

**ERRATA FOR
FDA ADVISORY COMMITTEE MEETING BRIEFING DOCUMENT**

EXPAREL[®]
(bupivacaine liposome injectable suspension)

**MEETING OF THE ANESTHETIC AND ANALGESIC DRUG
PRODUCTS ADVISORY COMMITTEE**

MEETING DATE: 14-15 February 2018

Available for Public Release

This document provides corrections to the original EXPAREL briefing document related to the conversion factor for oral oxycodone to IV morphine-equivalent doses (MED). In reviewing our data pertinent to MED conversions between different opioid medications that are used in assessing opioid rescue in our nerve block studies, we found that the schema which we had used in our sNDA, and that was included in Pacira’s briefing materials for the February 14/15, 2018 Anesthetic and Analgesic Drug Products Advisory Committee meeting, was inconsistent with the current consensus literature for such conversions (e.g., Shaheen 2009). Specifically, in studies 326 and 327, opioids were converted to IV MED by multiplying the oral (PO) oxycodone doses with the factor of 2.

We have recalculated all oxycodone doses to IV MED using the new schema that we believe is more consistent with how PO oxycodone is converted to IV MED. The schema for this conversion is as follows:

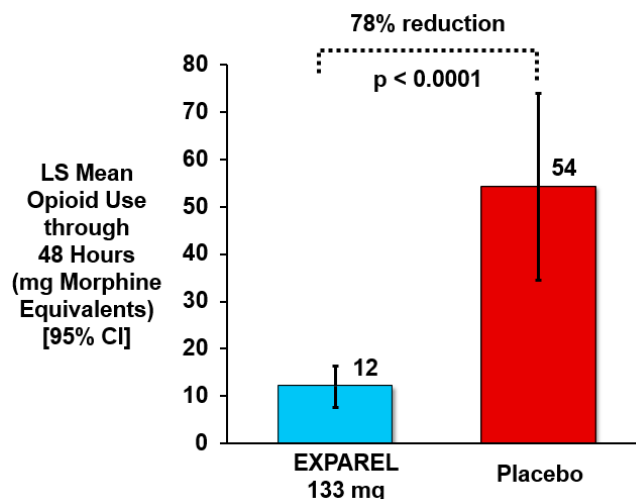
- PO oxycodone x 1.5 = PO morphine dose; and then PO morphine dose is multiplied by the factor of 0.5 to get the IV MED. Alternatively, PO oxycodone can be multiplied by the factor of 0.75 to provide IV MED.
 - For example, 10 mg PO oxycodone x 1.5 = 15 mg PO Morphine; Then 15mg PO morphine x 0.5 = 7.5 IV MED

OR

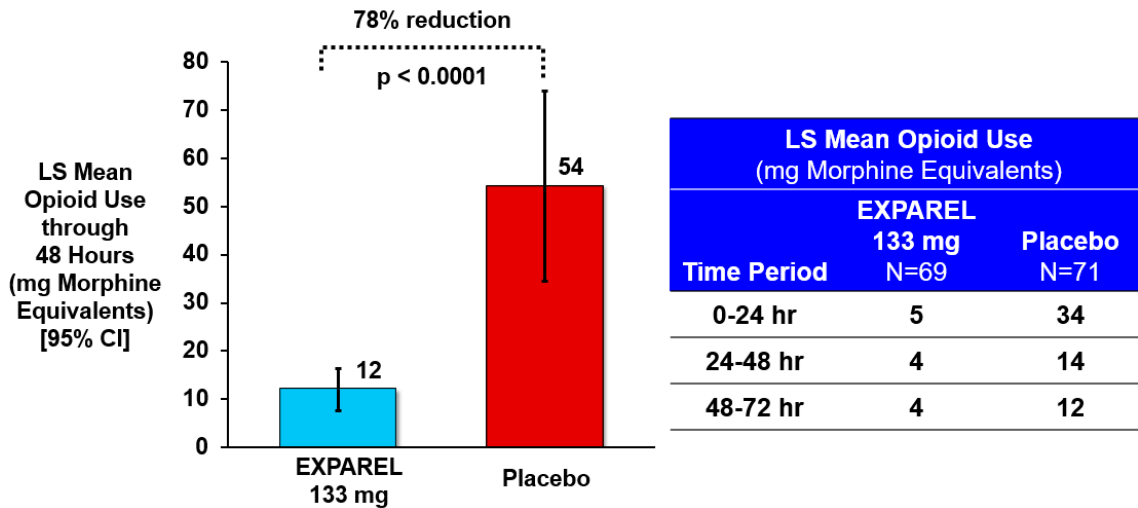
- 10 mg PO oxycodone x 0.75 = 7.5 IV MED

This updated schema does not affect the overall conclusions with respect to the use of opioid rescue medication in our pivotal trials. However, it does change the absolute magnitudes of some of the numbers. Changes to text are provided in **bold** type face.

- On Page 17 of the EXPAREL briefing document, the text should read: “The mean total amount of opioid rescue medication used was **78%** lower in the EXPAREL group than the placebo group (Figure 4; $p < 0.0001$).”
- Figure 4 on Page 17 should be replaced with the following:



- On Page 38, one bullet should be revised as “EXPAREL was associated with a **78%** reduction in the mean total opioid medication use ($p < 0.0001$) and a longer time to first opioid use ($p < 0.0001$).”
- On Page 48, the section on total opioid consumption should read: “EXPAREL was associated with a significant reduction (78%) in the mean total amount of opioid used by patients post-surgery. As shown in Figure 10, the LS mean morphine equivalents of opioids consumed through 48 hours was **12 mg** in the EXPAREL group compared to **54 mg** in the placebo group ($p < 0.0001$). Opioid use was lower in the EXPAREL group in all 24-hour time intervals throughout the study.”
- Figure 10 on Page 49 should be replaced with the following:



- Figure 19 on Page 55 should be replaced with the following:

