To: Purdue Field Force

From: Sales Training

Bulletin #: 194

Date: October 17, 2016

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**Hysingla® ER Pivotal Clinical Study – Prior Opioid Analgesic Use and Use of Rescue Medication**

**Background**

There have been some questions from the field regarding the Hysingla ER pivotal study and the opioid analgesics used by patients entering the study. In addition, there are questions around the use of rescue medication by patients in the Hysingla ER and placebo groups.

**Direction**

If asked about either of these topics related to the Hysingla ER pivotal study, please verbally use the information below to respond to your customer's inquiry. Keep in mind, additional details regarding the study design and results are described on page 10 of the Hysingla ER core visual aid.

**Key Facts/Points Regarding the Inclusion Criteria and Prior Opioid Use**

The inclusion criteria included:

- Adult patients aged 18 years or older with moderate to severe chronic lower back pain
  - Defined as low back pain lasting at least 3 months
- Opioid-naïve or opioid-experienced patients on a stable analgesic regimen and who were not responsive to their current analgesic regimen (i.e., had uncontrolled low back pain)
  - Uncontrolled low back pain defined as an "average pain over the last 14 days" score of 5 or greater at screening, as well as 3 or more "average pain over the last 24 hours" scores of 5 or greater during the screening period (on an 11-point Numeric Rating Scale (NRS) where 0=no pain and 10=pain as bad as you can imagine)
  - Opioid-experienced patients could be taking ≤ 100 mg/day of oral oxycodone or opioid equivalent 14 days prior to screening
- Patients willing to discontinue their current analgesic regimen

Of the 905 patients enrolled in the open-label conversion and dose-titration period, 48% were opioid-experienced and 52% of patients were opioid-naïve.

- In patients treated with opioids for their chronic low back pain, the most frequently used prior opioid medications (used by ≥ 5% of patients) were products containing hydrocodone (30%), followed by oxycodone (13%) and tramadol (8%).
- In patients taking non-opioid medications, the most frequently used prior non-opioid medications (used by ≥ 5% of patients) were ibuprofen (41%), naproxen (17%), acetaminophen (17%), and cyclobenzaprine (8%).

**Key Facts/Points Regarding the Use of Rescue Medication**

During the double-blind period, the Hysingla ER pivotal study protocol allowed the optional use of up to 6 tablets per day of 5 mg immediate-release (IR) oxycodone, depending on the randomized Hysingla ER dose for patients in both the placebo and Hysingla ER groups. Patients who were randomized to the highest Hysingla ER dose of 120 mg were those permitted to receive the maximum dose of 6 tablets or 30 mg per day of IR oxycodone.

- During the double-blind period, the facts regarding the resulting use of rescue medication are as follows:
  - 22% of patients in the Hysingla ER arm and 17% of patients in the placebo arm did not use any IR oxycodone rescue at all
  - For patients that used IR oxycodone rescue, in the Hysingla ER arm, on average, patients used approximately 0.7 tablets across all doses; the placebo group used 0.9 tablets (this means that in both groups, on average across all doses, they took less than 1 tablet per day)

If HCPs have additional questions regarding this information, please refer them to Medical Services or have them fill out an eMIRF.

As always, please make sure to provide fair balance in the discussion, and if the HCP informs you of any adverse events, please follow company policy and submit this information to Drug Safety and Pharmacovigilance.