FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC)
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
November 15, 2018

QUESTIONS

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1. **DISCUSSION**: Discuss how to define a clinically meaningful decrease in opioid use to support an opioid-sparing claim, considering the following options:

    a. Statistically significant difference in average opioid use, considering that minor differences in opioid use could reach statistical significance but may not be clinically-relevant and, conversely, that there could be a clinically-relevant decrease in opioid exposure for many patients that is not reflected by a substantial difference in mean opioid use between groups
    b. A reduction by an absolute amount (in morphine milligram equivalents, for example) or percentage decrease in opioid use
    c. A decrease in the duration of opioid analgesic therapy that is required in the inpatient setting, for example, opioid analgesics only being required for the immediate postoperative period (i.e., the day or night of the procedure)
    d. The number of patients who use no opioid in the hospital, even if they are prescribed opioids at discharge for use at home
    e. The number of patients who do not require opioid analgesics after discharge, regardless of analgesic regimen while hospitalized
    f. A reduction in opioid-related adverse reactions, e.g., nausea, vomiting, constipation, respiratory depression, sedation, urinary retention
    g. Other criteria for defining a clinically-meaningful decrease in opioid use

2. **DISCUSSION**: Discuss the pros and cons of the following study designs to assess opioid-sparing or, alternatively, a novel design to assess opioid-sparing:

    a. study drug vs. placebo with opioid restricted to rescue
    b. standard of care with add-on of study drug or placebo

3. **DISCUSSION**: Discuss how much difference in analgesia (if any) would be permissible in a study of an opioid-sparing drug, relative to the standard of care with an opioid.

4. **DISCUSSION**: Discuss the study design for a study of a novel non-opioid analgesic intended to be used in place of an opioid analgesic taking the following points into consideration:

    a. Discuss whether any evidence of efficacy is enough when evaluating a novel analgesic intended to replace an opioid, i.e., whether adequate analgesia is an acceptable outcome
    b. Discuss when the use of an active comparator is necessary to make a determination that a novel analgesic provides “opioid-level” analgesia in a setting usually managed with an opioid analgesic
    c. Discuss how the use of rescue medication should be taken into account in the evaluation of efficacy in this setting

QUESTIONS (cont.)

5. **VOTE**: Is any reduction in opioid use sufficient to warrant labeling as opioid sparing?

    a. If not, describe the criteria that would support such labeling.

6. **VOTE**: Is it sufficient to claim opioid-level analgesia for a novel analgesic based on the clinical trial population and without an opioid active comparator?

    a. If not, describe the type of comparisons that would provide support for a finding of opioid-level analgesia