Tatia Oden French Memorial Foundation Citizen Petition to FDA Fact Sheet

PETITION BACKGROUND

- On April 26, 2017, a Citizen Petition submitted to the FDA by the Tatia Oden French Memorial Foundation was accepted and made publically available via www.regulations.gov (ID #: FDA-2017-P-2563-0001). The petition requests that the FDA conduct a Sentinel query to assess rates and severity of adverse reactions associated with the unapproved use of misoprostol (marketed as Cytotec) for cervical ripening and induction of labor.
- If the petition is accepted, the Sentinel query will provide FDA with additional data and a better understanding of the adverse events associated with the use of Cytotec to induce labor or ripen the cervix during childbirth.
- Potential actions that FDA could take in response to the data gathered from this Sentinel study include: updates to existing Cytotec prescribing information, additional safety alerts, or other regulatory action deemed appropriate by the Agency.

ABOUT THE SENTINEL SYSTEM

- In May 2008, FDA created the Sentinel System, a nationwide collection of electronic health records providing FDA with surveillance capabilities that track adverse events by proactively assessing the safety of the products.
- The Sentinel system is a nationwide database of electronic health records of over 193 million patients from multiple data partners.
- The FDA typically relies on voluntary reporting from healthcare professionals and patients through the Adverse Event Reporting System (FAERS) to monitor the safety of drugs after they have been approved. The Sentinel System is designed to complement FAERS, which can alert the FDA to potential health risks but relies on limited data.

ABOUT CYTOTEC

- Cytotec (misoprostol) is a drug approved by the FDA for the oral treatment of peptic ulcers, specifically for reducing the risk of NSAID-induced gastric ulcers.
- The FDA classifies Cytotec as a Pregnancy Category X drug due to its abortifacient property. This means that the risks of prescribing the drug to pregnant women outweighs the potential benefits.
- Cytotec is also used off-label in pregnancy to induce labor and ripen the cervix. Side effects associated with this use have been documented, including hyper-stimulation of the uterus, meconium-stained amniotic fluid, amniotic fluid embolism, severe vaginal hemorrhage, higher rates of third and fourth-degree lacerations, high cesarean rates, fetal distress, higher incidence of infants referred to the neonatal intensive care unit, and death to mother and child.

STATS ABOUT MATERNAL MORTALITY IN THE U.S.

- Over the past 20 years, maternal morbidity and mortality rates have doubled in the United States.[i]
- The United States ranks 50th in the world for maternity mortality rates. Rates of maternal mortality fare even worse for certain groups.[ii]
    - Studies have shown that maternal mortality rates 4 times higher for African American women than for white women, and 3 times higher for Native American women.
    - The New York City Department of Health and Mental Hygiene show that maternal mortality was 12 times higher among black women than white women between 2006 and 2010.

ABOUT THE TATIA ODEN FRENCH MEMORIAL FOUNDATION

- The Tatia Oden French Memorial Foundation is a non-profit corporation formed in March 2003 to empower women around the issues of childbirth and pregnancy. It is presently focused on the issues of fully informed consent, the off-label use of drugs, and maternal mortality.
- The Foundation's history with FDA:
    - **November 2004**: The Foundation submitted a Citizen Petition to FDA requesting stronger warnings for Cytotec, which generated over 950 signatures in support.
    - **2005**: FDA published a Patient Information Sheet notifying the public of the risks associated with use of misoprostol in labor and delivery. The information sheet stated that FDA has not approved Cytotec for cervical ripening or labor induction and noted that serious side effects, including uterine rupture and death of the mother or child, may occur with the use of the drug for these purposes.
    - **March 2007**: Maddy Oden, Executive Director of the Tatia Oden French Memorial Foundation, met with the FDA's Office of Women's Health with 1,923 signatures on the Citizen Petition (70 of which were from women who had experienced catastrophic events after Cytotec inductions, including the loss of their baby or uterine rupture).
    - **November 2012**: FDA responded to the Foundation's Citizen Petition and issued revised labeling for Cytotec. The new labeling addressed three issues:
        - It recognized the obstetric use of Cytotec in labor induction
        - It created a new section on the labeling for obstetric use and safety information
        - It provided information regarding additional risk factors for uterine rupture
    - **October 2016**: An active MoveOn.org petition requesting that the FDA create a Medication Guide stating the serious adverse effects associated with Cytotec when used off label for labor induction. So far, the petition has over 4,000 signatures, many including negative personal experiences with the use of Cytotec for inductions.

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[i] MacDorman, MF; Declercq, E; Cabral, H; Morton, C. Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends from Measurement Issues. *Obstetrics & Gynecology*. September 2016, Vol. 128; 3, 447-455.

[ii] "Maternal Mortality Rates Much Higher for Minorities in US." *Medscape*. Oct 25, 2016.