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IMPORTANT PRESCRIBING INFORMATION

July 31, 2017

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Subject:	**Voluntary withdrawal of OPANA® ER (oxymorphone hydrochloride) Extended-Release tablets, for oral use.**

Dear Health Care Provider:
While the FDA still considers OPANA ER safe and effective when used appropriately as prescribed, manipulation followed by parenteral abuse has led to serious and sometimes fatal adverse events. While serious, life-threatening, or fatal respiratory depression may occur with overdose of all opioids, manipulation followed by parenteral abuse of OPANA ER has been purported to be associated with thrombotic microangiopathy, a condition characterized clinically by thrombocytopenia and microangiopathic hemolytic anemia. Endo Pharmaceuticals Inc., in cooperation with the United States Food and Drug Administration (FDA), is voluntarily withdrawing OPANA ER from the marketplace. This action does NOT affect FDA approved generic oxymorphone hydrochloride extended-release tablets. The generic tablets have not been associated with thrombotic microangiopathy when parenterally abused following manipulation.

It is estimated that OPANA ER (5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg) will no longer be available in pharmacies later this year and it is vital that healthcare providers and patients plan accordingly.

Switching patients to generic oxymorphone hydrochloride extended-release tablets:
As the FDA approved generic is bioequivalent to OPANA ER, no dosing alterations are required. While manipulated and parenterally injected generic oxymorphone hydrochloride extended-release tablets have not been implicated with thrombotic microangiopathy, like all opioids, generic oxymorphone hydrochloride extended-release tablets have been associated with serious, life-threatening, or fatal

respiratory depression. Sharing needles, unrelated to drug, is implicated in blood borne illnesses including, but not limited to, HIV/AIDs and Hepatitis C.

Oxymorphone hydrochloride extended-release tablets expose 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 oxymorphone hydrochloride extended-release tablets, and monitor all patients regularly for the development of these behaviors and conditions. Please see the oxymorphone hydrochloride extended-release tablets full prescribing information.

Switching patients to another extended-release/long-acting opioid formulation:
Switching extended-release/long-acting (ER/LA) opioid formulations is not formulaic. It requires patience and patient monitoring. It is safer to underestimate a patient's 24-hour requirements and provide rescue medication (e.g., immediate-release opioid) than to overestimate the 24-hour dosage and manage an adverse reaction due to an overdose. While useful tables of opioid equivalents are readily available, there is substantial inter-patient variability in the relative potency of different opioids. There are no established conversion ratios for conversion from other OPANA ER to other opioids defined by clinical trials. As a general guideline:

- Stop all forms of oxymorphone hydrochloride
- Start the new, ER/LA opioid formulation at the lowest FDA recommended dose regimen.
- Supplement the new, ER/LA opioid formulation with PRN ("as needed") immediate release opioid (rescue dosage).
- Close observation and frequent titration are warranted until pain management is stable on the new opioid. Monitor patients for signs and symptoms of opioid withdrawal, and for signs of oversedation/toxicity after converting patients to the new ER/LA opioid formulation.
- Refer to the FDA approved labeling of the new ER/LA opioid formulation for further information.

All ER/LA opioids expose 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 ER/LA opioids, and monitor all patients regularly for the development of these behaviors and conditions. Please see full prescribing information.

This action does NOT affect FDA approved generic oxymorphone hydrochloride extended-release tablets. The generic tablets have not been associated with thrombotic microangiopathy when parenterally abused following manipulation.

Reporting of adverse events:
Healthcare providers should report all suspected adverse events associated with the use of OPANA ER. If you become aware of a patient experiencing an adverse event

while taking OPANA ER, please contact Endo at 1-800-462-3636 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

If you need further information or assistance, we encourage you to contact Endo at 1-800-462-3636.

Respectfully,

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SVP, Research & Development, Branded Pharmaceuticals
Endo Pharmaceuticals Inc.
Enclosure: Opana ER Full Prescribing Information