The Medicines Company

8 Sylvan Way
Parsippany, NJ 07054

Re: Voluntary Discontinuation and Withdrawal from Market of IONSYS® (fentanyl iontophoretic transdermal system), CII

Dear Healthcare Provider,

The Medicines Company (MDCO) would like to advise you that it has decided to voluntarily discontinue the sale and distribution of IONSYS® (fentanyl iontophoretic transdermal system), CII, effective June 19, 2017. Please note that this is a business decision by MDCO and is not based on any safety or quality issues with the product.

IONSYS® is indicated for the short-term management of acute postoperative pain severe enough to require an opioid analgesic in the hospital and for which alternative treatments are inadequate. Please see reverse and attached Full Prescribing Information for important safety information for IONSYS®.

Healthcare Provider Action
Healthcare Providers with IONSYS® inventory should return all unused product to their wholesaler no later than September 1, 2017, for a refund. IONSYS® should not be returned to The Medicines Company directly.

In light of the planned discontinuation and withdrawal from the market, Healthcare Providers should not initiate new patients on IONSYS® and are advised to seek alternative therapies for the short-term management of acute postoperative pain in the hospital as soon as possible.

If you have any questions or require additional information concerning the discontinuation and withdrawal of IONSYS®, please contact The Medicines Company Global Health Science Center at (888) 977-6326.

Sincerely,

Loretta Itri, MD, FACP
Executive Vice President
Global Health Science and Regulatory Affairs
The Medicines Company

Enc.: IONSYS® (fentanyl iontophoretic transdermal system) Full Prescribing Information

WARNING: LIFE-THREATENING RESPIRATORY DEPRESSION; IONSYS® REMS; ADDICTION, ABUSE, AND MISUSE; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of IONSYS®. Monitor for respiratory depression, especially during initiation of IONSYS®. Only the patient should activate IONSYS® dosing.

IONSYS® Risk Evaluation and Mitigation Strategy (REMS) Program

- IONSYS® is for use only in patients in the hospital. Discontinue treatment with IONSYS® before patients leave the hospital.
- Because of the risk of respiratory depression from accidental exposure, IONSYS® is available through a restricted program called the IONSYS® REMS Program. Healthcare facilities that dispense IONSYS® must be certified in this program and comply with the REMS requirements.

Addiction, Abuse, and Misuse

IONSYS® exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing, and monitor regularly for development of these behaviors or conditions.

Cytochrome P450 3A4 Interaction

The concomitant use of IONSYS® with all cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug reactions and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in fentanyl plasma concentration. Monitor patients receiving IONSYS® and any CYP3A4 inhibitor or inducer.

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 IONSYS® 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.