist</td>
<td>Example</td>
</tr>
<tr>
<td>Inhibitors</td>
<td>Example</td>
</tr>
<tr>
<td>Other</td>
<td>Example</td>
</tr>
</tbody>
</table>

In clinical trials, the most common adverse reaction with morphine sulfate extended-release tablets were constipation, dizziness, sedation, nausea, vomiting, snoring, methaemoglobinemia, and pruritus. Other reported reactions included reduced libido and/or potency, headache, abdominal pain, constipation, dry mouth, dyspnea, dizziness, hallucinations, seizures, and respiratory depression. In clinical trials, morphine sulfate extended-release tablets were used in labor and delivery. In controlled labor and delivery trials involving more than 6000 parturients, the most frequent adverse reactions were hypotension, oversedation, sedation, pruritus, nausea, vomiting, and catheter blockage. In more than 5000 patients exposed to morphine sulfate extended-release tablets during labor, the most common adverse reactions were constipation, sedation, dizziness, pruritus, nausea, vomiting, respiratory depression, hypotension, oversedation, and pruritus.

In controlled trials of pregnancy, the most common adverse reaction with morphine sulfate extended-release tablets were constipation, dizziness, sedation, nausea, vomiting, snoring, methaemoglobinemia, and pruritus. Other reactions included reduced libido and/or potency, headache, abdominal pain, constipation, dry mouth, dyspnea, dizziness, hallucinations, seizures, and respiratory depression. In clinical trials, morphine sulfate extended-release tablets were used in labor and delivery. In controlled labor and delivery trials involving more than 6000 parturients, the most frequent adverse reactions were hypotension, oversedation, sedation, pruritus, nausea, vomiting, and catheter blockage. In more than 5000 patients exposed to morphine sulfate extended-release tablets during labor, the most common adverse reactions were constipation, sedation, dizziness, pruritus, nausea, vomiting, respiratory depression, hypotension, oversedation, and pruritus.

**Prolonged Use of Opioids**: Prolonged use of opioid analgesics during pregnancy may cause neonatal withdrawal syndrome. Risk Summary, 8.1 Pregnancy, 8.2 Post-Marketing Experience, 8.3 Pregnancy, 8.4 Lactation, 8.5 Nursing, 8.6 Pediatric Use, 8.7 Carcinogenesis, Mutagenesis, Impairment of Fertility, 12.3 Pregnancy, 12.4 Nursing,

**Adverse Reactions**: Adverse reactions were observed in clinical trials during the use of morphine sulfate extended-release tablets. These reactions were generally mild and transient. The most common adverse reactions observed were oversedation, respiratory depression, pruritus, nausea, vomiting, and sedation. Other reactions included constipation, dizziness, drowsiness, dry mouth, headache, insomnia, pruritus, and urinary retention. In general, adverse reactions were dose-related.

**Drug Interactions**: Drug interactions may occur with the use of morphine sulfate extended-release tablets. These interactions may increase the risk of adverse effects or decrease the efficacy of the drug. The concomitant use of cimetidine can potentiate morphine effects and increase risk of hypotension, respiratory depression, profound sedation, coma, and death. Morphine may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

**Warnings and Precautions**

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**Warnings and Precautions**

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Morphine is subject to misuse, addiction, and criminal diversion. Abuse similar to other opioids including fentanyl, hydrocodone, hydromorphone, methadone, and oxycodone may lead to overdose and death. Chronic use of opioids modifies reward systems and can lead to compulsive use and withdrawal symptoms when use is discontinued abruptly. These effects can be reversed by the use of other opioids at therapeutic doses. Risk of abuse includes use for non-medicine purposes, drug-seeking behavior, and use in combination with other CNS depressants, including alcohol, benzodiazepines, and tranquilizers.

9.1 Controlled Substance

Morphine sulfate extended-release tablets are controlled under the Controlled Substances Act and are subject to strict federal regulations. See “Guidance for Healthcare Providers: 2016 Minimum Data Set (MDS) for Unpaid Evaluations of Payers” (U.S. Department of Health and Human Services

9.2 Pregnancy

8.1 Lactation

Morphine is present in breast milk. Published lactation studies report variable concentrations of morphine in the milk of mothers who were not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of morphine sulfate extended-release tablets slowly while monitoring for signs of respiratory depression, sedation, and hypotension.

8.4 Pediatric Use

Clinical Considerations

The safety and effectiveness in pediatric patients below the age of 18 have not been established. See “Pediatric Use” (8.4) for information on the use of morphine sulfate extended-release tablets in pediatric patients.

8.5 Geriatric Use

In published animal studies, morphine administration adversely affected fertility and reproductive performance. Fetal and/or postnatal exposure to morphine in mice and rats has been shown to result in morphological changes in intracranial and neural brain and neuronal cell loss, alteration of a number of neuroanatomical and neurobehavioral systems, including opioid and non-opioid systems, and impairment in various learning and memory tests that appear to persist into adulthood. These studies were conducted with morphine treatment usually in the range of 4 to 20 mg/kg/day (0.7 to 3.2 times the HDD).

In a second study, decreased fetal body weights were reported following treatment of pregnant rabbits with increasing doses of morphine (10-56 mg/kg/day) during the pre-implantation period and 10 mg/kg/day (1.6 times the HDD) throughout the gestation period. No overt malformations were reported in either publication; although only limited endpoints were evaluated.

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8.3 Lactation

Risk Summary

Clinical Data

Infertility

As a result, chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible.

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8.2 Lactation

Risk Summary

Clinical Data

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The high drug content in extended-release formulations adds to the risk of adverse outcomes from abuse and overdose.

All patients treated with opioids require careful monitoring for signs of abuse and addiction, because use of opioid agonist products carries the risk of addiction to other appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, for its rewarding psychological or physiological effects. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develops after repeated substance use and includes a strong desire to take the drug, difficulties in controlling its use, persistent use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

"Drug-seeking" behavior is very common in persons with substance use disorders. Drug-seeking behavior includes emergency room visits near the outlet of a drug, refusal to undergo appropriate examination, testing, or referral, repeated "loss" of prescription, tampering with prescription and dispensing to provide pain or control for non-medical use (for other healthcare providers).

"Doctor shopping" (visiting multiple prescribers to obtain additional prescriptions) is common among drug abusers and people suffering from unattended addiction.

Prescription with interfering adequate pain relief could cause appropriate behavior in a patient with a poor understanding.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Healthcare providers should be aware that drug may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of overt addiction.

Morphine sulfate extended-release tablets, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Drug Specific Abuse of Morphine sulfate extended-release tablets.

Morphine sulfate extended-release tablets is for oral use only. Abuse of morphine sulfate extended-release tablets poses a risk of overdose and death. This risk is increased with concomitant abuse of morphine sulfate extended-release tablets with alcohol and other central nervous system depressants.

Taking oral, intranasal, crushed, or dissolved morphine sulfate extended-release tablets enhances drug release and increases the risk of overdose and death.

Due to the presence of tablets as one of the excipients in Morphine sulfate extended-release tablets, accidental ingestion of a single tablet may result in a fatal overdose, especially in children under 12 years of age and in individuals with severe hepatic impairment. The risk of fatal overdose increases with baseline hepatic dysfunction.

Abuse of Morphine sulfate extended-release tablets in an individual physically dependent on opioids may not occur to a clinically significant degree until several doses of tablets have been ingested. Tolerance may not occur to a clinically significant degree until several weeks of use. Tolerance may also develop to the respiratory depression and hypotension associated with opioid overdosage. The severity of the respiratory depression and hypotension may not be fully reversed with naloxone administration and may require prolonged ventilation with pressurized oxygen.

Due to the presence of talc as one of the excipients in morphine sulfate extended-release tablets, taking cut, broken, chewed, crushed, or dissolved morphine sulfate extended-release tablets enhances drug release and increases the risk of overdose and death.

Morphine sulfate extended-release tablets should not be abruptly discontinued (see Dosage and Administration (2.5). If morphine sulfate extended-release tablets is abruptly discontinued in a physically-dependent patient, withdrawal syndrome may occur. Some or all of the following can characterize this syndrome: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and malaise. Other signs and symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, atonic or spastic weakness, loss of appetite, nausea, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

In the absence of significant medical conditions, physicians should consider the following symptoms to be the manifestations of withdrawal syndrome: restlessness, anxiety, myalgia, joint pain, weakness, nausea, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

Abuse of Morphine sulfate extended-release tablets may also result in physical dependence and may exhibit respiratory difficulties and withdrawal signs (see Use in Specific Populations (8.2).)

10 OVERDOSAGE
Clinical Presentation
Acute overdosage with morphine sulfate extended-release tablets can be manifested by respiratory depression, somnolence progressing to respirations, skeletal muscle flaccidity, cold and clammy skin, and unresponsiveness. The clinical picture may resemble a morphine sulfate overdose, but clinical interpretation of the drug levels should be considered in evaluating the diagnosis of acute morphine sulfate overdose.

The physical signs of overdose include: pinpoint pupils, respiratory depression, sedation, and CNS depression progressing to respiratory arrest and death. Mortality is possible within minutes from respiratory depression.

Treatmet of Overdose

In cases of overdose, priorities are the re-establishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life support techniques.

The opioid antagonist naloxone or nalmefene, are specific antagonists to respiratory depression resulting from opioid overdosage. For clinically significant respiratory or circulatory depression secondary to morphine overdose, administration and opioid antagonists. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to morphine overdose.

Because the duration of reversal would be expected to be less than the duration of action of morphine in morphine sulfate extended-release tablets, carefully monitor the patient until spontaneous respiration is reliably reestablished. Morphine sulfate extended-release tablets will continue to release morphine and at the morphine load for 24 to 48 hours or longer following ingestion, necessitating prolonged monitoring. If the response to opioid antagonists is suboptimal or only brief in nature, administer additional antagonists as directed by the product's prescribing information.

In an individual physically dependent on opioids, administration of the usual dose of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal syndrome experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be initiated with care and by healthcare providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of overt addiction.

11 DESCRIPTION
Morphine sulfate extended-release tablets are for oral use and contain morphine sulfate, an opioid agonist.

Each tablet contains the following inactive ingredients: calcium carbonate, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, and titanium dioxide.

The tablets also contain: white to off-white crystalline powder. It has a solubility of 1 in 21 parts of water and 1 in 106 parts of alcohol, but is practically insoluble in chloroform or ether. The crystal water part measures the coefficient of the drug is 1.40 at physiological pH and the pH is 7.0 for the tertiary structures (from references at pH 7.4). Its molecular weight is 758.83 and its structural formula is:
12.1 Mechanism of Action

Morphine is a full opioid agonist and is relatively selective for the mu-opioid receptors, although it can bind to other opioid receptors at higher doses. The principal therapeutic action of morphine is analgesia. Like all full opioid agonists, there is a ceiling effect for analgesia with morphine. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug.

12.2 Pharmacokinetics

CNS Depressant/Alcohol Interaction

Additive pharmacodynamic effects may be expected when morphine sulfate extended-release tablets are used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

Effects on the Central Nervous System

Morphine produces respiratory depression by direct action on brainstem respiratory centers. The respiratory depression increases with increments in the brainstem respiratory centers that increases in carbon dioxide tension and electrical stimulation.

Morphine causes miosis, exertional tachycardia. Pupillary reactions are a sign of narcotic overdose but are no pathognomonic (e.g., intraocular hemorrhage or anterior ischaemia may produce similar findings). Marked mydriasis rather than miosis may be seen with hypoxia or overdose situations.

Effects on the Cardiovascular System

Morphine produces peripheral vasodilatation which may result in orthostatic hypotension or syncope. Manifestations of headodynamic release and peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or respiratory depression.

Effects on the Renal System

Morphine is demethylated. M6G has been shown to have analgesic activity but crosses the blood-brain barrier poorly, and there is some minor enterohepatic recycling.

The elimination of morphine occurs primarily as renal excretion of M3G and its effective half-life after oral administration is about 2 hours. Approximately 10% of the dose is excreted unchanged in urine. In some studies involving longer periods of plasma sampling, a longer terminal half-life of about 15 hours was reported. A small amount of the glucuronide conjugate is excreted in bile, and there is some minor enterohepatic recycling.

Effects on the Endocrine System

Effects on the Endocrine System

Morphine sulfate extended-release tablets are an extended-release tablet containing morphine sulfate. Morphine is released from morphine sulfate extended-release tablets faster and more slowly than from immediate-release oral preparations. Following oral administration of a given dose of morphine, the amount ultimately absorbed is essentially the same whether the source is morphine sulfate extended-release tablets or an immediate-release formulation. Because of pre-systemic elimination (i.e., metabolism in the liver and gut) and only about 40% of the administered dose reaches the central compartment.

The oral bioavailability of morphine is approximately 20 to 40%. When morphine sulfate extended-release tablets are given on a fixed dosing regimen, steady-state is achieved in about a day.

Food Effect

The effect of food upon the systemic bioavailability of morphine sulfate extended-release tablets has not been systematically evaluated for all strengths. One study, conducted with the 30 mg morphine sulfate extended-release tablets, showed no significant differences in Cmax and AUC (0-24h) values, not been systematically evaluated for all strengths. One study, conducted with the 30 mg morphine sulfate extended-release tablets, showed no significant differences in Cmax and AUC (0-24h) values,
Morphine pharmacokinetics are altered in patients with renal failure. The AUC is increased and clearance is decreased, and the metabolites, M6G and M3G, may accumulate to much higher plasma levels in patients with renal failure as compared to patients with normal renal function. Adequate studies of the pharmacokinetics of morphine in patients with severe renal impairment have not been conducted.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate the carcinogenic potential of morphine have not been conducted.

Mutagenesis

No formal immortal cell assays to assess the potential of morphine to impair fertility have been conducted.

No formal oncogenicity studies from the literature have demonstrated adverse effects on male fertility in the rat from exposure to morphine. One study in which male rats were administered morphine sulfate subchronically prior to mating (up to 30 mg/kg, twice daily) and during mating (20 mg/kg, twice daily) with untreated females, a number of adverse reproductive effects including reduction in total pregnancies and higher incidence of pseudopregnancies at 20 mg/kg (1.2 times the HDD) were reported.

Studies from the literature have also reported changes in hormonal levels in male rats (i.e., testosterone lowering) following treatment with morphine at 10 mg/kg or greater (1.6 times the HDD). Female rats that were administered morphine sulfate intraperitoneally prior to mating exhibited prolonged estrus cycles at 10 mg/kg/day (1.6 times the HDD).

Adrenal Insufficiency

Exposure of adult male rats to morphine has been associated with delayed sexual maturation and following mating to untreated females, smaller litters, increased pup mortality, and/or changes in reproductive outcome (i.e., death in adult offspring have been reported [estimated 5 times the plasma levels at the HDD]).

16 HOW SUPPLIED/STORAGE AND HANDLING

Morphine sulfate extended-release tablets 15 mg are round, blue-colored, film-coated tablets, debossed “N 200” on one side and plain on the other side. They are supplied as follows:

NDC 40032-541-01 opaque plastic bottles containing 100 tablets
NDC 40032-541-02 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 30 mg are round, lavender-colored, film-coated tablets, debossed “N 300” on one side and plain on the other side. They are supplied as follows:

NDC 40032-541-01 opaque plastic bottles containing 100 tablets
NDC 40032-541-04 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 60 mg are round, orange-colored, film-coated tablets, debossed “N 60” on one side and plain on the other side. They are supplied as follows:

NDC 40032-542-01 opaque plastic bottles containing 100 tablets
NDC 40032-542-02 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 90 mg are round, gray-colored, film-coated tablets, debossed “N 100” on one side and plain on the other side. They are supplied as follows:

NDC 40032-543-01 opaque plastic bottles containing 100 tablets
NDC 40032-543-03 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 120 mg are capsule-shaped, green-colored, film-coated tablets, debossed “N 150” on one side and plain on the other side. They are supplied as follows:

NDC 40032-544-01 opaque plastic bottles containing 100 tablets
NDC 40032-544-02 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 150 mg are round, gray-colored, film-coated tablets, debossed “N 150” on one side and plain on the other side. They are supplied as follows:

NDC 40032-544-01 opaque plastic bottles containing 100 tablets
NDC 40032-544-02 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 300 mg are capsule-shaped, green-colored, film-coated tablets, debossed “N 300” on one side and plain on the other side. They are supplied as follows:

NDC 40032-545-01 opaque plastic bottles containing 100 tablets
NDC 40032-545-02 opaque plastic bottles containing 500 tablets

Morphine sulfate extended-release tablets 500 mg are capsule-shaped, green-colored, film-coated tablets, debossed “N 500” on one side and plain on the other side. They are supplied as follows:

NDC 40032-546-01 opaque plastic bottles containing 100 tablets
NDC 40032-546-02 opaque plastic bottles containing 500 tablets

NDC 40032-547-01 opaque plastic bottles containing 100 tablets

NDC 40032-547-02 opaque plastic bottles containing 500 tablets

Interactions with Pseudopregnancy and Other CNS Depressants

Inform patients that the use of morphine sulfate extended-release tablets, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death [see Warnings and Precautions (5.2)]. Inform patients not to share morphine sulfate extended-release tablets with others and to take steps to protect morphine sulfate extended-release tablets from theft or misuse.

Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting morphine sulfate extended-release tablets or when the dosage is increased, and that it can occur even at recommended doses (see Warnings and Precautions (5.2)). Inform patients how to recognize respiratory depression and seek medical attention if breathing difficulties develop.

Accidental Ingestion

Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death [see Warnings and Precautions (5.2)]. Inform patients to take steps to store morphine sulfate extended-release tablets securely and to dispose of unused morphine sulfate extended-release tablets by flushing the tablets down the toilet.

Interactions with Pseudopregnancy and Other CNS Depressants

Inform patients and caregivers that potentially fatal additive effects may occur if morphine sulfate extended-release tablets are used with monoamine oxidase inhibitors or other CNS depressants, including alcohol, and to ask their healthcare provider for advice on the combined use of these medications unless supervised by a healthcare provider (see Warnings and Precautions (5.4), Drug Interactions (7)).

Serotonin Syndromes

Inform patients that the use of morphine sulfate extended-release tablets while using any drugs that inhibit monoamine oxidase (MAO) inhibitors may cause a potentially fatal serotonin syndrome resulting from concurrent administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and seek medical attention right away if symptoms develop. Inform patients to inform their physicians if they are taking, or plan to take serotonergic medications (see Drug Interactions (7)).

MAO Inhibition

Inform patients not to take morphine sulfate extended-release tablets while using any drugs that inhibit monoamine oxidase. Patients should not use MAOIs while taking morphine sulfate extended-release tablets (see Warnings and Precautions (5.4), Drug Interactions (7)).

Adrenocortical Insufficiency

Inform patients that overdosage could cause a rare but potentially life-threatening condition resulting from concurrent administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and seek medical attention right away if symptoms develop. Inform patients to inform their physicians if they are taking, or plan to take serotonergic medications (see Drug Interactions (7)).

Important Administration Instructions

Inform patients how to properly take morphine sulfate extended-release tablets, including:

1. Swallow morphine sulfate extended-release tablets whole (see Dosage and Administration (2.1))
2. Do not crush, chew, or dissolve the tablets (see Dosage and Administration (2.1))
3. Use morphine sulfate extended-release tablets exactly as prescribed to reduce the risk of life-threatening adverse reactions (e.g., respiratory depression) (see Warnings and Precautions (5.2)).
4. Do not discontinue morphine sulfate extended-release tablets without first discussing the need for a tapering regimen with the prescriber (see Dosage and Administration (2.1))

Reproduction

Inform patients that morphine sulfate extended-release tablets may cause orthostatic hypotension and syncope. Instruct patients how to recognize symptoms of low blood pressure and how to reduce the risk of serious consequences should hypotension occur (e.g., sit or lie down, carefully rise from a sitting or lying position) (see Warnings and Precautions (5.1))

Anaphylaxis

Inform patients that anaphylaxis has been reported with ingredients contained in morphine sulfate extended-release tablets. Advise patients how to recognize such a reaction and when to seek medical attention (see Contraindications (4), Adverse Reactions (6)).
**Medication Guide**

**Morphine Sulfate (mor' feen sul' fate) Extended-Release Tablets, CII**

**Use in Specific Populations (8.3)**

**Lactation**

Morphine sulfate passes into breast milk and may harm your baby. Inform female patients of reproductive potential that morphine sulfate extended-release tablets can cause withdrawal symptoms in your newborn baby that could be life-threatening. Inform female patients of reproductive potential that breastfeeding is not recommended during treatment with morphine sulfate extended-release tablets. Call your healthcare provider if the dose you are taking does not control your pain or if you experience problems with breastfeeding. Treatment with morphine sulfate extended-release tablets may cause decreased milk output and can put you at risk for opioid withdrawal in your newborn baby. Call your healthcare provider if you are breastfeeding while taking morphine sulfate extended-release tablets.

**Use in Specific Populations (8.3)**

**Infertility**

Inform male patients of reproductive potential that morphine sulfate extended-release tablets do not affect fertility and that fertility is reversible in both men and women. Inform male patients of reproductive potential that prolonged use of morphine sulfate extended-release tablets can impair the ability to perform such tasks until they know how they will react to the medication.

**Disposal of Unused Morphine Sulfate Extended-Release Tablets**

Do not take more than your prescribed dose. Take your prescribed dose every 8 to 12 hours, as directed by your healthcare provider. Do not change your dose. Take morphine sulfate extended-release tablets exactly as prescribed by your healthcare provider. Do not stop taking morphine sulfate extended-release tablets without talking to your healthcare provider. Do not share or give your morphine sulfate extended-release tablets to anyone else. Morphine sulfate extended-release tablets are made to dissolve slowly in your intestines.

**Before you start taking this medicine**

**Driving or Operating Heavy Machinery**

Inform patients that morphine sulfate extended-release tablets may impair the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication.

**When to take your medicine**

**When taking morphine sulfate extended-release tablets:**

- Take your morphine sulfate extended-release tablets by mouth. Do not confuse morphine sulfate extended-release tablets with other drugs that contain morphine, such as prescription cough and cold medicines or other prescription pain medicines.
- Take your morphine sulfate extended-release tablets exactly as prescribed by your healthcare provider. Do not change your dose or take your medicine more often or for a longer time than prescribed by your healthcare provider. Do not stop taking your medicine suddenly or change your dose without checking with your healthcare provider. Slowly decreasing your dose may help to prevent withdrawal symptoms.
- Do not take more than your prescribed dose. Take your prescribed dose every 8 to 12 hours, as directed by your healthcare provider. Do not change your dose. Take morphine sulfate extended-release tablets exactly as prescribed by your healthcare provider. Do not stop taking morphine sulfate extended-release tablets without talking to your healthcare provider. Do not share or give your morphine sulfate extended-release tablets to anyone else. Morphine sulfate extended-release tablets are made to dissolve slowly in your intestines.
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### Packaging

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### Marketing Information

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### Product Information

#### MORPHINE SULFATE

**morphine sulfate tablet, extended release**

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### Active Ingredient/Active Moiety

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### Inactive Ingredients

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</thead>
<tbody>
<tr>
<td>HYDROXYETHYL CELLULOSE (4000 MPA.S AT 1%)</td>
<td></td>
</tr>
<tr>
<td>HYDROXYPROPYL CELLULOSE, LOW SUBSTITUTED</td>
<td></td>
</tr>
<tr>
<td>HYPROMELLOSE 2208 (100 MPA.S)</td>
<td></td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td></td>
</tr>
<tr>
<td>SILICON DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>POLYVINYL ALCOHOL, UNSPECIFIED</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL 3350</td>
<td></td>
</tr>
<tr>
<td>TALC</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>D&amp;C RED NO. 27</td>
<td></td>
</tr>
<tr>
<td>FD&amp;C BLUE NO. 1</td>
<td></td>
</tr>
</tbody>
</table>

### Product Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Flavor</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>PURPLE (lavender)</td>
<td>ROUND</td>
<td>7mm</td>
<td>no score</td>
<td>n;30</td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>ANDA203602</td>
<td>12/16/2015</td>
<td></td>
</tr>
</tbody>
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### Product Information

#### MORPHINE SULFATE

**morphine sulfate tablet, extended release**

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Item Code (Source)</th>
<th>DEA Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>NDC:40032-542-01</td>
<td>CII</td>
</tr>
</tbody>
</table>

### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>MORPHINE SULFATE</td>
<td>(UNII: X3P646A2J0)</td>
<td>60 mg</td>
</tr>
</tbody>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYDROXYETHYL CELLULOSE (4000 MPA.S AT 1%)</td>
<td></td>
</tr>
<tr>
<td>HYDROXYPROPYL CELLULOSE, LOW SUBSTITUTED</td>
<td></td>
</tr>
<tr>
<td>HYPROMELLOSE 2208 (100 MPA.S)</td>
<td></td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td></td>
</tr>
<tr>
<td>SILICON DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>POLYVINYL ALCOHOL, UNSPECIFIED</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL 3350</td>
<td></td>
</tr>
<tr>
<td>TALC</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>D&amp;C YELLOW NO. 10</td>
<td></td>
</tr>
<tr>
<td>FD&amp;C YELLOW NO. 6</td>
<td></td>
</tr>
</tbody>
</table>

### Product Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Flavor</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORANGE</td>
<td>ROUND</td>
<td>7mm</td>
<td></td>
<td>n;60</td>
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</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
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<tr>
<td>ANDA</td>
<td>ANDA203602</td>
<td>12/16/2015</td>
<td></td>
</tr>
</tbody>
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### Product Information

#### MORPHINE SULFATE

**morphine sulfate tablet, extended release**

<table>
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<tr>
<th>Product Type</th>
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<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>NDC:40032-543-01</td>
<td>CII</td>
</tr>
</tbody>
</table>

### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>MORPHINE SULFATE</td>
<td>(UNII: X3P646A2J0)</td>
<td>100 mg</td>
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</tbody>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYDROXYETHYL CELLULOSE (4000 MPA.S AT 1%)</td>
<td></td>
</tr>
<tr>
<td>HYDROXYPROPYL CELLULOSE, LOW SUBSTITUTED</td>
<td></td>
</tr>
</tbody>
</table>

### Product Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Flavor</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (scored)</td>
<td>ROUND</td>
<td>7mm</td>
<td></td>
<td>n</td>
</tr>
</tbody>
</table>
**Product Information**

**Product Type**: HUMAN PRESCRIPTION DRUG  
**Route of Administration**: ORAL  
**DEA Schedule**: CII  

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>MORPHINE SULFATE (UNII: X3P646A2J0)</td>
<td>(MORPHINE - UNII:76I7G6D29C)</td>
<td>200 mg</td>
</tr>
</tbody>
</table>

**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
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**Product Characteristics**

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<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Flavor</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>GREEN</td>
<td>CAPSULE</td>
<td>14mm</td>
<td></td>
<td>n;200</td>
</tr>
</tbody>
</table>

**Packaging**

<table>
<thead>
<tr>
<th>Code</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:40032-544-01</td>
<td>100 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>12/16/2015</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NDC:40032-544-05</td>
<td>500 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>12/16/2015</td>
<td></td>
</tr>
</tbody>
</table>

**Marketing Information**

**Labeler** - Novel Laboratories, Inc. (793518643)

**Registrant** - Novel Laboratories, Inc. (793518643)

**Establishment**

Revised: 12/2019  
Novel Laboratories, Inc.