



Office of the City Manager

INFORMATION CALENDAR

February 13, 2007

To: Honorable Mayor and
Members of the City Council

From: *PK* Phil Kamlarz, City Manager

Submitted by: Fred Medrano, Director, Health and Human Services

Subject: Off-Label Use of the Drug Cytotec©

INTRODUCTION

On June 27, 2006, Council heard a presentation from Ms. Maddie Oden regarding the “off-label” use of the drug Cytotec© (generic name Misoprostol) to induce labor. Ms. Oden’s daughter Tatia Oden French tragically died in December 2001 of an amniotic fluid embolism during labor. Ms. Oden requested that Council send a letter to Alta Bates Hospital asking that there be a moratorium on the use of Misoprostol for inducing labor until there is proof of its safety for mother and child. Council referred the issue to the Community Health Commission (CHC), and also requested that the Health Officer report back to Council with a recommendation regarding sending a letter from the Mayor to Alta Bates Hospital.

On July 16, 2006, Ms. Oden made a presentation to the CHC. After discussion, the Commission determined that it is not within the purview of the Commission to make any recommendations on drugs administered at Alta Bates.

CURRENT SITUATION AND ITS EFFECTS

The off-label use of Misoprostol is common obstetrics practice in California, including in Bay Area hospitals. The drug is effective for this purpose, is endorsed by several United States specialty medical organizations, and is permitted under federal Food and Drug Administration (FDA) regulations. Medical practice is regulated by the State of California. Efforts to regulate the use of Misoprostol (or any other drug) on the local level would be misguided. Local governments lack the expertise to assess the efficacy or risks of medications – both in general and in specific patient circumstances. Women who receive Misoprostol should be provided with information about its risks and benefits, as well as treatment alternatives. Such informed consent is considered the standard of medical practice in California.

BACKGROUND

Misoprostol for the induction of labor: Misoprostol (brand name Cytotec ©) is used to prevent ulcers in people who take some anti-inflammatory or pain medicines, including aspirin, which can cause ulcers. The “off-label” use of Misoprostol to induce labor has become quite popular. Off-label use is the prescription of medications for indications other than those for which the medication received federal Food and Drug Administration approval. Off-label use is permitted by the FDA and is very common.¹

The FDA place a “black-box” warning on Misoprostol, to warn that it should not be used by pregnant women as it may induce abortion. The physician prescribing information also indicates that Misoprostol causes uterine hyperstimulation, and may increase risk of uterine rupture or amniotic fluid embolism.ⁱⁱ

The American College of Obstetrics and Gynecology supports the off-label use of Misoprostol, and states that it can be used safely and effectively for labor induction.ⁱⁱⁱ The American Academy of Family Physicians also endorses the use of Misoprostol for labor induction. Critical reviews of the published medical literature on this issue suggest that there are no differences in the rates of cesarean delivery, serious neonatal or maternal morbidity, or neonatal or maternal mortality between women who received Misoprostol and those who received oxytocin or prostaglandin E₂. However, clinical trials to evaluate the use of Misoprostol to induce labor have involved nearly 10,000 women, the numbers are still too small to determine whether there may be an increased risk of extremely rare events (such as rupture of the uterus or amniotic fluid embolism) associated with Misoprostol versus other drugs used to induce labor.^{iv,v,vi} It should be noted that labor induction is often intended to prevent complications or C-section when there is a concern about continuation of pregnancy (e.g. baby too big, risk of infection, etc.).

Informed consent: Another question that has surfaced in the discussion about the use of Misoprostol for the induction of labor is that of informed consent. The American Medical Association Code of Ethics maintains that the physician has an ethical obligation to help the patient make choices from among the therapeutic alternatives consistent with good medical practice.^{vii} Informed consent is a “process of communication between a patient and physician that results in the patient's authorization or agreement to undergo a specific medical intervention.”^{viii} Informed consent is also a well-established doctrine in the field of medical liability law, which now extends to the dispensing of pharmaceuticals.^{ix} In California, failure to get informed consent is considered negligence; a doctor who fails to obtain informed consent for non-emergency treatment may be subject to a medical malpractice lawsuit, or charged with a civil and/or criminal offense.^x

Regulation of the practice of medicine: The Medical Board of California is the State agency that regulates the practice of medicine; it licenses medical doctors, investigates complaints, disciplines those who violate the law, conducts physician evaluations, and facilitates rehabilitation where appropriate.^{xi} The laws governing the practice of medicine are contained in the **Business and Professions Code** Medical Practice Act Sections 2000 et seq.^{xii} Local governments do not have a role in the regulation of the practice of medicine in California.

POSSIBLE FUTURE ACTION

The City Council could send a letter to Alta Bates Summit Medical Center encouraging a review of policies and procedures related to informed consent to ensure that all providers implement informed consent processes that are consistent with best practices.

FISCAL IMPACTS OF POSSIBLE FUTURE ACTION

None

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ⁱ The FDA “recognizes that, in certain circumstances, off-label uses of approved products are appropriate, rational, and accepted medical practice. Prescribing a medication for an off-label indication is common in the treatment of pregnant women and is not considered experimental if based on sound scientific evidence.” (Goldberg A, Greenberg M, Darney P. Misoprostol and Pregnancy. (2001) *New England Journal of Medicine*.344(1):38-47.) “Off-label drug use is common in obstetrics and includes many drugs which would be considered mandatory in everyday practice” (Alfitevic Z, Weeks A. Oral misoprostol for induction of labour. *Cochrane Database of Systematic Reviews* 2006 Issue 2 CD001338. DOI:10.1002/14651858.) The Federal Food, Drug and Cosmetic Act explicitly allows off-label use (Sec.906 - 21 U.S.C. 396 – Practice of Medicine). An FDA statement entitled “Use of Approved Drugs for Unlabeled Indications” states that “The Food, Drug and Cosmetic Act does not limit the manner in which a physician may use an approved drug. Once a product has been approved for marketing, a physician may prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling. Such “unapproved” or, more precisely, “unlabeled” uses may be appropriate and rational in certain circumstances, and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature.” (FDA Drug Bull. 1982; 12:4–5) .

ⁱⁱ FDA Prescribing Information for Health Professionals. <http://www.fda.gov/cder/foi/label/2002/19268slr037.pdf>

ⁱⁱⁱ Induction of labor with misoprostol. ACOG committee opinion no.228. Washington, D.C.: American College of Obstetricians and Gynecologists, November 1999; Induction of labor. ACOG practice bulletin no. 10. Washington, D.C.: American College of Obstetricians and Gynecologists, November 1999.

^{iv} Alfitevic Z, Weeks A. Oral misoprostol for induction of labour. *Cochrane Database of Systematic Reviews* 2006 Issue 2 CD001338. DOI:10.1002/14651858. <http://www.cochrane.org/reviews/en/ab001338.html>

^v Royal College of Obstetricians and Gynaecologists. Induction of labour. Evidence-based Clinical Guideline Number 9 2001 http://www.rcog.org.uk/resources/public/pdf/rcog_induction_of_labour.pdf

^{vi} Goldberg A, Greenberg M, Darney P. Misoprostol and Pregnancy. (2001) *New England Journal of Medicine*.344(1):38-47

^{vii} AMA Resources/Standards on Medical Ethics. <http://www.ama-assn.org/ama/pub/category/8488.html>

^{viii} The California Patient’s Guide. <http://www.calpatientguide.org/ii.html>

^{ix} “The responsibility to warn patients of risks rests with the prescribing physician rather than with the manufacturer of the drug; the manufacturer has the responsibility to provide the physician with appropriate information. A physician who fails to warn a patient or a manufacturer who fails to warn physicians of risks associated with a particular drug may incur liability for that error.” (AMA Health Law *Virtual Mentor*. 2006; 8:520-523. <http://www.ama-assn.org/ama/pub/category/16566.html>)

^x While a statutory definition of "Informed Consent" has never been written into California law, it has been extensively discussed in case law and is well understood within the medical and legal communities to mean that a patient "receive sufficient information to make a meaningful decision" regarding their own healthcare. *Cobbs v. Grant* (1972) 8 Cal.3d 229.The California Patient’s Guide. <http://www.calpatientguide.org/ii.html>

^{xi} http://www.medbd.ca.gov/Pubs_Consumerinfo.pdf

^{xii} <http://www.leginfo.ca.gov/cgi-bin/displaycode?section=bpc&group=01001-02000&file=2000-2029>

