September XX, 2008

Dear Valued Customer,

We would like to thank you for your continued support and inform you that the temporary supply shortage on DURAGESIC® (fentanyl transdermal system) CII has been resolved. You should be able to confidently order all five strengths of DURAGESIC® from your supplier.

If you're still having difficulty obtaining branded DURAGESIC® please e-mail duragesic@its.jnj.com and we will try our best to assist you, but this should not be the case.

Boxed Warning

DURAGESIC® (fentanyl transdermal system) CII contains a high concentration of a potent Schedule II opioid agonist, fentanyl. Schedule II opioid substances which include fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone have the highest potential for abuse and associated risk of fatal overdose due to respiratory depression. Fentanyl can be abused and is subject to criminal diversion. The high content of fentanyl in the patches (DURAGESIC®) may be a particular target for abuse and diversion.

DURAGESIC®
is indicated for management of persistent, moderate to severe chronic pain that:

- **Requires continuous, around-the-clock opioid administration for an extended period of time, and**
- **Cannot be managed by other means such as nonsteroidal analgesics, opioid combination products, or immediate-release opioids**

DURAGESIC® should ONLY be used in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to DURAGESIC® 25 mcg/hr. Patients who are considered opioid-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid.

Because serious or life-threatening hypoventilation could occur, DURAGESIC® is contraindicated:

- **In patients who are not opioid-tolerant**
- **In the management of acute pain or in patients who require opioid analgesia for a short period of time**
- **In the management of postoperative pain, including use after outpatient or day surgeries (e.g., tonsillectomies)**
- **In the management of mild pain**
- **In the management of intermittent pain (e.g., use on an as needed basis [p.r.n.])**

Boxed Warning **(continued)**

(See CONTRAINDICATIONS section of the full Prescribing Information for further information.)

Since the peak fentanyl levels occur between 24 and 72 hours of treatment, prescribers should be aware that serious or life-threatening hypoventilation may occur, even in opioid-tolerant patients, during the initial application period.

The concomitant use of DURAGESIC® with all cytochrome P450 3A4 inhibitors such as (ritonavir, ketoconazole, itraconazole, troleandomycin, clarithromycin, nelfinavir, nefazodone, amiodarone, amprenavir, aprepitant diltazem, erythrocin, fluconazole, fosamprenavir, grapefruit juice, and verapamil) may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. Patients receiving DURAGESIC® and any CYP3A4 inhibitors should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted. (See CLINICAL PHARMACOLOGY Drug Interactions, WARNINGS, PRECAUTIONS, and DOSAGE AND ADMINISTRATION sections of the full Prescribing Information for further information.)

The safety of DURAGESIC® has not been established in children under 2 years of age. DURAGESIC® should be administered to children only if they are opioid-tolerant and 2 years of age or older. (See PRECAUTIONS - Pediatric Use section of the full Prescribing Information.)

DURAGESIC® is ONLY for use in patients who are already tolerant to opioid therapy of comparable potency. Use in non-opioid tolerant patients may lead to fatal respiratory depression. Overestimating the DURAGESIC® dose when converting patients from another opioid medication can result in fatal overdose with the first dose. Due to the mean elimination half-life of 17 hours of DURAGESIC®, patients who are thought to have had a serious adverse event, including overdose, will require monitoring and treatment for at least 24 hours.

DURAGESIC® can be abused in a manner similar to other opioid agonists, legal or illicit. This risk should be considered when administering, prescribing, or dispensing DURAGESIC® in situations where the healthcare professional is concerned about increased risk of misuse, abuse, or diversion.

Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse, and addiction. Patients at increased risk of opioid abuse may still be appropriately treated with modified-release opioid formulations; however, these patients will require intensive monitoring for signs of misuse, abuse, or addiction.

DURAGESIC® patches are intended for transdermal use (on intact skin) only. Do not use a DURAGESIC® patch if the seal is broken or the patch is cut, damaged, or changed in any way. Using a patch that is cut, damaged, or changed in any way can expose the patient or caregiver to the contents of the patch, which can result in an overdose of fentanyl that may be fatal.

Avoid exposing the DURAGESIC® application site and surrounding area to direct external heat sources such as heating pads or electric blankets, heat or tanning lamps saunas, hot tubs and heated water beds while wearing the system. Avoid taking hot baths or sunbathing. There is a potential for temperature-dependant increases in fentanyl released from the system resulting in possible overdose and death. Patients wearing DURAGESIC® systems who develop fever or increased core body temperature due to strenuous exertion should be monitored for opioid side effects and the DURAGESIC® dose should be adjusted if necessary.

IMPORTANT SAFETY INFORMATION

In clinical trials, the five most common side effects >10% associated with DURAGESIC® (fentanyl transdermal system) CII were nausea 23%, vomiting 22%, somnolence 17%, constipation 14%, and diaphoresis 14%.

DURAGESIC® should be prescribed only by persons knowledgeable in the continuous administration of potent opioids, in the management of patients receiving potent opioids for treatment of pain, and in the detection and management of hypoventilation (including the use of opioid antagonists).

All patients and their caregivers should be advised to avoid exposing the DURAGESIC® application site to direct external heat sources, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, and heated water beds, etc., while wearing the system. There is a potential for temperature-dependent increases in fentanyl released from the system resulting in possible overdose and death.

Death and other serious medical problems have occurred when people were accidentally exposed to DURAGESIC®. Placing DURAGESIC® in the mouth, chewing it, swallowing it, or using it in ways other than indicated may cause choking or overdose that could result in death.

DURAGESIC® has been reported as being abused by other methods and routes of administration, resulting in uncontrolled delivery of the opioid. Such misuse could pose a significant risk to the abuser that could result in overdose and death. Concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

Respiratory depression is the chief hazard of opioid agonists, including fentanyl, the active ingredient in DURAGESIC®. Respiratory depression is more likely to occur in elderly or debilitated patients. Please see WARNINGS section of full Prescribing Information for a list of patients in whom DURAGESIC® should not be used or should be used with extreme caution.

The concomitant use of DURAGESIC® with other central nervous system depressants, including but not limited to other opioids, sedatives, hypnotics, tranquilizers (eg, benzodiazepines), general anesthetics, phenothiazines, skeletal muscle relaxants, and alcohol, may cause respiratory depression, hypotension, and profound sedation or potentially result in coma. When such combined therapy is contemplated, the dose of one or both agents should be significantly reduced. DURAGESIC® may be expected to have additive CNS depressant effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

Patients, family members, and caregivers should be instructed to keep patches (new and used) out of the reach of children and others for whom DURAGESIC® was not prescribed. A considerable amount of active fentanyl remains in DURAGESIC® even after used as directed. Accidental or deliberate application or ingestion by a child or adolescent will cause respiratory depression that could result in death.

Used patches should be folded so that the adhesive side of the patch adheres to itself, and flushed down the toilet immediately upon removal. Patients should dispose of any patches remaining from a prescription as soon as they are no longer needed. Unused patches should be removed from their pouches, folded so that the adhesive side of the patch adheres to itself, and flushed down the toilet.

Please see accompanying full Prescribing Information, including Boxed Warning.

Sincerely,

DURAGESIC Brand Team

www.duragesic.com

PriCara®, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.

PriCara
Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.