FDA's Response to the Citizen Petition from the National Advocates for Pregnant Women

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Outline

- Definition of a Citizen Petition
- Citizen Petition assertions and requests
- FDA responses

What is a Citizen Petition ?

- A request from a member of the public that FDA take or refrain from taking an administrative action
  - Examples: petition to change a drug's labeling, petition to remove a drug from the market, petition to issue a rule or guidance
- FDA creates a public docket (at www.regulations.gov) for each petition
- FDA responds to the petitioner's requests and arguments, and posts the official written response to the public docket

Citizen Petition submitted by the National Advocates for Pregnant Women

- Received October 17, 2013
- Objected to the Neonatal Opioid Withdrawal Syndrome (NOWS) warnings for Extended Release (ER)/Long Acting (LA) opioid analgesics
- Included objections that pertained predominantly to the importance of the use of opioids as maintenance treatment for addiction, rather than use of opioids for analgesia

Citizen Petition Assertions and Requests

- The NOWS-related warnings were medically inaccurate, and NOWS did not present a serious risk
- FDA's conclusion that NOWS was life-threatening was erroneous and FDA should remove the NOWS boxed warning and all references to NOWS as “life-threatening” from ER/LA opioid analgesic labeling, including in the medication guide and patient counseling information
- *“NOWS is not associated with adverse long-term outcomes”*

Citizen Petition Assertions and Requests

- The NOWS-related warnings were inconsistent with leading national and international expert opinion on opioid use during pregnancy and FDA regulations
- Prescribing information should add the following:

  "Opioid dependent pregnant women should be particularly encouraged to enter treatment since opioid substitution therapy can lessen the risk of fetal demise and dramatically improve neonatal outcome."

Citizen Petition Assertions and Requests

- NOWS-related warnings failed to consider the negative medical consequences of this labeling for maternal and fetal health
- NOWS labeling was

  " likely to increase erroneous and counterproductive child welfare actions against pregnant women and parents who receive opioid substitution therapy."

FDA Response to Citizen Petition (CP)

- FDA responded on April 16, 2014*
- CP request: Remove the boxed warning
- **FDA Response**:
  - NOWS boxed warning pertained to ER/LA opioids used for *analgesia,* not for maintenance treatment for addiction
  - Prominence of the Warning emphasized the need for providers to be prepared for NOWS

*http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm363722.htm

FDA Response to Citizen Petition

- CP assertion: NOWS is not a serious risk
- **FDA Response:** FDA disagreed
- FDA statute defines a serious risk as an adverse drug reaction that results in:
  - Death
  - Immediate risk of death
  - Inpatient hospitalization or prolongation of hospitalization
  - Incapacity or disruption of ability to conduct normal life functions
  - A birth defect
  - A medical intervention to prevent the above
- NOWS may result in almost all of the above

FDA Response to Citizen Petition

- CP assertion: NOWS is not life-threatening
- **FDA Response:** FDA clarified the NOWS language to state the following:
  - That NOWS is potentially life-threatening **if not recognized and treated**
  - The revised language is consistent with the American Academy of Pediatrics Clinical Report on Neonatal Drug Withdrawal (2012) and with the medical literature

FDA Response to Citizen Petition

- CP assertion/request: “NOWS is not associated with adverse long-term outcomes”
- **FDA Response:** FDA disagreed
- Some literature suggests that NOWS may be associated with long-term effects on neurologic and cognitive functioning
- More research is needed

FDA Response to Citizen Petition

- CP assertion: NOWS warnings not consistent with national or international guidelines
- **FDA Response:** There are no national or international guidelines regarding the use of opioids for analgesia during pregnancy, other than for labor analgesia
- FDA does not oppose national or international guidelines on the maintenance treatment of opioid addiction in pregnancy

FDA Response to Citizen Petition (continued)

- American College of Obstetricians and Gynecologists (ACOG),Substance Abuse and Mental Health Services Administration (SAMHSA), and the World Health Organization (WHO) recommend that pregnant women be treated with methadone or buprenorphine:
  - Avoid maternal and obstetrical complications associated with heroin and/or opioid addiction
  - Avoid complications associated with withdrawal (fetal death and high risk of relapse)

FDA Response to Citizen Petition

- CP request: Addition of specific labeling language that recommended that opioid-dependent pregnant women enter treatment

- **FDA Response:** FDA disagreed
- FDA does not oppose this recommendation as a clinical practice guideline
- Inclusion of a clinical practice guideline is not consistent with current FDA labeling practices.

FDA Response to Citizen Petition

- CP assertion: NOWS warnings could have negative maternal/fetal consequences

- **FDA Response:** Warnings were for ER/LA opioid analgesics
- The impact of untreated pain in pregnancy is not known
- FDA's intent is not to discourage the use of opioids in pregnant women when medically indicated
- Purpose of NOWS warning was to provide risk information to inform prescribing and risk-benefit considerations in pregnant women who are prescribed ER/LA opioid products for analgesia

Conclusion

In recognition of issues raised by the Citizen Petition and stakeholders regarding labeling of opioids approved for treatment of addiction, FDA is convening this Advisory Committee for recommendations regarding effective communication strategies.