Important Prescribing Information for [N]ABSTRAL® - a Fentanyl Citrate Sublingual Tablet Approved by Health Canada on February 17, 2011

April 2011

Important Safety Information

- Patient Selection: ABSTRAL® is indicated only in adult cancer patients with breakthrough pain who are already receiving, and who are tolerant to, opioid therapy for their persistent baseline cancer pain.
- ABSTRAL® is contraindicated for use in opioid non-tolerant patients including those using opioids intermittently, on an as needed basis.
- ABSTRAL® is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room.
- ABSTRAL® should not be used in patients who are receiving partial opioid agonists such as buprenorphine or agents with some opioid effects such as tramadol, as the safety of their concomitant use has not been established.
- ABSTRAL® is not interchangeable and should never be switched on a mcg per mcg basis with any other fentanyl medication. The substitution of ABSTRAL® for any other fentanyl product on a mcg per mcg basis may result in fatal overdose.
- Regardless of the dose of baseline opioid or the dose of any breakthrough pain medication the patient may have taken previously, ABSTRAL® treatment should **always** be started at the lowest dose of 100 mcg and titrated incrementally.
- ABSTRAL® single doses should be separated by at least 2 hours.
- ABSTRAL® should only be used once per breakthrough cancer pain episode.

Dear Healthcare Professional:

Paladin Labs Inc. is introducing ABSTRAL®, a unique formulation of fentanyl.

ABSTRAL® (fentanyl citrate sublingual tablet) is indicated for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their persistent baseline cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg/day morphine equivalents for a week or longer.

ABSTRAL® contains fentanyl, an opioid agonist controlled substance, with an abuse liability similar to other opioid analgesics. This should be considered when prescribing or dispensing ABSTRAL® in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

ABSTRAL® must not be used in opioid non-tolerant patients as there is an increased risk of life-threatening respiratory depression and deaths have occurred under these circumstances.

ABSTRAL® is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room.

ABSTRAL® is contraindicated in patients with severe respiratory depression or severe obstructive lung disease, and is also contraindicated in patients with known intolerance or hypersensitivity to fentanyl or to any ingredient in the formulation or component of the container.

When prescribing, do not switch patients from any other fentanyl product to ABSTRAL® as ABSTRAL® is not equivalent on a mcg per mcg basis with any other fentanyl product.

All patients MUST begin treatment using one 100 mcg ABSTRAL® sublingual tablet and must be titrated incrementally to a dose that provides adequate analgesia with tolerable side effects.

Special care must be used when dosing ABSTRAL®. Single doses should be separated by at least 2 hours. ABSTRAL® should only be used once per breakthrough cancer pain episode.

Patients and their caregivers must be instructed that ABSTRAL® contains a medicine in an amount which can be fatal in children. All ABSTRAL® packages must be kept out of the reach of children and other patients who did not receive a prescription from a physician, at all times.

The concomitant use of ABSTRAL® with CYP3A4 inhibitors (e.g. erythromycin, clarithromycin, ketoconazole, ritonavir, verapamil and aprepitant) may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

More complete information on potential drug interaction with fentanyl drug products are available in the product monograph, on the www.e-therapeutics.ca drug interaction section or may be provided on request by contacting Paladin Labs Medical Services at 1-888-550-6060.

Adverse Reactions

The adverse reactions seen with ABSTRAL® are typical opioid side effects. Frequently, opioid-associated adverse reactions will cease or decrease in intensity with continued use of ABSTRAL®. Expect opioid side effects and manage them accordingly.

The most serious adverse reactions associated with all opioids including ABSTRAL® are respiratory depression (potentially leading to apnea or respiratory arrest), circulatory depression, hypotention, and shock. Follow all patients regularly for symptoms of respiratory depression.

The most common side effects of ABSTRAL® are nausea, vomiting, constipation, dry mouth, somnolence, dizziness, headache, tiredness and short breath.

Detailed prescribing information can be obtained from the Canadian Product Monograph, which is available:

- upon request through Paladin Labs Medical Services at 1-888-550-6060
- for download at www.paladinlabs.com/abstral
- online at Health Canada's Drug Product Database link: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php

Paladin Labs Inc. has created the ABSTRAL® Educational Programme. This programme has been implemented to mitigate the risk of ABSTRAL® overdose, abuse, addiction, and serious complications due to medication errors by: helping to assure proper patient selection, including avoidance of the use of ABSTRAL® in opioid non-tolerant patients; reducing the risk of exposure to ABSTRAL® in persons for whom it was not prescribed, including accidental exposure in children; and training prescribers, pharmacists, and patients about proper dosing and administration. The educational materials will be available upon request, through our sales representatives and for download at www.paladinlabs.com/abstral. These materials consist of:

- Product Monograph
- Prescriber and Pharmacist Guide
- Patient and Caregiver Guide
- Information on How to Open ABSTRAL®

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

• Report online at www.healthcanada.gc.ca/medeffect
• Call toll-free at 1-866-234-2345
• Complete a Canada Vigilance Reporting Form and:
- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

Paladin Labs Inc. is committed to supplying you with high quality products and ensuring the highest level of patient care. Please do not hesitate to contact our Medical Services at 1-888-550-6060 or consult our website at www.paladinlabs.com/abstral if you need any additional information and/or copies of the educational materials concerning ABSTRAL®.

Sincerely yours,

Patrice Larose, B.Pharm., Ph.D.
Vice President, Scientific Affairs