



## FDA APPROVES LAZANDA® - FIRST FENTANYL NASAL SPRAY - FOR THE MANAGEMENT OF BREAKTHROUGH PAIN IN CANCER PATIENTS

On Average, More than Half of Patients with Cancer Experience.

Debilitating Breakthrough Pain.

**Reading, England and Bedminster, NJ, 30 June 2011:** Archimedes Pharma Ltd., and its subsidiary, Archimedes Pharma U.S. Inc., today announced that the U.S. Food and Drug Administration (FDA) has approved Lazanda® (fentanyl) nasal spray for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Lazanda marks the first FDA product approval for Archimedes Pharma. Lazanda is marketed as PecFent® (fentanyl pectin nasal spray) in Europe, where it is presently available in five countries.

"Lazanda is an important new option for patients with cancer who experience excruciating breakthrough pain," says Jeffrey H. Buchalter, chief executive officer of Archimedes Pharma. "Lazanda, which uses our patented PecSys® drug delivery system, is designed to deliver medicine in a rapid, but controlled manner, and provides patients with an effective alternative to manage their breakthrough pain."

Breakthrough pain in cancer (BTPc) is an intense, sudden pain that is often unpredictable and debilitating and occurs despite otherwise appropriate opioid therapy for background pain. BTPc has a different profile from background pain. BTPc often has high intensity, a rapid onset, usually reaching maximum intensity within five minutes, and a short duration, lasting between 30 and 60 minutes per episode. On average, BTPc affects more than half of patients with cancer and often interferes with patients' health and ability to engage in daily living activities.

"As the first fentanyl nasal spray in the U.S., Lazanda provides a new approach to managing the often debilitating and inadequately-treated episodes of breakthrough pain that many patients with cancer experience," said Donald Taylor, M.D., director at Taylor Research LLC., and clinical investigator for Lazanda. "Current treatment options typically utilize short-acting oral opioid medications that cannot provide pain relief with an onset of action or duration of effect that matches the time course of a BTPc episode. Lazanda's rapid and controlled availability is a much better match for the nature of an episode of breakthrough pain, giving physicians a new and powerful tool for treating cancer breakthrough pain."

Lazanda will be available in the second half of this year through a Risk Evaluation and Mitigation Strategy (REMS) program, which is intended to minimize the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors. Under the Lazanda® REMS program, pharmacies, distributors, and health care professionals who prescribe to outpatients are required to enroll in the program to dispense, distribute, and prescribe Lazanda.

"We fully support the FDA mandate to implement a REMS program for Lazanda as an important way to provide patients, healthcare providers, and pharmacists with the information they need about the appropriate and safe use of Lazanda," said Buchalter. "Archimedes Pharma looks forward to working closely with health care professionals to ensure safe and consistent access to Lazanda for the patients who are seeking relief from unbearable episodes of breakthrough pain in cancer."

## About Lazanda® (fentanyl) nasal spray.

Lazanda contains fentanyl, which is a Schedule II controlled substance, and uses Archimedes Pharma's patented drug delivery system, PecSys®.

Lazanda, incorporating PecSys technology, delivers fentanyl in a rapid, but controlled manner and is designed to deliver a fine mist spray to a mucus membrane, in this case the nasal membrane. Each spray of Lazanda forms a gel when it contacts the nasal mucosa; the active ingredient is then rapidly absorbed across the mucus membrane and directly into the blood stream.

The efficacy of Lazanda for the management of breakthrough pain in adult cancer patients was established in a double-blind, placebo-controlled clinical study in which Lazanda showed a statistically significant improvement compared with placebo on the primary endpoint, the sum of the pain intensity difference at 30 minutes (SPID30). More than 500 patients evaluated in the clinical trial program (which included three phase III clinical trials) contributed to the understanding of the tolerability and safety profile of Lazanda. The most common adverse events associated with Lazanda were consistent with opioid treatment and included vomiting, nausea, pyrexia (fever), and constipation.

### IMPORTANT SAFETY INFORMATION.

#### WARNINGS: POTENTIAL FOR ABUSE AND IMPORTANCE OF PROPER PATIENT SELECTION.

**Lazanda contains fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics.** Lazanda can be abused in a manner similar to other opioid agonists, legal or illicit. Consider the potential for abuse when prescribing or dispensing Lazanda in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Schedule II opioid substances, which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone, have the highest potential for abuse and risk of fatal overdose due to respiratory depression. Serious adverse events, including deaths, in patients treated with other oral transmucosal fentanyl products have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of Lazanda for any other fentanyl product may result in fatal overdose.

**Lazanda is indicated only for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.** Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/day, 25 mcg of transdermal fentanyl/hour, 30 mg of oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for one week or longer.

**Lazanda is contraindicated in opioid non-tolerant patients** and is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products. When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl product to Lazanda. Patients beginning treatment with Lazanda must begin with titration from the 100 mcg dose. (see Dosage and Administration)

When dispensing, do not substitute a Lazanda prescription for any other fentanyl product. Substantial differences exist in the pharmacokinetics of Lazanda compared to other fentanyl products that could result in clinically important differences in the rate and extent of absorption of fentanyl and could result in fatal overdose.

Special care must be used when dosing with Lazanda. If the breakthrough pain episode is not relieved, patients must wait at least 2 hours before taking another dose of Lazanda. (see Dosage and Administration)

Lazanda is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that Lazanda contains a medicine in an amount that can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. Lazanda must be kept out of the reach of children at all times. (see Patient/Caregiver Instructions)

The concomitant use of Lazanda with cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

Because of the risk for misuse, abuse, addiction, and overdose, Lazanda is available only through a restricted program, required by the Food and Drug Administration, called the Lazanda REMS (Risk Evaluation and Mitigation Strategy) program. Under the Lazanda REMS program, healthcare professionals who prescribe to outpatients, pharmacies, and distributors must enroll in the program to prescribe, receive, dispense, and distribute Lazanda, respectively. [see Warnings and Precautions]. Further information is available at [www.LazandaREMS.com](http://www.LazandaREMS.com) or by calling 1-855-841-4234.

### Contraindications.

- Lazanda is contraindicated in the management of pain in opioid non-tolerant patients, because life-threatening hypoventilation could occur at any dose in patients not already taking around-the-clock opioid therapy.
- Lazanda is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room.
- Lazanda is contraindicated in patients with known intolerance or hypersensitivity to any of its components or the drug fentanyl. Anaphylaxis and hypersensitivity have been reported in association with the use of other oral transmucosal fentanyl products.

### Warnings And Precautions.

- Patients must not be converted to Lazanda from other fentanyl products because it is not equivalent to other fentanyl products on a mcg per mcg basis, and such substitution could result in a fatal overdose; do not substitute Lazanda for another fentanyl product when being dispensed.
- Serious or fatal respiratory depression can occur even at recommended doses in patients using Lazanda. Respiratory depression is more likely to occur in patients with underlying respiratory disorders and elderly or debilitated patients, in opioid non-tolerant patients, or when opioids are given in conjunction with other drugs that depress respiration.
- Lazanda could be fatal to individuals for whom it is not prescribed and for those who are not opioid tolerant.
- Patients and their caregivers must be instructed that Lazanda contains medicine in an amount that could be fatal to a child and thus must keep both used and unused bottles in their child-resistant container and out of the reach of children at all times and all residual fentanyl must be emptied before disposal.
- Patients on concomitant CNS depressants must be monitored for a change in opioid effects and adjust the dose of Lazanda.
- Concomitant use with potent cytochrome P450 3A4 inhibitors may increase depressant effects including hypoventilation, hypotension, and profound sedation. Monitor and consider dosage adjustment if warranted.
- Cautiously adjust the dose of Lazanda in patients with chronic obstructive pulmonary disease or preexisting medical conditions predisposing them to respiratory depression.
- Administer Lazanda with extreme caution in patients particularly susceptible to intracranial effects of CO<sub>2</sub> retention, such as those with evidence of increased intracranial pressure or impaired consciousness.
- Patients taking Lazanda must be warned that opioid analgesics impair the mental and/or physical ability required for the performance of potentially dangerous tasks (e.g., driving a car or operating machinery).
- Use Lazanda with caution in patients with bradyarrhythmias.
- Lazanda is not recommended for use in patients who have received MAO inhibitors within 14 days, because severe and unpredictable potentiation by MAO inhibitors has been reported with opioid analgesics.

### Drug Interactions.

- Potential interactions may occur when Lazanda is given concurrently with agents that affect CYP3A4 activity. Monitor patients for signs of opioid toxicity who begin therapy with, or increase the dose of, inhibitors of CYP3A4 or stop therapy with, or decrease the dose of, inducers of CYP3A4. Monitor patients who are taking vasoconstrictive nasal agents to treat allergic rhinitis for potentially impaired pain management.

### Use In Specific Populations.

- Safety and efficacy below 18 years of age have not been established.
- There are no adequate and well-controlled studies of Lazanda in pregnant women. Do not use Lazanda during labor and delivery or in women who are nursing.
- Lazanda should be administered with caution in patients with impaired renal or hepatic function and titrated to clinical effect in patients with severe renal or hepatic disease.

**Adverse Reactions.**

- Most common adverse events during titration (frequency  $\geq 5\%$ ): nausea, vomiting, and dizziness.
- Most common adverse events during maintenance (frequency  $\geq 5\%$ ): vomiting, nausea, pyrexia, and constipation.
- Please see the accompanying full Prescribing Information including boxed warning. For more information please see [www.lazanda.com](http://www.lazanda.com).

**About Archimedes Pharma.**

Archimedes Pharma is an international specialty pharmaceutical company providing novel and advanced treatments to address unmet needs for people living with serious or life-threatening chronic and debilitating illnesses. Archimedes Pharma markets a diverse portfolio of speciality products and has operations in the U.S. and throughout Europe. Archimedes Pharma U.S. Inc. is a subsidiary of Archimedes Pharma Ltd. For more information, please visit: [www.archimedespharma.com](http://www.archimedespharma.com).

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