Press Release

Daiichi Sankyo, Inc. and Inspirion Delivery Sciences LLC Announce U.S. Availability of MorphaBond™ ER (morphine sulfate) Extended-Release Tablets CII, an Abuse-Deterrent Formulation

Basking Ridge, NJ and Morristown, NJ (November 3, 2017) – Daiichi Sankyo, Inc. and Inspirion Delivery Sciences LLC (Inspirion) announced today that MorphaBond™ ER (morphine sulfate) extended-release tablets, CII is now available throughout the United States. MorphaBond ER is an abuse-deterrent opioid agonist 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. However, abuse by intranasal, intravenous, and oral routes is still possible. MorphaBond ER is available in four dosage strengths: 15, 30, 60 and 100 mg.

"Daiichi Sankyo is deeply committed to responsibly bringing medicines to patients in pain and to being a part of the solution to the abuse of controlled substances," said Ken Keller, President, Administrative and Commercial, Daiichi Sankyo, Inc. "We are pleased to provide a treatment option that allows healthcare professionals to manage their patients' chronic pain in a form that is expected to reduce the potential for intranasal and intravenous abuse."

MorphaBond ER is the only single-agent, extended-release morphine that is approved by the U.S. Food and Drug Administration with labeling that describes its potential to deter abuse by both intranasal and intravenous administration. However, abuse by intranasal, intravenous and oral routes is still possible. MorphaBond ER is formulated with SentryBond™, a patent-protected technology that uses multiple overlapping abuse-deterrent barriers designed with the intent to make the tablet more difficult to adulterate for misuse and abuse while retaining its extended-release properties even if manipulated.

"Abuse-deterrent opioid formulations are an important part of a comprehensive approach to addressing the opioid crisis," said Inspirion's CEO, Stefan Aigner, MD, CFA. "We're pleased to see our licensing partners at Daiichi Sankyo, a company with a strong commitment to responsible marketing of prescription medications, bring MorphaBond ER to market."

PP-US-MB-0382
11/17

Daiichi Sankyo will lead the commercialization of MorphaBond ER in collaboration with Inspirion as part of a previously-announced License Agreement.

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, physicians should reserve MorphaBond ER 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. MorphaBond ER is not indicated as an as-needed (prn) analgesic.

MorphaBond ER should be prescribed only by healthcare professionals who are knowledgeable in the use of opioids for the management of chronic pain.

To reflect Daiichi Sankyo Inc.'s commitment to bringing innovative medicines to patients in pain in a responsible manner and contribute to the larger effort of preventing controlled substance abuse, misuse, addiction and overdose, the Company has established *Commitments in Pain Care*. The program is designed to engage and educate key stakeholders around responsible pain management, including patients and caregivers, healthcare professionals, advocates, employees and others. *Commitments in Pain Care* underscores the Company's dedication to undertaking the marketing and distribution of its pain medicines, as well as engagement with stakeholders, with a great sense of responsibility and professionalism. To learn more about *Commitments in Pain Care*, please visit: www.CommitmentsInPainCare.com.

Please see Important Safety Information, including BOXED WARNING and Indication below.

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

MORPHABOND™ ER (morphine sulfate) extended-release tablets, for oral use, CII is an opioid agonist 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, reserve MORPHABOND ER 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.

MORPHABOND ER is not indicated as an as-needed (prn) analgesic.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: ADDICTION, ABUSE, and MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

MORPHABOND™ ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing MORPHABOND ER, and monitor all patients regularly for the development of these behaviors or conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of MORPHABOND ER. Monitor for respiratory depression, especially during initiation of MORPHABOND ER or following a dose increase. Instruct patients to swallow MORPHABOND ER tablets whole; crushing, chewing, or dissolving MORPHABOND ER tablets can cause rapid release and absorption of a potentially fatal dose of morphine.

Accidental Ingestion

Accidental ingestion of even one dose of MORPHABOND ER, especially by children, can result in a fatal overdose of morphine.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of MORPHABOND ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants

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 of MORPHABOND ER and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

CONTRAINDICATIONS

MORPHABOND ER is contraindicated in patients with: significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment; concurrent use of monoamine oxidase inhibitors (MAOIs) or use MAOIs within the last 14 days; known or suspected gastrointestinal obstruction, including paralytic ileus; and hypersensitivity (e.g., anaphylaxis) to morphine.

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse

MORPHABOND ER contains morphine, a Schedule II controlled substance, and thus exposes its users to the risks of addiction, abuse, and misuse. As extended-release products such as MORPHABOND ER 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. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed MORPHABOND ER and in those who obtain the drug illicitly. Addiction can occur at recommended doses and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing MORPHABOND ER, and monitor all patients receiving MORPHABOND ER for development of these behaviors or conditions. Patients at increased risk may be prescribed extended-release opioid formulations such as MORPHABOND ER, but use in such patients necessitates intensive counseling about the risks of proper use of MORPHABOND ER along with intensive monitoring for signs of addiction, abuse, and misuse.

Abuse or misuse of MORPHABOND ER by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of morphine and can result in overdose and death.

Opioid agonists such as MORPHABOND ER are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing MORPHABOND ER. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper storage and disposal of unused drug.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended, and if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status. Carbon dioxide (CO2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of MORPHABOND ER, the risk is greatest during the initiation of therapy or following a dosage increase. Closely monitor patients for respiratory depression, especially within the first 24-72 hours of initiating therapy with and following dosage increases with MORPHABOND ER.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of MORPHABOND ER during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of MORPHABOND ER with benzodiazepines or other CNS system depressants (eg, non-benzodiazepine sedatives/hypnotics, tranquilizers, muscle relaxants, general anesthetics, anxiolytics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly 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 than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response.

Advise both patients and caregivers about the risks of respiratory depression and sedation when MORPHABOND ER is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs.

Life -Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of MORPHABOND ER in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: MORPHABOND ER-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of MORPHABOND ER.

Elderly, Cachectic, or Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients. Monitor such patients closely, particularly when initiating and titrating MORPHABOND ER and when MORPHABOND ER is given concomitantly with other drugs that depress respiration. Alternatively, consider the use of non-opioid analgesics in these patients.

Interaction with Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors (MAOIs) may potentiate the effects of morphine, including respiratory depression, coma, and confusion. MORPHABOND ER should not be used in patients taking MAOIs or within 14 days of stopping such treatment.

Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Severe Hypotension

MORPHABOND ER may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension after initiating or titrating the dosage of MORPHABOND ER. In patients with circulatory shock, MORPHABOND ER may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of MORPHABOND ER in patients with circulatory shock.

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

In patients who may be susceptible to the intracranial effects of CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), MORPHABOND ER may reduce respiratory drive, and the resultant CO2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with MORPHABOND ER. Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of MORPHABOND ER in patients with impaired consciousness or coma.

Risks of Use in Patients with Gastrointestinal Conditions

MORPHABOND ER is contraindicated in patients with gastrointestinal obstruction, including paralytic ileus. The morphine in MORPHABOND ER may cause spasm of the sphincter of Oddi. Opioids may cause increases in the serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

Increased Risk of Seizures in Patients with Seizure Disorders

The morphine in MORPHABOND ER may increase the frequency of seizures in patients with seizure disorders, and may increase the risk of seizures occurring in other clinical settings associated with seizures.

Withdrawal

Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who have received or are receiving a course of therapy with a full opioid agonist analgesic, including MORPHABOND ER. In these patients, mixed agonists/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms. When discontinuing MORPHABOND ER, gradually taper the dosage. Do not abruptly discontinue MORPHABOND ER.

Risks of Driving and Operating Machinery

MORPHABOND ER may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of MORPHABOND ER and know how they will react to the medication.

Adverse Reactions

In clinical trials, the most common adverse reactions with morphine sulfate extended-release were constipation, dizziness, sedation, nausea, vomiting, sweating, dysphoria, and euphoric mood.

Drug Interactions

- Concomitant use of benzodiazepines or other CNS depressants can increase the risk of respiratory depression, profound sedation, coma and death.
- The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
- Mixed agonist/antagonist and partial agonist opioid analgesics may reduce the analgesic effect of MORPHABOND ER and/or may precipitate withdrawal symptoms.

- Morphine may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
- MAOI interactions with opioids may manifest as serotonin syndrome or opioid toxicity.
- The concomitant use of cimetidine can potentiate morphine effects and increase risk of hypotension, respiratory depression, profound sedation, coma, and death.
- Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
- The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
- The concomitant use of PGP-inhibitors can increase the exposure to morphine by about two-fold and can increase risk of hypotension, respiratory depression, profound sedation, coma, and death.

These are not all the possible side effects of MORPHABOND ER. Please see Full Prescribing Information, including **BOXED WARNINGS**, and Medication Guide. Patients and health care providers may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About SentryBond™

The SentryBond technology platform combines inactive excipients with active pharmaceutical ingredients (API) in a tablet that uses multiple overlapping barriers to frustrate abuse for various methods of manipulation and routes of administration. SentryBond is designed to maintain the extended release properties of MorphaBond ER, even if manipulated. SentryBond technology imparts its abuse-deterrent characteristics via physical and chemical methods, without the use of antagonist or aversive agents. SentryBond technology is covered by an issued U.S. patent, with additional U.S. and global patent applications pending.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit:

www.daiichisankyo.com. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.

About Inspirion Delivery Sciences

Inspirion Delivery Sciences LLC is a privately held specialty pharmaceutical company that is dedicated to advancing solutions in the field of prescription drug abuse deterrence through continued innovation. Recognizing the serious unmet public health need to combat the escalating crisis of prescription opioid abuse and misuse, Inspirion began pioneering the development of novel abuse-deterrent technologies. For more information, visit the Company's website at www.inspirionds.com.

Contact

Alyssa Dargento
Daiichi Sankyo, Inc.
adargento@dsi.com
908-992-6632

PP-US-MB-0382
11/17