Anaphylactoid syndrome of pregnancy
Immediate steps to save lives

Enhancing recovery after repeat C/S

Genitourinary syndrome of menopause
Not a normal part of aging

Long-term maternal benefits of lactation
Good for baby, good for mother

LEGALLY SPEAKING
Oxytocin – frequently used, possibly abused
A new choice for balanced control

Balcoltra™ offers a balance of high efficacy and low dose\(^1\)

- Low-dose levonorgestrel/ethinyl estradiol combination oral contraceptive (COC)\(^1\)
- Familiar 21/7 dosing\(^1\)
- Cycle control with 4% breakthrough bleeding and 1 unintended pregnancy per 100 woman-years\(^1\)

Visit balcoltra.com to learn more about how Balcoltra may help your patients.

*Most eligible patients will pay no more than $21 per co-pay. Patients should present this coupon with their prescription to their participating pharmacy. For each Balcoltra prescription, patients pay the first $21 of their out-of-pocket expense and Avion will cover up to $100 of their remaining expense. This offer is good for 21 uses. Cardholders with questions, please call 1-877-838-3846 (8:30 AM - 5:30 PM ET, Monday-Friday).

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**INDICATIONS AND USAGE**

Balcoltra is a progestin/estrogen combination oral contraceptive (COC) indicated for use by females of reproductive potential to prevent pregnancy.

**IMPORTANT SAFETY INFORMATION**

**WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS**

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs are contraindicated in women who are over 35 years of age and smoke.

**CONTRAINDICATIONS**

Balcoltra is contraindicated in women with a high risk of arterial or venous thrombotic diseases, liver tumors (benign or malignant) or liver disease, undiagnosed abnormal uterine bleeding, during pregnancy, with breast cancer or other estrogen- or progestin-sensitive cancer (now or in the past), hypersensitivity to any of the components, or in women who are currently taking Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir (with or without dasabuvir).

**WARNINGS AND PRECAUTIONS**

- Discontinue Balcoltra if an arterial thrombotic event or venous thromboembolic event (VTE) occurs, and at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of VTE as well as during prolonged immobilization. Balcoltra should not be started any earlier than 4 weeks after delivery, in women who are not breastfeeding. The use of COCs increases the risk of VTE. The risk of VTE is highest during the first year of use of COCs and when re-starting hormonal contraception after a break of 4 weeks or longer. Use of COCs also increases the risk of arterial thromboses such as strokes and myocardial infarctions. Use COCs with caution in women with cardiovascular disease risk factors.
- If jaundice occurs, treatment should be discontinued.
- Balcoltra should not be prescribed for women with uncontrolled hypertension or hypertension with vascular disease. An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women with extended duration of use. If Balcoltra is used in women with well-controlled hypertension, monitor blood pressure and stop treatment if blood pressure rises significantly.
- Women who are prediabetic or diabetic should be monitored while using Balcoltra. Alternate contraceptive methods should be considered for women with uncontrolled dyslipidemia.
- Patients using Balcoltra who have a significant change in headaches or who develop new headaches that are recurrent, persistent, or severe should be evaluated, and Balcoltra should be discontinued if indicated.
- Irregular bleeding and spotting sometimes occurs in patients on COCs, especially during the first three months of use. If bleeding persists or occurs after previously regular cycles on Balcoltra, check for causes such as pregnancy or malignancy.
- This product contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Sensitivity to tartrazine is frequently seen in patients who have aspirin hypersensitivity.

**ADVERSE REACTIONS**

In a clinical trial with levonorgestrel 0.1 mg and ethinyl estradiol 0.02 mg, the most common adverse reactions (incidence ≥2%) were headache (14%), metrorrhagia (8%), dysmenorrhea (7%), nausea (7%), abdominal pain (4%), breast pain (4%), emotional lability (3%), acne (3%), depression (2%), amenorrhea (2%), and vaginal moniliasis (2%).

**DRUG INTERACTIONS**

Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the effectiveness of COCs or increase breakthrough bleeding.

Patients should be counseled that COCs do not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Please see full Prescribing Information, including BOXED WARNING, for Balcoltra.

**REFERENCES**

Balcoltra™ (levonorgestrel 0.1 mg and ethinyl estradiol 0.02 mg tablets and ferrous bisglycinate 36.5 mg tablets) for oral administration

brief summary of prescribing information

For additional information, refer to the full Prescribing Information.

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

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INDICATIONS AND USE

Balcoltra is indicated for use by females of reproductive potential to prevent pregnancy.

DOSAGE AND ADMINISTRATION

Patients should take one tablet by mouth at the same time every day in the order directed on the blister pack.

Contraindications

Balcoltra is contraindicated in individuals with:

- A high risk of arterial or venous thrombosis diseases, including in women:
  - Breast cancer or other estrogen- or progestin-sensitive cancer or history of these cancer
  - Hypersensitivity of any of the components
  - Co-administration with Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir

Warnings and precautions

Thrombotic Disorders and Other Vascular Problems

Stop Balcoltra if an arterial thrombotic event or venous thromboembolic (VTE) event occurs, or unexplained visual loss, proptosis, diplopia, papilledema or retinal vascular lesions occur. If possible, stop at least 4 weeks before major surgery or other surgery known to have an elevated risk of VTE as well as during the following prolonged immobilization. Start no earlier than days 4 weeks after delivery in women who are not breastfeeding.

In women who are not on COCs, the use of COCs increases the risk of VTE; however, pregnancy increases the risk of VTE as much or more than the use of COCs. Discontinue Balcoltra prior to starting medications, such as COCs. If breastfeeding, stop Balcoltra if breast pain, feeding difficulties, or changes in milk production occur. If breastfeeding needs to be continued, use alternative contraception.

Bleeding irregularities and Amenorrhea

Evaluate irregular bleeding or amenorrhea.

Unscheduled (breakthrough or intracyclic) bleeding and spotting sometimes occur in patients on COCs, especially during the first three months of use. If bleeding is irregular or if spotting occurs after previously regular cycles, check for causes such as pregnancy or malfunction. If pathology and pregnancy have been excluded, bleeding irregularities may resolve over time or with a change to a different contraceptive product.

Carbohydrate and Lipid Metabolic Effects

Monitor prediabetic and diabetic women taking Balcoltra, as COCs may decrease glucose tolerance. Consider an alternative contraceptive method for women with uncontrolled diabetes.

Women with hypertriglyceridemia, or a family history thereof, may experience increases in triglycerides or cholesterol with subsequent COC use. If the patient has adhered to the prescribed regimen and misses two consecutive periods, rule out pregnancy.

FD&C Yellow No. 5 Allergic-type Reaction

This product contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions including bronchial asthma in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

Depression

Carefully observe women with a history of depression and discontinue Balcoltra if depression recurs to a serious degree.

Cardiovascular Disorders and Cervix

Balcoltra is contraindicated in women who currently have or had breast cancer because breast cancer may be hormonally sensitive.

Effect on Binding Globulins

The estrogen component of COCs may raise the serum concentrations of albumin, haptoglobin, and cortisol-binding globulin. The dose of replacement thyroid hormone or cortisol therapy may need to be increased.

Monitoring

A woman who is taking COCs should have her blood pressure checked periodically with her healthcare provider.

Hereditary Angiogena

In women with hereditary angioedema, exogenous estrogens may induce or exacerbate symptoms of angioedema.

Hepatic Impairment

The pharmacokinetics of Balcoltra has not been studied in patients with moderate or severe hepatic impairment. Use Balcoltra with caution in women with hepatic impairment. Use Balcoltra with caution in women with severe renal impairment.

OVERDOSAGE

There have been no reports of serious ill effects from overdose of oral contraceptive pills, including ingestion by children. Overdosage may cause withdrawal bleeding in females and nausea.

The FDA-approved product labeling can be found at www.balcoltra.com, or call 1-888-612-8466.

Drugs interactions

Consult the labeling of concurrently used drugs to obtain more information about interactions with hormonal contraceptives. Drugs that induce certain enzymes, including CYP3A4, may decrease the effectiveness of COCs or increase breakthrough bleeding.

Counsel women to use an alternative method of contraception as a back-up method when enzyme inducers are used with COCs, and to continue back-up contraception for 28 days after discontinuing the enzyme inducer for contraceptive reliability.

Pregnancy

Balcoltra is contraindicated in pregnancy because there is no reason to combine the contraceptive effects of Balcoltra with the effects of pregnancy. Discontinue Balcoltra if pregnancy occurs. Based on epidemiologic studies and meta-analyses, there is little or no increased risk of birth defects in the children of females who inadvertently use COCs during early pregnancy.

Use in Specific Populations

Pregnant Women

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Breastfeeding

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IT COULD BE POSTPARTUM DEPRESSION (PPD).

LEAVE NO MOM BEHIND

PPD is the most common complication of childbirth.1-5

Without proper screening, more than 50% of PPD cases may go undiagnosed.7,14

Get a validated screening tool at KnowPPD.com/epds

The American College of Obstetricians and Gynecologists (ACOG) recommends screening patients at least once during the perinatal period using a standardized, validated tool.15

Some examples of these tools include the Edinburgh Postnatal Depression Scale (EPDS) and the Patient Health Questionnaire-9 (PHQ-9).

It only takes ~5 minutes to know your patient’s score.15

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**OESﾎ**

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invitae.com
Fertility banking – how secure is it?

Recent cryopreservation tank failures have focused a spotlight on procedures used by IVF facilities to safeguard patients’ reproductive tissue. The information here may help ob/gyns and their patients better understand the processes, management, and maintenance of IVF systems.

Cryopreservation of gametes (sperm and oocytes) and embryos has been an essential component of assisted reproductive technology (ART) for many years. Cryopreservation of semen, first employed successfully in the 1950s, has potentiated safe intrauterine insemination, effectively eliminating transmission of sexually transmitted disease with current practices of quarantining and retesting before use. It has also been effectively utilized for fertility preservation for men facing surgery, chemotherapy or radiation for malignancy likely to render them sterile, and prior to vasectomy. Embryo cryopreservation, successfully first performed in the 1980s, offered an option for storage and successful subsequent use of supernumerary embryos created with in vitro fertilization (IVF). It is now relied on for patients having a host of genetic tests performed on their embryos to allow time to receive results before transfer, for women seeking fertility preservation for a variety of reasons and other women that have temporary or permanent contraindications to proceeding with fresh embryo transfer or pregnancy.

More recently, it has been appreciated that frozen embryo transfers often produce higher success rates than fresh cycles and result in safer pregnancies for mothers and babies. These advantages include a lower incidence of preterm deliveries and small for gestational age neonates. Cryopreservation of oocytes developed in the late 1990s has potentiated fertility preservation for women for the same indications used for sperm freezing. In addition, the well-recognized age-related decline in fertility in women, attributed to diminishing oocyte quantity and quality, has created new and exponential demand for fertility preservation for so-called “social” reasons. Successful cryopreservation of oocytes has been the most technically challenging process but survival rates greater than 90% have now been reported.¹

The success of these technologies has rapidly led to a very large inventory of cryopreserved tissues around the world. Many couples and individuals electing to cryopreserve gametes and embryos have an indefinite time horizon for their use, which adds to the challenge of storing large quantities of tissue over long periods. For the most part, fertility clinics have admirably met this challenge. One of the highest priorities of a fertility clinic and its laboratory is to safeguard any cryopreserved reproductive tissue (e.g. sperm, eggs, and embryos) in storage at the clinic. Such storage requires the highest level of surveillance to maintain appropriate cryogenic conditions and immediate reaction and action when
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conditions do not meet the needed standards. In many cases, reproductive tissues are irreplaceable and may represent the only opportunity for future offspring for the affected patient.

Cryopreservation with all of these techniques is a safe, reliable methodology that has generally been taken for granted by patients and health care professionals. However, cryopreservation of human tissue is subject to two primary problems: microbial contamination (not addressed in this commentary) and failure of the requisite equipment to maintain cryogenic conditions. Recent well-publicized simultaneous failures of cryogenic storage tanks at two American fertility centers earlier this year created considerable alarm throughout the industry after thousands of cryopreserved sperm, egg, and embryo specimens were placed at risk. Cryogenic storage tank failure occurs when either the cryogenic storage tank’s temperature is inadequate for storage of reproductive tissue or the volume of cryoprotectant (liquid nitrogen, LN₂) required to maintain the cryogenic storage tank is insufficient. As a result of either of these conditions, the reproductive tissue may completely or partially thaw, causing irreversible damage or even destruction of the reproductive tissue.

These recent events have received extensive coverage and created legitimate concerns regarding the safety and reliability of cryopreservation systems. The following information is intended to address concerns and queries regarding the processes, management, and maintenance of systems associated with reproductive tissue cryopreservation and storage.

How are reproductive tissues cryopreserved?
For sperm, a preliminary analysis is performed on the semen sample to assess sperm count and motility. After the analysis, the semen is mixed with a glycerol-based cryopreservation media, placed into several individual vials and slowly exposed to LN₂ vapors. Approximately 30 to 60 minutes later, the vials are transferred to cryogenic storage tanks for permanent storage. Oocytes and embryos are cryopreserved utilizing essentially the same methodology but with special modifications. Previously, oocytes and embryos were placed into dehydrating cryoprotectant solutions that removed water from the cells and then replaced the water to protect from ice damage during cryopreservation process. Next the oocytes or embryos were placed into an automated freezer that slowly cooled down to -30º C. Today, oocytes and embryos are cryopreserved by a technique called “vitrification,” whereby the process of cryopreservation is so rapid that the water molecules inside oocytes and embryos do not have the time to form ice crystals and they instantly solidify into a glass-like structure. Slow freezing and vitrification have several other key differences, including the volume of cryoprotectant used (10- to 100-fold greater with slow freezing), devices used for storage and thermodynamic stability (favoring vitrification). Most labs now perform vitrification exclusively. There are also two options for freezing medium: liquid nitrogen and nitrogen vapor. Most of the publicized tank failures have involved nitrogen vapor but vapor is used almost exclusively for shipment of cryopreserved tissues. Sperm, oocytes, and embryos can be cryopreserved indefinitely, with several published articles reporting live births from reproductive tissues stored for more than several decades.⁵³

How are cryopreserved reproductive tissues typically stored?
Cryogenic storage tanks filled with LN₂ are considered reliably safe and are the standard for most fertility clinics worldwide. These insulated metal containers have walls with two or more vacuumed layers to allow holding and maintenance of LN₂ at its basal temperature of -196º C, far below the conditions necessary to maintain the viability of cryopreserved reproductive tissues. These tanks do not require

Q. Have you broached the topic of frozen embryos with your patients? What was their response?

<table>
<thead>
<tr>
<th>Response</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donate to other couples or agencies</td>
<td>17%</td>
</tr>
<tr>
<td>Discard</td>
<td>6%</td>
</tr>
<tr>
<td>Give to researchers</td>
<td>0%</td>
</tr>
<tr>
<td>Preserve for future pregnancy attempts</td>
<td>33%</td>
</tr>
<tr>
<td>I have not had this discussion with my patients</td>
<td>44%</td>
</tr>
</tbody>
</table>

Data from Contemporary OB/GYN poll. June 2018.
Electrical power to maintain temperature and are not affected by power outages. Two types of cryogenic storage tanks are currently used in fertility clinics. Both can be utilized for both the vapor and total immersion phase of LN₂ storage. The first type is a small waist-high aluminum cryogenic tank that resembles a large thermos and is frequently placed on a wheeled base to allow for easy evacuation. This type of tank must be filled manually with LN₂. Larger aluminum or steel cryogenic storage tanks that resemble chest-type freezers are also available but are not movable. These can function in both the vapor or total immersion phase of LN₂. Larger cryogenic storage tanks can also be attached to LN₂ supply tanks or manifold that will automatically fill the storage tanks when a sensor detects low levels of LN₂ or an insufficient temperature level. Inside the cryogenic storage tanks are different storage layout systems to hold the many varied cryopreservation devices.

How are cryogenic storage tanks maintained and monitored?

Cryogenic storage tanks are usually stored in a secure access room. All tanks are connected to an alarm system that is capable of remotely alerting laboratory staff members in event of a significant temperature variation or LN₂ level deviation. In the event of an alarm, standard protocol calls for laboratory staff to immediately report to the laboratory at any time to investigate the cause of the alarm. The alarm system is tested monthly and should undergo preventative maintenance at least once a year. Standard protocols for following these regimens is essential to reduce the contribution of human error to catastrophic failure.

CONTINUED ON PAGE 33

BENCH TO BEDSIDE

Each month
Contemporary OB/GYN

sorts through the enormous pile of published research, bulletins and releases to find the advances of most importance to clinicians.

TAILORx trial finds chemotherapy not beneficial for all breast cancer patients

According to research published in The New England Journal of Medicine, chemotherapy is not more beneficial than treatment with hormone therapy alone for women with hormone receptive (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, and axillary node-negative breast cancer. Contemporaryobgyn.net/TAILORx

USPSTF recommends alcohol screening for adults, pregnant women

Public comments are being solicited on a new systematic review from the US Preventive Services Task Force (USPSTF) on unhealthy alcohol use. The panel’s recommendations include screening pregnant women for alcohol use, which is in keeping with guidance from the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO). Contemporaryobgyn.net/USPSTFalcohol

Live birth in world’s first in utero stem cell transplant trial

The first birth from a groundbreaking trial of in utero stem cell transplantation suggests that fetal therapy may be a viable new option for alpha thalassemia (ATM). The delivery at 37 weeks’ gestation, which occurred in February at UCSF, was announced by researchers there who are conducting a phase 1 clinical trial to demonstrate the safety, feasibility, and efficacy of performing in utero stem cell transplantation (SCT) on fetuses affected with ATM. Contemporaryobgyn.net/TransplantBirth

Study: Mifepristone pretreatment improves management of first-trimester pregnancy loss

Pretreatment with mifepristone followed by treatment with misoprostol resulted in a higher likelihood of successful management of first-trimester pregnancy loss than treatment with misoprostol alone, according to a study published in The New England Journal of Medicine. Contemporaryobgyn.net/mifepristone

Are patients less satisfied with MDs who reduce opioids?

Results of new research suggest that reducing dosages for chronic pain may not lead to patient dissatisfaction with care. The findings, published in The American Journal of Managed Care, are from a retrospective cohort study by Kaiser Permanente Southern California. Contemporaryobgyn.net/opioidMDs
Genitourinary syndrome of menopause
Underdiagnosed and undertreated

As the US population ages, incidence of GSM is likely to rise, and ob/gyns must be proactive in counseling and treating patients

by NANETTE SANTORO, MD, AND IVY LIN, MD

Introduction
Genitourinary syndrome of menopause (GSM) is a relatively new term that describes the constellation of lower urogenital tract signs and symptoms associated with a low-estrogen state. Prior nomenclature such as vulvovaginal atrophy and atrophic vaginitis failed to encompass the frequent urinary symptoms associated with menopause. GSM, which arose from a 2013 terminology consensus conference by the International Society for the Study of Women’s Sexual Health (ISSWSH) and North American Menopause Society (NAMS), is seen as a more generalizable and inclusive term with fewer negative connotations that should replace older jargon.

GSM describes the genital, sexual and urinary changes in the lower genital tract associated with menopause. It is a chronic disorder that is unlikely to improve over time without treatment. The estrogen receptors present throughout the lower genitourinary tract respond to the decrease in circulatory estrogen after menopause with thinning of the vaginal and uro-epithelium, an increase in vaginal pH, decreases in collagen and tissue elasticity and fewer blood vessels. Physiologically, this manifests with symptoms of vaginal dryness, vaginal irritation, vaginal itching and may affect sexual function due to dyspareunia and diminished lubrication (Table 1). It is important to note that GSM also includes urologic signs and symptoms. Postmenopausal patients are more prone to recurrent urinary tract infections (UTIs), dysuria, urinary frequency and urgency.

Prevalence
GSM can be clinically detected in up to 90% of postmenopausal women undergoing evaluation. However, only about one-third of menopausal women report vulvovaginal symptoms when surveyed. According to the 2010 United States census, there are approximately...
50 million women over age 51, the average age of menopause. That means approximately 17 million women experience GSM symptoms, a number that is likely increasing due to population demographics. Studies have shown that many of these women rate their symptoms as either moderate or severe. Affected women perceive declines in quality of life similar to those of patients with chronic conditions such as arthritis, chronic obstructive pulmonary disease (COPD) and irritable bowel syndrome. GSM symptoms also negatively impact sexual satisfaction in over half of patients and strain personal relationships.

Despite the prevalence of GSM, the condition continues to be under-recognized and undertreated due to a combination of patient and provider factors. Only about one-quarter of women ever discuss their symptoms with a provider. Frequently, the burden falls on the patient to initiate the conversation. The most common barrier to patients discussing GSM is a belief that their symptoms should just be accepted as a natural part of aging and menopause. Other women fail to even link their symptoms with menopause. This demonstrates a large gap in patient knowledge and an opportunity to educate patients on GSM as a medical condition. Providers need to take the initiative in screening and patient education. However, studies have shown that providers are doing a poor job at this. One study found that only 13% of providers queried their patients for GSM symptoms. Even after diagnosis, the majority of women with GSM go untreated despite studies demonstrating a negative impact on quality of life. Hesitation to prescribe treatment by providers as well as patient-perceived concerns over safety profiles limit use of topical vaginal therapies.

**Treatment**

The primary goal of GSM treatment is symptom relief. Options include lifestyle changes and non-hormonal and hormonal treatments. Hormonal therapies include both topical and systemic approaches. Vaginal lasers marketed for GSM have also recently arrived on the market. The theory behind laser therapy is that collagen growth is stimulated, thereby strengthening the vagina. However, medical evidence from controlled, randomized clinical trials (RCTs) on which to base a recommendation is lacking at this time.

**Lifestyle modifications**

Tobacco abuse has been associated with increased atrophic vaginal changes as well as menopause at a younger age. Tobacco cessation should be encouraged. Some providers recommend regular sexual intercourse, including the Society of Obstetricians and Gynaecologists of Canada. While more sexual activity is associated with fewer atrophic changes and GSM, it is unclear whether this finding reflects the fact that intercourse improves symptoms, or rather, that patients with fewer symptoms and less dyspareunia are more likely to engage in intercourse. The latter may well be the more likely explanation. General vulvar hygiene should be maintained with the goal of keeping the area dry and free of irritants. Cotton underwear is preferable, as well as avoidance of fragrance-containing products.

**Non-hormonal therapy**

Non-hormonal therapies for GSM include vaginal moisturizers and lubricants. Vaginal moisturizers function to replace natural vaginal secretions while vaginal lubricants reduce friction during intercourse. Moisturizers commonly contain molecules that are capable of retaining large amounts of water and releasing them slowly. Examples include hyaluronic acid and polycarbophil gel. Some moisturizers have a low pH to help

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**TABLE 1** Common signs and symptoms of GSM

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal dryness</td>
<td>Loss of vaginal rugae</td>
</tr>
<tr>
<td>Irritation, burning, itching of vagina and</td>
<td>Vaginal tissue paleness</td>
</tr>
<tr>
<td>vulva</td>
<td></td>
</tr>
<tr>
<td>Decreased lubrication during intercourse</td>
<td>Thin, dry, friable tissue of vagina and</td>
</tr>
<tr>
<td></td>
<td>vulva</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>Cervix smaller, retracted</td>
</tr>
<tr>
<td>Postcoital bleeding</td>
<td>Decreased size of labia minora</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Decreased pubic hair density</td>
</tr>
<tr>
<td>Increased urinary frequency and urgency</td>
<td>Prominent urethral meatus</td>
</tr>
<tr>
<td></td>
<td>Recurrent urinary tract infections</td>
</tr>
</tbody>
</table>
acidify the vaginal environment back to premenopausal physiologic levels; however, products with a pH of less than three should be avoided. Lubricants are also typically water-based but contain additional oil, glycerin, or silicone. The osmolality of the lubricant should also be taken into account. Certain brands are markedly hyperosmolar, such as Astroglide, KY Jelly, and Replens. Although these agents are often effective, their high osmolality can theoretically dehydrate the adjacent vaginal epithelium and cause irritation.12 Vaginal moisturizers and lubricants provide temporary relief and may be sufficient for patients with only mild symptoms. Other non-hormonal options such as black cohosh or soy have not been shown to improve GSM.13 These are not recommended for treatment.

Vaginal estrogen and alternatives

The gold standard pharmacologic treatment for GSM is still vaginal estrogen, especially for patients who are not suffering from systemic symptoms of menopause. Low-dose vaginal estrogen is effective and safe (Table 2).14-17 Vaginal formulations act locally to target GSM symptoms, and result in minimal, transient elevations of circulating estradiol. Oral estrogen preparations should be reserved for primary treatment of vasomotor and other systemic menopausal symptoms. Patients who are on systemic hormonal therapy (HT) may still have GSM symptoms and therefore may get additional benefit from topical estrogen if they do not note sufficient improvement after a few months of systemic dosing. Vaginal estrogen, supplied as either estradiol or conjugated equine estrogen, comes in a variety of low-dose formulations including creams, rings and tablets. The different formulations are all considered equally effective. A new vaginal estrogen in the form of an estradiol soft gel is currently in phase III trials, formulated to not require an applicator for insertion and to dissolve faster, with less vaginal discharge than other preparations.18

Ultimately, the specific vaginal estrogen formulation should be personalized for individual patients according to cost, convenience and preference. Patients are typically instructed on daily use during initiation, then to decrease frequency to twice weekly. Cessation of treatment is expected to lead to a return of symptoms. Compounded estrogen products are not recommended for use due to variability in production with inconsistent strengths, no data on individual pharmacokinetics of a vaginally administered dose, and lack of safety data.

Various studies have demonstrated the safety of vaginal estrogen. Women using low-dose vaginal estrogen tablets and rings have a very small increase in serum estradiol levels that remains well within the normal postmenopausal range.19 Data from the Women’s Health Initiative have also demonstrated the relative safety of vaginal estrogen preparations. Over 45,000 women using either vaginal estrogen cream or tablet were followed. On average, women used vaginal estrogen for a median duration of two years for a median follow-up of seven years.20 Vaginal estrogen users had similar rates of endometrial cancer, invasive breast cancer and pulmonary embolism/deep vein thrombosis as non-users. In fact, risks of coronary heart disease, fracture and all-cause mortality were lower in vaginal estrogen users.20

Multiple studies have investigated the endometrial safety of vaginal estrogen, including two randomized controlled trials (RCTs) that documented no difference in endometrial hyperplasia or cancer with endometrial biopsy samples after 12 months of vaginal estrogen exposure.21,22 Additional progestin for endometrial protection, therefore, is not thought to be needed during low-dose vaginal estrogen use. Contraindications to vaginal estrogen use include unexplained uterine bleeding, endometrial hyperplasia or cancer and use of aromatase inhibitors (AIs).

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Commercially available low-dose vaginal estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulation</td>
<td>Brand name</td>
</tr>
<tr>
<td>Cream</td>
<td>Estrace</td>
</tr>
<tr>
<td>Cream</td>
<td>Premarin</td>
</tr>
<tr>
<td>Ring</td>
<td>Estring</td>
</tr>
<tr>
<td>Tablet</td>
<td>Vagifem</td>
</tr>
</tbody>
</table>

Download a patient education handout at contemporaryobgyn.net/treatingGSM
The packaging for vaginal estrogen contains the same information as for systemic estrogen. The package insert includes a "black box" warning, which states an increased risk of: "endometrial cancer, cardiovascular disorders, breast cancer and probable dementia." This warning, which understandably frightens patients, is applied by the US Food and Drug Administration (FDA) to any estrogen-containing pharmaceutical. Yet all of the data supporting this warning derives from clinical trials involving systemic hormone exposure at much higher doses. With the current abundant data that exist demonstrating the differences in safety profiles and serum estrogen levels between vaginal estrogen and oral estrogen, NAMS and other organizations have teamed up to recommend to the FDA that the boxed warning be removed from topical estrogen preparations.23

Alternatives to estrogen for treatment of GSM include selective estrogen receptor modulators (SERM). SERMs act to stimulate estrogen receptors in certain tissues while blocking them in others. The most well-known SERMs were designed to treat breast cancer. Specific SERMs are now on the market to treat GSM and serve as pharmacologic alternatives for women who are not candidates for estrogen use. Ospemifene has been available since 2013 and is approved for treatment of dyspareunia due to GSM as a daily oral tablet. Studies have demonstrated improvement in GSM symptoms compared to placebo.24 Ospemifene acts as an agonist on vaginal epithelium while avoiding a stimulatory effect on endometrial and breast tissue. Endometrial safety, based on endometrial thickness, has been demonstrated out to one year of use.25 Ospemifene has an antagonistic effect on breast tissue in ex vivo studies, however, its use and safety in patients with a history of breast cancer has yet to be studied.26 Side effects of ospemifene that may limit its use include an increase in hot flashes, need for daily, systemic administration, and delayed therapeutic effect.24 Many women do not see benefits until about six months after initiation. Venous thromboembolism (VTE) risk is also a concern for any SERM and the safety of ospemifene appears similar to other SERMs, with a small increase in risk that is not as much as the risk seen with estrogen. Lasofoxifene is another SERM not yet approved for use in the United States. It has been shown to help GSM symptoms while also improving bone density and decreasing breast cancer risk in a postmenopausal population.27,28 However, lasofoxifene has also been associated with an increase in endometrial polyps, though not necessarily hyperplasia or cancer.29 Lasofoxifene seems promising as a possible treatment option in patients with a history of breast cancer but as of now, it remains in phase III development. We suggest use of ospemifene for patients who fail over-the-counter treatments and who have contraindications to vaginal estrogen treatment or who strongly want to avoid estrogen therapy. Providers should be aware that ospemifene packaging contains a black box warning regarding VTE risk.

The newest alternative to vaginal estrogen treatment is vaginal dehydroepiandrosterone (DHEA), also known as prasterone, which was approved in 2016 for dyspareunia related to GSM. Prasterone likely works by local conversion of androstenedione and testosterone into estrone and estradiol. In RCTs, prasterone has been shown to decrease dyspareunia compared to placebo in postmenopausal women.30 Prasterone increases circulating DHEA, testosterone, and estrone, however, hormone levels are maintained within normal postmenopausal ranges after 12 weeks.31 Studies regarding prasterone safety in patients with a history of cancer, specifically, breast cancer, have not been conducted yet. Prasterone is a vaginal insert that, unlike vaginal estrogen, requires daily administration.

Though there have not been head-to-head trials comparing ospemifene or prasterone against vaginal estrogen, the efficacy of vaginal estrogen has been well demonstrated and its safety profile is far lengthier than that of the current alternatives. In addition, vaginal estrogen does not require daily administration unlike ospemifene or prasterone. We still recommend vaginal estrogen as a first-line option for patients who seek pharmaceutical treatment for GSM.

Fractional carbon dioxide (CO₂) laser therapy, popularly called "vaginal rejuvenation," has been proffered as an attractive alternative to hormonal therapy. Laser treatments use CO₂ wavelengths to ablate and coagulate mucosal tissue, thereby stimulating wound healing and tissue remodeling with increased collagen.
Managing obstetric emergencies: Anaphylactoid syndrome of pregnancy (aka AFE)

Ob/gyns must be ready to move quickly when a patient exhibits the sudden and unexpected signs of anaphylactoid syndrome (ASP).

by STEVEN L. CLARK, MD

Anaphylactoid syndrome of pregnancy (ASP) remains a puzzling and deadly condition despite decades of recognition and research. It is a leading cause of maternal mortality, yet it likely has been overdiagnosed, with many unexplained peripartum maternal deaths historically attributed to ASP. The aim of this discussion is to shed light on more recent research and our current understanding of this life-threatening obstetric emergency.

Typical presentation

Women with ASP may present with the classic triad of hypoxia, hypotension, and coagulopathy resulting in sudden cardiovascular collapse or cardiac arrest. In less typical cases, one or more of these signs may be blunted or absent. ASP usually occurs during labor or within minutes of delivery, either vaginal or cesarean. Patients may experience symptoms of anxiety, a sense of impending doom, confusion, or shortness of breath which are accompanied by abnormal vital signs (Table 1), loss of consciousness, or cardiopulmonary arrest. Seizures may also occur with this condition, which may be mistaken for eclampsia. Fetal heart rate (FHR) tracing and uterine contraction monitoring may reveal uterine tachysystole as a direct result of maternal catecholamine release; this initial shock reaction also includes shunting of uterine blood from the uterus and placenta to transiently maintain blood pressure and perfusion of maternal vital organs. Both of these processes result in signs of fetal hypoxia and FHR abnormalities, which often precede maternal cardiopulmonary manifestations.

Coagulopathy is also a major component of classic ASP, although some patients may expire before their clotting status can be assessed. Disseminated intravascular coagulation (DIC) can result in massive hemorrhage and may be detected clinically by bleeding from the vagina, during cesarean, or from the incision postoperatively, in-

Table 1: Vital signs associated with ASP

- Suspect ASP in a patient who has the triad of hypoxia, hypotension, and coagulopathy either in labor or near time of delivery.
- ASP is a diagnosis of exclusion, easy to confuse with other conditions such as pulmonary embolus or sepsis.
- High-quality CPR is the first step in management together with activation of emergency team members such as nursing, MFM, critical care and the blood bank.

DR CLARK is Professor, Baylor College of Medicine/Texas Children’s Hospital, Houston.
travenous sites or the bladder (hematuria.) In the acute care setting, presence of coagulopathy may be the only clinical feature distinguishing ASP from massive pulmonary embolism; however, the latter occurs primarily in the postpartum period whereas ASP is primarily an intrapartum condition.

Etiology and mechanism

Most cases of ASP occur peripartum, during labor (70%) or within minutes of delivery (30%). Originally, it was hypothesized that fetal squamous cells entering the maternal circulation and obstructing the pulmonary vascular tree were responsible for the hemodynamic manifestations of this condition. This was based on autopsy reports of eight women who died during labor in whom such squamous cells were identified. Based on this presumed pathophysiologic mechanism, this syndrome was originally designated amniotic fluid embolism but it is now known as anaphylactoid syndrome of pregnancy (ASP). This is because we now have an improved understanding of the pathophysiology of the condition, based on recent research.\(^2,4\)

Subsequent studies demonstrated presence of squamous cells in pregnant women with other conditions, and the clinical similarity of this condition to other manifestations of the systemic inflammatory response syndrome (SIRS) cast doubt upon the theory involving squamous cells. Recent evidence also demonstrates that an insufficient number of squamous cells exist in amniotic fluid to cause any significant obstruction of the pulmonary vasculature, even were the entire content of the term amniotic cavity infused into the maternal circulation.\(^7\)

Because the clinical picture of ASP mimics an allergic or proinflammatory reaction, and it occurs at the time when fetal tissue is likely to enter the maternal circulation, it appears that the mechanism of ASP involves an abnormal host (maternal) immunological response to a common physiologic phenomenon. Specifically, fetal antigens enter the maternal circulation during labor or delivery and elicit a proinflammatory response driven by endogenous mediators including cytokines. This SIRS-like process may include pulmonary vasoconstriction, direct pulmonary injury and capillary leak (acute respiratory response syndrome) and depression of myocardial contractility. DIC and hemorrhage are downstream effects of systemic activation of inflammatory mediators and the coagulation cascade. Unfortunately, at present there are no identifiable clinical risk factors for pre-labor identification of at-risk maternal-fetal pairs nor are there any preventative measures for ASP.

Diagnosis

In the past, diagnosis of ASP was commonly made at the time of autopsy when fetal squamous cells were detected in the maternal pulmonary circulation. In fact, in some countries, the case definition of ASP still includes pathological diagnosis of fetal squamous cells/debris in the maternal pulmonary circulation, despite clear evidence that this finding is non-diagnostic.\(^2,4,6,8,9\)

We support the recommendation of the Society for Maternal-Fetal Medicine (SMFM) that ASP is a clinical diagnosis and often one of exclusion, involving elimination of other more common causes of maternal cardiovascular instability or coagulopathy. (Table 2).\(^10\)

A multispecialty expert panel including representatives of the Society for Maternal-Fetal Medicine, the National Institutes of Health and the Centers for Disease Control have published a set of diagnostic criteria for AFE for use in development and evaluation of studies of AFE/ASP (Table 1).\(^10\) These criteria were developed to address the problem of a body of existing literature heavily populated with patients who did not actually have ASP. Such errors have contributed to confusion and misunderstanding regarding the nature of this condition, risk factors and prognosis.

Retrospective review of cases of suspected AFE/ASP by experts have found that up to 50% of cases coded as AFE/
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Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered <37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

**Limitation of use:** While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. **It is not intended for use in women with multiple gestations or other risk factors for preterm birth.**

**Important Safety Information for Makena® (hydroxyprogesterone caproate injection)**

- Do not use Makena in women with any of the following conditions:
  - Current or history of thrombosis or thromboembolic disorders
  - Known or suspected breast cancer, other hormone-sensitive cancer or history of these conditions
  - Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
  - Cholestatic jaundice of pregnancy
  - Liver tumors, benign or malignant, or active liver disease
  - Uncontrolled hypertension
- Makena should be discontinued if thrombosis or thromboembolism occurs
- Allergic reactions, including urticaria, pruritus and angioedema, have been reported with use of Makena or with other products containing castor oil
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- Administered in ~15 seconds

**DISCREET**

- Shorter, thinner, nonvisible needle
- Administered in the back of the upper arm—no need for patients to disrobe

**ADMINISTRATION FRIENDLY**

- Protective needle guard to help minimize accidental needle-sticks
- Appointment flexibility—no need for private exam rooms

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More than Makena.

- Women receiving Makena should be monitored if they:
  - Are prediabetic or diabetic
  - Have conditions that may be affected by fluid retention, such as preeclampsia, epilepsy, cardiac or renal dysfunction
  - Have a history of clinical depression; Makena should be discontinued if depression recurs
  - Develop jaundice; consider whether benefit of use warrants continuation
  - Develop hypertension

- Certain pregnancy-related fetal and maternal complications or events were numerically increased in Makena-treated subjects as compared to placebo subjects, including miscarriage (2.4% vs. 0%) and stillbirth (2% vs. 1.3%), admission for preterm labor (16% vs. 13.8%), preeclampsia or gestational hypertension (8.8% vs. 4.6%), gestational diabetes (5.6% vs. 4.6%), and oligohydramnios (3.6% vs. 1.3%)

- In a study where the Makena intramuscular injection was compared with placebo, the most common adverse reactions reported with Makena intramuscular injection (reported incidence in ≥2% of subjects and higher than in the control group) were: injection site reactions (pain [35%], swelling [17%], pruritus [6%], nodule [5%]), urticaria (12%), pruritus (8%), nausea (6%), and diarrhea (2%)

- In studies where the Makena subcutaneous injection using auto-injector was compared with Makena intramuscular injection, the most common adverse reaction reported with Makena Auto-Injector use (and higher than with Makena intramuscular injection) was injection site pain (10% in one study and 34% in another)

Please see brief summary of full Prescribing Information on the following page.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please consult full prescribing information.

INDICATIONS AND USAGE

Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered ≥37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity. Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

CONTRAINDICATIONS

Do not use Makena in women with any of the following conditions:
- Control group.
- Pain, which was reported after at least one injection by 34.8% of the Makena group.
- The most common adverse reaction with intramuscular injection was injection site pain.
- Makena is not indicated for use in women under 16 years of age. Safety and efficacy data are insufficient to determine a drug-associated risk of adverse developmental outcomes as none of the Makena-treated women received the drug during the first trimester of pregnancy. In animal reproduction studies, intramuscular administration of hydroxyprogesterone caproate to pregnant rats during gestation at doses 5 times the human dose equivalent based on a 60-kg human was not associated with adverse developmental outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Data: Animal Data Reproduction studies of hydroxyprogesterone caproate administered to various animal species have been reported in the literature. In nonhuman primates, embryo lethality was reported in rhesus monkeys administered hydroxyprogesterone caproate up to 2.4 and 24 times the human dose equivalent, but not in cynomolgus monkeys administered hydroxyprogesterone caproate up to 2.4 times the human dose equivalent based on a 60-kg human. There were no teratogenic effects in either strain of monkey. Reproduction studies have been performed in mice and rats at doses up to 85 and 5, respectively, times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to hydroxyprogesterone caproate. Lactation Risk Summary: Low levels of progestins are present in human milk with the use of progestin-containing products, including hydroxyprogesterone caproate. Published studies have reported no adverse effects of progestins on the breastfed child or on milk production. Pediatric Use Makena is not indicated for use in women under 16 years of age. Safety and effectiveness in patients less than 16 years of age have not been established. A small number of women aged 18 years and older were studied, but safety and efficacy are expected to be the same in women aged 16 years and above as for users 18 years and older. Hepatic Impairment No studies have been conducted to examine the pharmacokinetics of Makena in patients with hepatic impairment. Makena is extensively metabolized and hepatic impairment may reduce the elimination of Makena. 

Table 1 Selected Fetal Complications

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Makena n/N</th>
<th>Control n/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage (&lt;20 weeks)</td>
<td>5/209</td>
<td>0/107</td>
</tr>
<tr>
<td>Stillbirth (≥20 weeks)</td>
<td>6/305</td>
<td>2/153</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Makena N=310</th>
<th>Control N=153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission for preterm labor1</td>
<td>16.0</td>
<td>13.8</td>
</tr>
<tr>
<td>Preeclampsia or gestational hypertension</td>
<td>8.8</td>
<td>4.6</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>5.6</td>
<td>4.6</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>3.6</td>
<td>1.3</td>
</tr>
</tbody>
</table>

1Other than delivery admission

Common Adverse Reactions: The most common adverse reaction with intramuscular injection was injection site pain, which was reported after at least one injection by 34.8% of the Makena group and 32.7% of the control group. Table 3 lists adverse reactions that occurred in ≥2% of subjects and at a higher rate in the Makena group than in the control group.

Table 3 Adverse Reactions Occurring in ≥2% of Makena-Treated Subjects and at a Higher Rate than Control Subjects

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Makena N=310</th>
<th>Control N=153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site pain</td>
<td>34.8</td>
<td>32.7</td>
</tr>
<tr>
<td>Injection site swelling</td>
<td>17.1</td>
<td>7.8</td>
</tr>
<tr>
<td>Urticaria</td>
<td>12.3</td>
<td>11.1</td>
</tr>
<tr>
<td>Pruritus</td>
<td>7.7</td>
<td>5.9</td>
</tr>
<tr>
<td>Injection site pruritus</td>
<td>5.8</td>
<td>3.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.8</td>
<td>4.6</td>
</tr>
<tr>
<td>Injection site nodule</td>
<td>4.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

In the clinical trial using intramuscular injection, 2.2% of subjects receiving Makena were reported as discontinuing therapy due to adverse reactions compared to 2.6% of control subjects. The most common adverse reactions that led to discontinuation in both groups were urticaria and injection site pain/swelling (1% each). Pulmonary embolus in one subject and injection site cellultis in another subject were reported as serious adverse reactions in Makena-treated subjects. Two clinical studies were conducted in healthy post-menopausal women, comparing Makena administered via subcutaneous auto-injector to Makena administered as an intramuscular injection. In the first study, injection site pain occurred in 3/30 (10%) of subjects who used the subcutaneous auto-injector vs. 2/30 (7%) of subjects receiving intramuscular injection. In the second study, injection site pain occurred in 20/59 (34%) of subjects who used the subcutaneous auto-injector vs. 5/61 (8%) of subjects receiving intramuscular injection.

Postmarketing Experience

The following adverse reactions have been identified during postapproval use of Makena. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Body as a whole: Local injection site reactions (including erythema, urticaria, rash, irritation, hypersensitivity, warmth); fatigue; fever; hot flashes/flushes • Digestive disorders: Vomiting • Induction: Urinary tract infection • Nervous system disorders: Headache, dizziness • Pregnancy, puerperium and perinatal conditions: Cervical incompetence, premature rupture of membranes • Reproductive system and breast disorders: Cervical dilation, shortened cervix • Respiratory disorders: Dyspnea, chest discomfort

DRUG INTERACTIONS

In vitro drug-drug interaction studies were conducted with Makena. Hydroxyprogesterone caproate has minimal potential for CYP1A2, CYP2A6, and CYP2B6 related drug-drug interactions at the clinically relevant concentrations. In vitro data indicated that there were no clinically relevant concentrations of hydroxyprogesterone caproate to not inhibit the activity of CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. No in vivo drug-drug interaction studies were conducted with Makena.

USE IN SPECIFIC POPULATIONS

Pregnancy Risk Summary: Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Fetal, neonatal, and maternal risks are discussed throughout labeling. Data from the placebo-controlled clinical trial and the infant follow-up safety study did not show a difference in adverse developmental outcomes between children of Makena-treated women and children of control subjects. However, these data are insufficient to determine a drug-associated risk of adverse developmental outcomes as none of the Makena-treated women received the drug during the first trimester of pregnancy. In animal reproduction studies, intramuscular administration of hydroxyprogesterone caproate to pregnant rats during gestation at doses 5 times the human dose equivalent based on a 60-kg human was not associated with adverse developmental outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Data: Animal Data Reproduction studies of hydroxyprogesterone caproate administered to various animal species have been reported in the literature. In nonhuman primates, embryo lethality was reported in rhesus monkeys administered hydroxyprogesterone caproate up to 2.4 and 24 times the human dose equivalent, but not in cynomolgus monkeys administered hydroxyprogesterone caproate at doses up to 2.4 times the human dose equivalent, every 7 days between days 20 and 146 of gestation. There were no teratogenic effects in either strain of monkey. Reproduction studies have been performed in mice and rats at doses up to 85 and 5, respectively, times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to hydroxyprogesterone caproate.

Liver Tumors, Benign or Malignant, or Active Liver Disease

• Cholestatic jaundice of pregnancy

Pediatric Use

• Undiagnosed abnormal vaginal bleeding unrelated to pregnancy

Other than delivery admission

• Known or suspected breast cancer, other hormone-sensitive cancer, or history of these conditions

• Undiagnosed abnormal vaginal bleeding unrelated to pregnancy

• Chronic hepatitis or hepatic impairment may reduce the elimination of Makena.

• No studies have been conducted to examine the pharmacokinetics of Makena.
ASP have other more likely diagnoses, making use of population-based studies derived from administrative coding data particularly problematic.11 These criteria have been validated; while their use will reliably exclude women without ASP from research databases, they will also exclude a small number of women with atypical presentations of this condition.12

Prognosis and recurrence

Reported mortality from ASP/AFE has decreased significantly over the last several decades, in part due to recognition of the existence of less severe, atypical presentations. Recent reports suggest a survival rate of up to 80%.13 However, heavy contamination of administrative coding-based studies with patients who do not have this condition suggest caution in interpretation of such mortality data. In reports based on actual medical records review by experts in critical care obstetrics, both incidence of ASP and survival rates are generally lower.2,11 In women whose initial presentation includes cardiopulmonary arrest, prognosis remains poor. After recovery from hemodynamic derangements and coagulopathy, many patients will have acute lung injury/acute respiratory distress syndrome. Hypoxic brain injury may also be sustained due to the initial severe hypoperfusion and hypoxia. Echocardiography may reveal evidence of right ventricular overload and dilation, pulmonary artery hypertension, and contractile dysfunction of the left ventricle.14-16 Risk of recurrence with ASP is unknown, however, to date no recurrences have been reported. Given the apparent uncommon and unique interaction between patient and fetus-specific antigen involved in this condition, recurrence would not be expected with a different fetus.

Management strategy

When faced with sudden peripartum cardiopulmonary collapse or suspected ASP, the obstetrician’s initial role is to recognize the various possible etiologies. If ASP is suspected based on the triad of hypoxia, hypotension, and coagulopathy in addition to timing around time of delivery, the first step is to provide high-quality cardiopulmonary resuscitation (CPR) as indicated (Table 3).

Treatment is primarily supportive. An important concurrent step is to ask for help from team members including nursing, obstetrics partners or maternal-fetal medicine experts, anesthesia personnel, critical care personnel, and the blood bank. Left lateral uterine displacement, or in a potentially viable fetus (≥23 weeks’ gestation) delivery during resuscitation efforts may increase cardiac preload and improve the effectiveness of CPR by relieving inferior vena cava pressure caused by the gravid uterus. Intubation will likely be needed for ongoing respiratory support. Even prior to clinical signs of hemorrhage, we recommend notifying the blood bank and perhaps activating a massive transfusion protocol if suspicion for ASP is high as at least 80% of these women will develop DIC.4 Based on the presumed pathophysiology of ASP, a novel regimen of atropine, ondansetron and ketorolac has been proposed.17 Although survival with use of this regimen has been described and may reasonably be incorporated into standard treatment approaches for ASP, its actual efficacy is uncertain.

The Amniotic Fluid Embolism Foundation, a unique collaboration between private and academic institutions, has been established both to assist patients and families who have encountered ASP and to promote research efforts. Information regarding participation in an ongoing national registry of ASP cases is also available through the foundation website, at https://www.afesupport.org/.

**DISCLOSURES** The author reports no potential conflicts of interest with regard to this article.

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Round-up of authoritative sources for further reading.

STATEMENTS AND GUIDELINES

Amniotic fluid embolism: Diagnosis and management
Guideline from the Society for Maternal-Fetal Medicine with the assistance of Luis D. Pacheco, MD; George Saade, MD; Gary D. V. Hanks, MD; Steven L. Clark, MD

MATERNAL MORTALITY IN THE MEDIA
A collection of articles and reports from the mainstream media to help you stay up to date. Recent coverage includes an update on the Maternal Health Accountability Act of 2017 (S1112), a congresswoman’s editorial on why she introduced the MOMMA Act, and a look at why Pennsylvania’s maternal death rate has doubled in 20 years.
http://www.contemporaryobgyn.net/modern-medicine-feature-articles/maternal-mortality-media

JOURNAL ARTICLES AND REFERENCES

UpToDate
Chapter on amniotic fluid embolism syndrome with literature review current through May 2018

OB HOSPITAL CLOSURES
To help illustrate the impact these closures have on their patients, Contemporary OB/GYN will post links to these reports on our Hospitals Closures page. Among the latest: An ob/gyn sues a hospital chain for killing his practice; a group of clergy led a federal complaint saying a hospital closure is a civil rights violation; and hospitals in Houston are taking steps to reduce the maternal mortality rate.
http://www.contemporaryobgyn.net/modern-medicine-feature-articles/ob-hospital-closures

Cardiac arrest during pregnancy: ongoing clinical conundrum
This recently published study from Carolyn Zelop, MD, and Stephanie Martin, DO, discusses the specifics of dealing with maternal cardiac arrest that occurs during pregnancy. https://www.ajog.org/article/S0002-9378(17)32806-5/abstract

DR. ZELOP is Director of Ultrasound, Fetal Echocardiography and Perinatal Research at Valley Hospital in Ridgewood, New Jersey, and Clinical Professor of Obstetrics and Gynecology at NYU School of Medicine, New York. She works actively with ACOG and the American Heart Association (AHA) on issues of maternal cardiac arrest and mortality. Dr. Zelop is the Series Editor of the Contemporary OB/GYN series on maternal mortality.

DR. MARTIN is Medical Director and Co-owner of Clinical Concepts in Obstetrics, LLC, Scottsdale, Arizona.

“This unique population of young, yet critically ill women can respond to appropriate treatment and may be more salvageable than most patients requiring CPR.”
ERAS: Improved outcomes post-cesarean

by ELIZABETH CHEROT, MD

The concept of an enhanced recovery program following elective surgery was developed more than 15 years ago.1,2 It refers to multimodal care pathways designed to accelerate patient recovery by reducing the surgical stress response and supporting the patient’s physiologic function. These procedures and anesthesia-specific pathways form an integrated continuum, as the patient moves from home through the preoperative, intraoperative, and postoperative phases of surgery and returns home again.3

A key component of enhanced recovery after surgery (ERAS) is patient and family engagement, which helps patients better prepare for surgery, hospitalization and discharge. The aim of enhanced recovery is to optimize multiple aspects of patient care, improve recovery, and facilitate earlier discharge with increasing patient satisfaction and quality of care. One of the central elements of our ERAS protocol is the application of multimodal pain interventions to reduce the reliance on opioid-based medications.

Much of the work establishing the benefits of enhanced recovery has been conducted on patients undergoing colorectal surgery, but the same concepts have since been used in gynecology, urology and orthopedics.4 Despite demonstrated success in Europe, the transition to evidence-based enhanced recovery has been slow in surgical and anesthesia practice in the United States, partly because of a lack of awareness, and also due to reluctance of some healthcare team members to embrace change.5 Until recently, there has been little interest in enhanced recovery after cesarean delivery. However, since 2012, multiple obstetrical units in the United Kingdom have introduced enhanced recovery programs in obstetrics and have demonstrated improved quality of care and significant savings with superior patient satisfaction.6-10

The Saint Peter’s/Axia experience with ERAS

The relative lack of experience with enhanced recovery after obstetrical surgery in the United States provided us with a unique opportunity to pioneer this process at Saint Peter’s University Hospital and within Axia Women’s Health. Axia Women’s Health is comprised of more than 250 physicians at over 100 patient care centers located in New Jersey and Pennsylvania. Axia provides patients a full spectrum of care in obstetrics, gynecology, fertility, maternal fetal medicine and women’s imaging centers. We launched our ERAS obstetrical pathway in 2016 for low-risk patients with the diagnosis of repeat cesarean delivery. The four tenets of our program are:

1. Improved preoperative assessment, planning and preparation before admission;
2. Reduced physical stress of surgery;
3. A structured approach to immediate perioperative and postoperative management, including pain relief;
4. Early mobilization.

To improve perioperative assessment, planning and preparation for admission, our team partnered with SeamlessMD, a leading provider of clinical intelligence platforms, to develop a smartphone application to engage and empower our patients. Our patient application has a wide range of capabilities, including the ability to provide preoperative education, timely reminders, and remote monitoring. Our analytics dashboard collects patient-generated data from across the platform. For instance, patients are prompted to report their mood, appearance of their incision, success of breastfeeding, extent of mobilization, pain scores and narcotic use for 2 weeks postoperatively. Our dashboard is monitored and becomes actionable, preventing readmissions and complications while empowering patients.

All patients receive a detailed explanation about ERAS from their obstetrician and download their application during their 36-week prenatal visit. We provide “bite-size” information at the right time using appropriate language delivered by interactive multimedia. We push notifications to patients daily about their surgery, and pre- and postoperative care. Involving patients and their families is fundamental to ERAS.

DR CHEROT is Vice-President of Medical Affairs at Axia Women’s Health, Voorhees, NJ. Her clinical care center is Brunswick Hills Ob/Gyn in East Brunswick, NJ.
and empowers patients to take a significant role in and ownership over decisions regarding their care. The information significantly reduces their fear and challenges preconceived ideas about the operation, pain, recovery and length of stay.

Our second aim was to reduce the physical stress of surgery, so all patients receive a preoperative complex carbohydrate drink and 40 mg of famotidine the evening before their procedure. On the morning of surgery, patients have a second clear complex carbohydrate drink 2 to 3 hours before their scheduled cesarean delivery. This physiologically improves cortisol, insulin and glucose levels and thus recovery. Intraoperatively, we warm patients by placing a whole body warmer on the operating table to prevent hypothermia, and by warming preoperative intravenous (IV) fluids, thus controlling perioperative temperature management. We allow skin to skin in the operating room for early breastfeeding and continue this in the recovery room.

We also reduce the stress of surgery by giving all patients triple antiemetic prophylaxis with 4 mg IV ondansetron, 10 mg dexamethasone, and 10 mg metoclopramide intraoperatively. We also have a standard intraoperative protocol with a subarachnoid block with 0.75% bupivacaine and fentanyl. Additionally, 0.15 mg intrathecal morphine is added to the subarachnoid medications for postoperative pain control.

For our pain management protocol, we give two very effective non-opioid medications in alternating doses around the clock. A patient receives pain medication every 3 hours for the first 24 hours automatically. We give the nonsteroidal anti-inflammatory drugs ketorolac 30 mg IV and 1000 mg acetaminophen IV in alternating sequences. These medications are not on-demand, thus eliminating the up and down roller-coaster effect; patients are no longer over-sedated nor behind on pain control. Starting 24 hours after surgery, patients are switched to 600 mg of ibuprofen and 650 mg of acetaminophen by mouth. These are also distributed in alternating sequence and not on demand. Starting on postoperative Day 2 and only for breakthrough pain, 2 mg of hydromorphone by mouth is available on an as-needed basis.

Lastly, we improve mobilization. There is evidence to suggest that mobilization reduces incidence of venous thromboembolism and pulmonary complications. After transfer to the post-partum floor when full motor function is confirmed, patients are helped to a chair and subsequently walk a few steps with assistance. We remove Foley catheters six hours after surgery and remove IV catheters on Day 0. By removing the Foley catheters on postoperative Day 0, patients are getting up to use the bathroom and on postoperative Day 1 they are eating all meals out of bed and walking the length of the hallways.

Outcomes with ERAS for cesarean
After launching our ERAS program in the fall of 2016, we enrolled over 100 patients in the first year. Our length of stay was reduced from 3.7 days to 2.45 days. As a result of implementing our protocol, our patients have been able to reduce narcotic use five- to six-fold. Most patients do not receive narcotic pain relief in the hospital or after discharge. Other benefits and advantages of our ERAS include minimizing disruption of eating and drinking before surgery and post-delivery, as well as increasing early skin-to-skin contact with their newborns. Patients are ambulating earlier and have their indwelling catheters removed on postoperative Day 0. We have had a 68% response rate to our patient engagement application and an increase in patient satisfaction. Patients appear to be comforted by the ability of providers to monitor their progress through our dashboard after discharge. Axia Women’s Health providers can log in to the web-based dash board from their office and follow all postoperative patients. Providers can follow patient’s pain and mood scores that they have entered on their smart phone application. We follow their breastfeeding success and patients can even send descriptions and pictures of their incision. Axia Women’s Health developed our application with SeamlessMD as a strategy to engage patients in the ERAS protocol. Developing similar communication approaches are likely important to the success of any ERAS protocol.

Conclusion
At this ob/gyn’s institution, a program that helped patients better prepare for surgery, hospitalization, and discharge resulted in shorter lengths of stay and less use of narcotics.
gen formation. Treatment usually consists of a series of short in-office procedures six weeks apart that can cost thousands of dollars. Early case series and other clinical studies have demonstrated improvement in GSM symptoms, however, these studies suffer from small sample sizes (few with more than 20 women), a lack of randomization, no placebo-treated control group, and short follow-up (20 weeks). One small (sample size 45) RCT comparing CO2 laser with vaginal estrogen, each agent alone, both combined, with a no-treatment control group, demonstrated that in the combined treatment group, symptom improvement was greater than treatment with vaginal estrogen alone. However, laser therapy alone was associated with worse dyspareunia.32,33

Larger studies demonstrating long-term safety and efficacy, as well as an analysis of cost-effectiveness, are needed before this modality can be recommended. Moreover, laser therapy for GSM is not FDA-approved at this time. The American College of Obstetricians and Gynecologists’ most recent position statement on laser therapy from May 2016 emphasizes the importance of accurately informing patients of a treatment’s FDA status. It advises providers to be wary regarding new trends based on “promotions or marketing.”34

Breast cancer and GSM
A history of breast cancer complicates treatment of GSM, especially for women with hormone receptor-positive histology. GSM complaints are common in this patient population, especially among patients treated with AIs. First-line therapy should always include non-hormonal vaginal moisturizers and lubricants. If those fail, low-dose vaginal estrogen can be considered. An individualized decision should be made in conjunction with the patient’s oncologist. Few studies have demonstrated vaginal estrogen safety in breast cancer patients. One prospective cohort study followed 69 women with a history of breast cancer who used vaginal estrogen for an average of one year. The study found no increased risk of breast cancer recurrence.35 However, this study was limited by its small sample size and relatively brief follow-up. Larger and longer-term studies are needed to provide more confidence that low-dose vaginal estrogen will not affect breast cancer recurrence rates. If vaginal estrogen is to be used for compassionate reasons, preparations that result in the lowest systemic estradiol concentrations are recommended and treatment should be for the shortest duration possible. Patients using AIs may be at risk if they use vaginal estrogen. A small study demonstrated a rise in serum estradiol levels in six women using Vagifem while taking AIs, thereby eliminating the goal of maximally suppressing estrogen levels.36 Clearly, this is a setting in which shared decision-making with an informed patient is of paramount importance.

Conclusion
GSM continues to be underreported and undertreated, despite the large number of postmenopausal women suffering from this chronic condition. Patients may suffer silently, perceiving their symptoms to be a natural aspect of aging, or may be hesitant to bring up this sensitive issue with their providers. Providers have much room to improve on screening patients for GSM.

Treatment should always start non-pharmacologically with topical moisturizers and lubricants. For those who require prescription therapy, we recommend vaginal estrogen in cream, ring or tablet form. Multiple formulations may need to be trialed before finding a price point acceptable to the patient as insurance coverage varies greatly. Systemic estrogen therapy should be reserved for primary treatment of other, body-wide menopausal symptoms. Patients taking systemic estrogen may still suffer from GSM and could benefit from additional vaginal estrogen therapy. Ospemifene is an alternative prescription option for GSM that is approved by the FDA and may be a good option for patients with a history of breast cancer or who want to avoid estrogen, however, it may increase hot flashes and requires daily oral dosing. The need for more long-term data on prasterone prohibits us from recommending it as a treatment option at this time. Laser therapies also require larger studies on long-term efficacy, safety and cost-effectiveness.

DISCLOSURES The authors report no potential conflicts of interest with regard to this article.

FOR REFERENCES VISIT contemporaryobgyn.net/TreatingGSM
Solosec™ (secnidazole) is the first and only bacterial vaginosis (BV) treatment designed to deliver a complete course of therapy in just one oral dose\textsuperscript{1,2}

To learn how Solosec may make it easy for patients to complete treatment, visit solosechcp.com/journal.

**INDICATION**

SOLOSEC™ (secnidazole) 2g oral granules is a 5-nitroimidazole antimicrobial agent indicated for the treatment of bacterial vaginosis in adult women.

**SELECT IMPORTANT SAFETY INFORMATION**

- **SOLOSEC** is contraindicated in patients with a history of hypersensitivity to secnidazole, other ingredients of the formulation, or other nitroimidazole derivatives.
- Vulvo-vaginal candidiasis may develop with SOLOSEC and require treatment with an antifungal agent.
- Potential risk of carcinogenicity in patients taking single-dose of SOLOSEC to treat bacterial vaginosis is unclear. Chronic use should be avoided.
- SOLOSEC is a single-dose therapy for oral use. The entire contents of SOLOSEC packet should be sprinkled onto applesauce, yogurt or pudding and consumed once within 30 minutes without chewing or crunching the granules. SOLOSEC is not intended to be dissolved in any liquid.
- In clinical studies, the most common adverse events occurring in (≥2%) of patients receiving SOLOSEC 2g oral granules were vulvovaginal candidiasis (9.6%), headache (3.6%), nausea (3.6%), dysgeusia (3.4%), vomiting (2.5%), diarrhea (2.5%), abdominal pain (2.0%), and vulvovaginal pruritus (2.0%).

Please see Brief Summary of Prescribing Information on adjacent page.

To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceuticals, Inc. at 1-844-SOLOSEC (1-844-765-6732) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Rx Only

This Brief Summary does not include all the information needed to use SOLOSEC™ safely and effectively. See full Prescribing Information for SOLOSEC.

SOLOSEC (secnidazole) 2g oral granules

Single oral dose

Initial U.S. approval: 2017

INDICATIONS AND USAGE

SOLOSEC is a nitroimidazole antimicrobial indicated for the treatment of bacterial vaginosis in adult women.

DOSEAGE AND ADMINISTRATION

Administer a single 2-gm packet of granules once orally, without regard to the timing of meals. Sprinkle entire contents of packet onto yogurt, applesauce, or pudding and consume all of the mixture within 30 minutes without chewing or crunching the granules. A glass of water may be taken after the administration of SOLOSEC to aid in swallowing. SOLOSEC is not intended to be dissolved in any liquid.

CONTRAINDICATIONS

Hypersensitivity. SOLOSEC is contraindicated in patients with a history of hypersensitivity to secnidazole, other ingredients of the formulation, or other nitroimidazole derivatives.

WARNINGS AND PRECAUTIONS

Vulvovaginal Candidiasis. The use of SOLOSEC may result in vulvovaginal candidiasis and may require treatment with an antifungal agent.

Potential Risk for Carcinogenicity. Carcinogenicity has been seen in mice and rats treated chronically with nitroimidazole derivatives, which are structurally related to secnidazole. It is unclear if the positive tumor findings in lifetime rodent studies of these nitroimidazoles indicate a risk to patients taking a single dose of SOLOSEC to treat bacterial vaginosis. Avoid chronic use of SOLOSEC.

Drug Resistance. Prescribing SOLOSEC in the absence of proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

ADVERSE REACTIONS

Clinical Trials Experience. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflect exposure to 589 patients, of whom 518 received a 2g dose of SOLOSEC. SOLOSEC was evaluated in 3 clinical trials of patients diagnosed with bacterial vaginosis: 2 placebo-controlled trials (Trial 1 n=215, Trial 2 n=189) and 1 uncontrolled safety trial (Trial 3 n=321).

All patients received a single oral dose of study medication or placebo. Trial 1 evaluated a 1g (this dose is not approved) dose (n=71) and a 2g dose (n=72) of SOLOSEC. Trial 2 evaluated a 2g dose (n=125). The population was female, aged 15 to 54 years. Patients in the placebo-controlled trials were primarily Black or African American (54%) or Caucasian (41%). There were no deaths in the trials. Two patients in Trial 3 discontinued due to vulvovaginal candidiasis in the SOLOSEC-treated arm.

Most Common Adverse Reactions

Among 197 patients treated with a single 2g dose of SOLOSEC in the 2 placebo-controlled trials, Trial 1 and 2, adverse reactions were reported by approximately 29% of patients. Table 1 displays the most common adverse reactions (≥2% in SOLOSEC-treated patients) in these 2 trials.

Table 1: Adverse Reactions Occurring (≥2% SOLOSEC-Treated Patients) in the Pooled Placebo-Controlled Trials 1 and 2 in Adult Women with Bacterial Vaginosis

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>SOLOSEC N=197 n (%)</th>
<th>Placebo N=136 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>19 (9.6)</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>7 (3.6)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (3.6)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (2.5)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (2.0)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Vulvovaginal pruritus</td>
<td>4 (2.0)</td>
<td>2 (1.5)</td>
</tr>
</tbody>
</table>

Among the 321 patients in an uncontrolled trial, Trial 3, adverse reactions were reported in 30% of patients. Vulvovaginal candidiasis (8.4%), nausea (5.3%), vomiting (2.5%) and dysgeusia (3.4%) were the most common adverse reactions reported in this trial.

Postmarketing Experience. The following adverse reactions have been reported during use of other formulations of secnidazole 2g outside of the United States. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Reported adverse reactions were nausea, dysgeusia, abdominal pain, headache, and vomiting.

DRUG INTERACTIONS

Oral Contraceptives. There was no clinically significant drug interaction between secnidazole and the combination oral contraceptive, ethinyl estradiol plus norethindrone. SOLOSEC can be co-administered with combination oral contraceptives (eg, ethinyl estradiol plus norethindrone).

USE IN SPECIFIC POPULATIONS

Pregnancy. Limited available data with SOLOSEC use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. In animal reproduction studies, there were no adverse developmental outcomes when secnidazole was administered orally to pregnant rats and rabbits during organogenesis at doses up to 4 times the clinical dose.

Lactation. Breastfeeding is not recommended. Discontinue breastfeeding for 96 hours after administration of SOLOSEC.

Pediatric Use. The safety and effectiveness of SOLOSEC in pediatric patients below the age of 18 years have not been established.

Geriatric Use. Clinical studies with secnidazole did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Nitroimidazoles, which have similar chemical structures to secnidazole, have been associated with tumors affecting the liver, lungs, mammary, and lymphatic tissues in animals after lifetime exposures. It is unclear if these positive tumor findings in lifetime rodent studies of these nitroimidazoles indicate a risk to patients taking a single dose of SOLOSEC to treat bacterial vaginosis. Avoid chronic use of SOLOSEC.

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Secnidazole was positive in the bacterial reverse mutation assay, but was negative for the rat micronucleus test and mouse lymphoma test. In a rat fertility study, females were dosed for 2 weeks prior to mating until Day 7 of gestation with males that were dosed for a minimum of 28 days before cohabitation. No parental toxicity or adverse effects on mating performance, estrous cycles, fertility or conception was observed at doses of up to the maximum tolerated dose (300 mg/kg/day, approximately 1.4 times the recommended dose based on AUC comparisons).

PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (Patient Information).

Manufactured for and Distributed by: Lupin Pharmaceuticals, Inc. Baltimore, MD 21202

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NP-SOL-0004
Long-term maternal benefits of breastfeeding

Longer durations of breastfeeding are associated with improved health outcomes for mothers and should be supported by ob/gyns.

by ADETOLA LOUIS-JACQUES, MD, AND ALISON STUEBE, MD, MSC

Breastfeeding is associated with improved health outcomes for mothers. The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (ACOG) recommend exclusive breastfeeding for the first six months of life with introduction of complementary foods at six months and continued breastfeeding through the infant’s first year of life and beyond as mutually desired. Current breastfeeding rates are below the Healthy People 2020 (HP2020) target established by the United States Department of Health and Human Services.

Current breastfeeding rates are below the Healthy People 2020 (HP2020) target established by the United States Department of Health and Human Services.

Breastfeeding may help reverse the metabolic changes accompanying pregnancy and adverse pregnancy outcomes, both of which are associated with increased metabolic disease risks later in a woman’s life.

Breastfeeding and women’s health

Pregnancy is associated with metabolic changes such as increased in-
sulin resistance, hyperlipidemia, and visceral fat accumulation. Persistence of the metabolic changes that occur during pregnancy has been theorized to increase a woman’s lifetime metabolic disease risk. Lactation may play a role in reversing these changes more rapidly. Also, adverse pregnancy outcomes such as preeclampsia, gestational diabetes and preterm delivery are associated with a higher maternal incidence of cardiometabolic diseases later in life. Breastfeeding is associated with risk reduction in these cardiometabolic diseases. For example, up to 50% of women with gestational diabetes develop Type 2 diabetes mellitus (T2D) within five years postpartum, and greater than one to three months of lactation is associated with approximately 80% reduction in the cumulative incidence of T2D at five years postpartum.

The association between breastfeeding and women’s health has been studied extensively (Table 2). A longer duration of breastfeeding has been associated with a risk reduction in breast cancer, ovarian cancer, endometrial cancer, metabolic syndrome, hypertension, myocardial infarction, and T2D. Sustained breastfeeding is associated with greater maternal benefit. In a recent cost analysis, Bartick et al. modeled maternal and child health outcomes using current national rates in comparison to optimal breastfeeding (defined as 90% of mothers exclusively breastfeeding each child for six months and continuing to breastfeed for 12 months). Across the lifetime of a cohort of women born in a single year, they found current suboptimal breastfeeding rates were associated with an excess of 2,619 premature maternal deaths (95% CI 1,978 to 3,259).

Studies reveal an association between breastfeeding and improved maternal health; however, this association may not be causal. First, most studies are observational because it is unethical to randomize women to breastfeed or formula-feed. Randomized trials of breastfeeding have focused on types of support. As an example, the PROBIT study conducted in Belarus in the 1990s consisted of 17,046 mother-infant pairs. All moth-

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Healthy people 2020 breastfeeding goals and current rates in United States by race/ethnicity in 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categories</td>
<td>Ever breastfed %</td>
</tr>
<tr>
<td>Healthy people 2020 goals</td>
<td>81.9</td>
</tr>
<tr>
<td>U.S. rates</td>
<td>82.5</td>
</tr>
<tr>
<td>RACE/ETHNICITY</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>84.8</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>85.7</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>68.0</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
<td>80.7</td>
</tr>
<tr>
<td>Non-Hispanic Hawaiian/Pacific Islander</td>
<td>79.9</td>
</tr>
<tr>
<td>Non-Hispanic American Indian/Alaska Native</td>
<td>79.5</td>
</tr>
</tbody>
</table>

Most medications are compatible with breastfeeding, but inappropriate information may lead to unnecessary cessation of lactation.
Initiated breastfeeding and there was a small difference (8%-15%) in absolute breastfeeding rates between the intervention and control groups over the first postpartum year, limiting the ability to detect differences in health outcomes.25 Secondly, outcomes may be confounded by differences in health behaviors: mothers who breastfeed are more likely to be white, married, better educated, wealthier, leaner, and less likely to use tobacco or recreational drugs when compared with women who do not breastfeed.5 Finally, baseline metabolic risk factors such as obesity and insulin resistance may negatively impact lactogenesis and breastfeeding duration.26

**Clinical practices that support breastfeeding**

Despite the maternal health benefits associated with breastfeeding, anticipatory guidance from ob/gyns is inconsistent: In one study, breastfeeding was discussed at 29% of initial prenatal visits and conversations lasted 39 seconds on average.27 The World Health Organization/ UNICEF Ten Steps to Successful Breastfeeding increases breastfeeding success (Table 3).28 The 10 steps are evidence-based practices that have been demonstrated to increase breastfeeding initiation and duration. Other strategies that improve breastfeeding

<table>
<thead>
<tr>
<th>Maternal condition</th>
<th>Cases averted in population (95% CI)</th>
<th>Deaths averted in population (95% CI)</th>
<th>Cases averted per 100,000 women (95% CI)</th>
<th>Deaths averted per 100,000 women (95% CI)</th>
<th>Women needed to treat to avert a case (95% CI)*</th>
<th>Women needed to treat to avert a death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>5,023 (3,965 - 6,021)</td>
<td>838 (434 - 1,245)</td>
<td>252 (199 - 302)</td>
<td>42 (22 - 62)</td>
<td>397 (331 - 503)</td>
<td>2,379 (1,602 - 4,596)</td>
</tr>
<tr>
<td>Ovarian cancer (premenopausal)</td>
<td>22 (−71 - 112)</td>
<td>8 (−58 - 71)</td>
<td>1 (−4 - 6)</td>
<td>0.4 (−3 - 4)</td>
<td>92,713 (−28,274 to −17,788)</td>
<td>237,079 (−34,379 to 28,254)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>12,320 (10,537 - 14,162)</td>
<td>473 (154 - 789)</td>
<td>618 (520 - 710)</td>
<td>24 (8 - 40)</td>
<td>162 (141 - 189)</td>
<td>4,218 (2,529 - 12,952)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35,982 (34,122 - 38,144)</td>
<td>322 (98 - 543)</td>
<td>1,805 (1,711 - 1,913)</td>
<td>16 (5 - 27)</td>
<td>55 (52 - 58)</td>
<td>6,192 (3,671 - 20,259)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>8,487 (7,520 - 9,583)</td>
<td>986 (677 - 1,295)</td>
<td>426 (377 - 481)</td>
<td>49 (34 - 65)</td>
<td>235 (208 - 265)</td>
<td>2,023 (1,540 - 2,946)</td>
</tr>
<tr>
<td>Total maternal deaths</td>
<td>n/a</td>
<td>2,619 (1,978 - 3,259)</td>
<td>n/a</td>
<td>131 (99 - 163)</td>
<td>n/a</td>
<td>761 (612 - 1,008)</td>
</tr>
</tbody>
</table>

*Adapted with permission from Bartick MC, et al.10

1 Number needed to treat in this case refers to number of women needed to optimally breastfeed.

2 Following Altman (1998) for numbers needed to treat where the results are not statistically significant, we show a confidence interval from a negative value, which would indicate a number needed to harm through infinity to a positive value, indicating a number needed to benefit, effectively an interval in the real projective line that includes the mean value.

Totals may not always add up due to rounding. Totals do not include results that are not statistically significant, nor do the confidence intervals for the totals include the confidence intervals for the non-significant findings.

<table>
<thead>
<tr>
<th>Maternal death</th>
<th>Cases averted in population (95% CI)</th>
<th>Deaths averted in population (95% CI)</th>
<th>Women needed to treat to avert a death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>5,023 (3,965 - 6,021)</td>
<td>838 (434 - 1,245)</td>
<td>2,379 (1,602 - 4,596)</td>
</tr>
<tr>
<td>Ovarian cancer (premenopausal)</td>
<td>22 (−71 - 112)</td>
<td>8 (−58 - 71)</td>
<td>4,218 (2,529 - 12,952)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>12,320 (10,537 - 14,162)</td>
<td>473 (154 - 789)</td>
<td>6,192 (3,671 - 20,259)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35,982 (34,122 - 38,144)</td>
<td>322 (98 - 543)</td>
<td>6,192 (3,671 - 20,259)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>8,487 (7,520 - 9,583)</td>
<td>986 (677 - 1,295)</td>
<td>2,023 (1,540 - 2,946)</td>
</tr>
<tr>
<td>Total maternal deaths</td>
<td>n/a</td>
<td>2,619 (1,978 - 3,259)</td>
<td>761 (612 - 1,008)</td>
</tr>
</tbody>
</table>

Enabling optimal breastfeeding would prevent over 2,000 women’s deaths annually in the United States.
rates include access to breast pumps, group prenatal classes, peer counseling, and clinic appointments for breastfeeding problems.29-31

Providers are encouraged to initiate education on the benefits and management of breastfeeding from the first prenatal appointment and continue throughout pregnancy. Prescriptions for breast pumps and training in usage can be provided to women planning to return to work. Maternal risk factors for breastfeeding difficulties such as obesity, variations in breast anatomy and primiparity should be reviewed and anticipatory guidance provided.32

One common cause of iatrogenic early weaning is inaccurate information on medication use. Health care providers often provide inaccurate information about medication use during breastfeeding.33,34 Most medications are compatible with breastfeeding, but inappropriate information may lead to unnecessary cessation of lactation.35 Reliable up-to-date resources on medication in lactation include Lactmed (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm), the Infant Risk Center (http://www.infantrisk.com), and MotherToBaby.org.

In the intrapartum period, providers should emphasize the importance of skin-to-skin contact in the immediate postpartum period and breastfeeding initiation within the first hour after birth. Postpartum, referral to sources of lactation support such as La Leche League, peer counselors, and hospital support groups may enable women to achieve their breastfeeding goals. Breastfeeding problems should be addressed by assessment of the mother-infant dyad in conjunction with an International Board-Certified Lactation Consultant.

Ob/gyns can play an important role by: (1) Developing knowledge and skills in basic lactation management; (2) Encouraging and supporting women to initiate and sustain breastfeeding; (3) Being a resource for mothers experiencing difficulties with breastfeeding; (4) Promoting the integration of the Ten Steps into maternity care; and (5) Advocating for policies that help women achieve their breastfeeding goals, such as paid maternity leave and break time for milk expression.1

**Conclusions**

Breastfeeding is associated with substantial differences in health outcomes for mothers. Lactation is a core component of reproductive physiology, and thus in the domain of women’s health providers.1,36 Enabling women to meet their breastfeeding goals is therefore an integral part of women’s health care.

**DISCLOSURES** The authors report no potential conflicts of interest with regard to this article.

**FOR REFERENCES VISIT** contemporaryobgyn.net/BreastfeedingBenefits

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**TABLE 3**

<table>
<thead>
<tr>
<th>Critical management procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a. Comply fully with the International Code of Marketing of Breast-milk Substitutes and relevant World Health Assembly resolutions.</td>
</tr>
<tr>
<td>1b. Have a written infant feeding policy that is routinely communicated to staff and parents.</td>
</tr>
<tr>
<td>1c. Establish ongoing monitoring and data-management systems.</td>
</tr>
<tr>
<td>2. Ensure that staff have sufficient knowledge, competence and skills to support breastfeeding.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key clinical practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Discuss the importance and management of breastfeeding with pregnant women and their families.</td>
</tr>
<tr>
<td>4. Facilitate immediate and uninterrupted skin-to-skin contact and support mothers to initiate breastfeeding as soon as possible after birth.</td>
</tr>
<tr>
<td>5. Support mothers to initiate and maintain breastfeeding and manage common difficulties.</td>
</tr>
<tr>
<td>6. Do not provide breastfed newborns any food or fluids other than breast milk, unless medically indicated.</td>
</tr>
<tr>
<td>7. Enable mothers and their infants to remain together and to practise rooming-in 24 hours a day.</td>
</tr>
<tr>
<td>8. Support mothers to recognize and respond to their infants’ cues for feeding.</td>
</tr>
<tr>
<td>9. Counsel mothers on the use and risks of feeding bottles, teats and pacifiers.</td>
</tr>
<tr>
<td>10. Coordinate discharge so that parents and their infants have timely access to ongoing support and care.</td>
</tr>
</tbody>
</table>
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Providers fell below the standard of care by negligently increasing and maintaining the oxytocin at unsafe levels, causing the uterine rupture. The result was a lack of oxygen to the fetus, which caused the subsequent brain injury. The patient’s expert obstetrician testified that the patient’s uterine contractions were adequate when the oxytocin dose reached 14 MU/minute, but the dose continued to be increased.

**THE VERDICT**

The parties reached a $3.5 million settlement.

### Hysterectomy, bowel perforation, multiple complications

A Mississippi woman underwent a hysterectomy in 2011, performed by her gynecologist. Two days later, she returned to the emergency room with complaints of pain. The following day, she was seen by her gynecologist and admitted to the hospital. A general surgery consult was ordered. Exploratory laparotomy performed the next day revealed an abscess and a 1-cm bowel perforation, which was repaired. Despite the repair, the patient endured a rigorous course of recovery. She developed pneumonia, respiratory failure, underwent multiple surgeries, and had recurrent abscesses and fistulas.

The woman sued the gynecologist, alleging he was negligent in perforating her bowel and failing to timely recognize the injury. Her expert opined that such an injury can sometimes be a surgical complication, but it was not in this case as it was alleged the gynecologist was rushed in performing this procedure because he had a patient at another hospital waiting for a cesarean delivery.

The gynecologist denied all liability and argued the perforation happened days after the operation within an abscess. He claimed it would have been obvious to him if it occurred during surgery.

**THE VERDICT**

The jury deliberated for two and a half hours at the conclusion of an eight day trial and returned a defense verdict.

### Severe hemorrhage, life-threatening complications

In 2013, a 46-year-old North Carolina woman was suffering with a history of increasingly frequent and painful menstrual periods. Her gynecologist was unable to prescribe oral contraceptives due to the patient’s hypertension and recommended a hysteroscopy with resection of a submucosal fibroid, a dilation and curettage, and endometrial ablation.

During the procedure, the gynecologist encountered the 2-cm fibroid and attempted to morcellate it from the anterior wall down to a normal-appearing uterine cavity. Although the estimated blood loss was noted to be less than 100 mL the patient began hemorrhaging immediately. During that operation, the woman’s bladder was lacerated twice. After hours of attempting to repair the damage, a urologist was called in to assist. Postoperatively the patient suffered a stroke, respiratory failure, kidney failure, permanent sterility, and significant bladder complications.

The woman sued the gynecologist alleging all the complications she suffered were the result of the gynecologist’s actions.

**THE VERDICT**

The case settled for a confidential amount at mediation.

### Alleged catheter tip found in bladder years after hysterectomy

An Alabama woman underwent a hysterectomy in 2009. As part of the procedure, a Foley catheter was inserted in the bladder and the balloon was inflated. The catheter was removed a week later when the patient went to see the gynecologist. At that time, she complained of pain and the gynecologist was called back in to speak with her. Subsequently, she suffered persistent pain and infections related to her bladder. Three months later, the woman’s primary care physician referred her to a urologist, who ordered a computed tomography scan of the bladder. The report noted a “linear band of hyper dense material...” which could represent some minimal areas of hemorrhage or debris” but no further investigation was done. Over two years later, the patient continued...
The first trial began in July of 2017 but ended in a mistrial after the jury heard inadmissible evidence about the defendants’ liability insurance. The second trial lasted eight days and the jury found in favor of all the defendants.

The patient sued her healthcare providers, including the gynecologist, urologist, primary care physician, radiologist, and hospital. She criticized the gynecologist for not having removed the catheter tip, and the others for not having discovered its continuing presence in a timelier fashion. According to the gynecologist, he tested the balloon and examined the tip of the catheter after it was removed. Both were intact. The patient later questioned whether he actually checked the integrity of the catheter. The notes in the medical records did not indicate that he had performed this check when the catheter was removed.

The defendants responded with a denial of any breach of the standard of care. The gynecologist could not remember who inserted the catheter or who took it out and further expressed uncertainty that any catheter had been removed from the patient in his office. Finally, the gynecologist and the urologist questioned whether the item removed from the patient’s bladder was a catheter tip, although the pathology report stated the contrary.

The obstetrician asserted that her evaluation and determination based on the patient’s symptoms were reasonable and within the standard of care. She also maintained that because the symptoms were determined to be a result of the pregnancy, it was not necessary to note that in the chart. She also argued that it would have taken close to a month to determine the diagnosis and any treatment would have only minimized the probability of a cardiac arrhythmia, not prevented it.

The jury deliberated for almost two and a half hours at the conclusion of an 11-day trial and returned a defense verdict.

Medical Analysis

This tragic case presentation underscores the need to educate all clinicians about the increasing prevalence of cardiac complications during pregnancy. Cardiac disease including cardiomyopathy is the leading etiology of maternal death as detailed in our opening January editorial - http://bit.ly/CVmorbidity. While the physiologic changes of pregnancy can lead to maternal complaints of breathlessness and fatigue, pregnancy can unmask congenital or acquired cardiac disease. Cardiac conditions that may precede pregnancy or be pregnancy-associated can be life-threatening including: cardiomyopathy, valvular disease or arrhythmias. Attributing these symptoms to “just pregnancy” is a diagnosis of exclusion. Any patient with persistent signs and symptoms of dyspnea requires thorough evaluation with EKG and echocardiogram.

Dr. Zelop is Director of Ultrasound, Fetal Echocardiography and Perinatal Research at Valley Hospital in Ridgewood, New Jersey, and Clinical Professor of Obstetrics and Gynecology at NYU School of Medicine, New York. She works actively with ACOG and the American Heart Association (AHA) on issues of maternal cardiac arrest and mortality. Dr. Zelop is the Series Editor of the Contemporary OB/GYN series on maternal mortality.
Fertility banking security

Because redundancy is an essential feature of all critical monitoring systems, nitrogen levels are measured in all tanks at least three times per week, if not daily to ensure temperature uniformity. A yardstick-like instrument is used to measure the level of LN$_2$ and these data are graphically charted to detect increased consumption of LN$_2$ which may be a signal that a tank is failing. If the cryogenic storage tank does not have an autofill mechanism, it is manually filled with LN$_2$ to a pre-determined level.

All cryogenic storage tanks are checked daily for signs of frost or condensation that may indicate impending tank failure. If there are any signs of malfunction, a tank must be replaced. At least one empty back-up tank should be readily available and filled with LN$_2$ in the event of a tank failure emergency.

When a natural disaster is anticipated or another event that would potentially preclude access to the tanks or delivery of additional LN$_2$, undamaged cryogenic storage tanks should be capable of maintaining appropriate temperatures for at least six weeks to ensure safety of the reproductive tissues.

What is a failure of a cryogenic storage tank?

A catastrophic failure occurs when a cryogenic storage tank’s vacuum is abruptly lost without warning. Unless a backup tank is available and the contained cryopreserved reproductive tissues are immediately transferred, loss of the cryopreserved specimens is imminent. Other tank failures occur when there is slow deterioration of the tank’s vacuum due to mechanical insult, overfill with LN$_2$, inertial stress, and metal or weld fatigue. Signs of frost or condensation are the most common signs of impending cryogenic storage tank failure and increased LN$_2$ consumption. Most manufacturers guarantee the tank’s vacuum for five years and cite a lifespan of ten years.

How often does a cryogenic storage tank failure happen?

There are no national or international agencies that track incidence of cryogenic storage tank failures and most available information is anecdotal. However, a generalized industry opinion is that catastrophic tank failures are rare. Known cryogenic storage tank failures with complete loss of productive tissues occur once or twice a decade. A survey of cryostorage centers in UK and Ireland cited three failures from 17 respondents using nitrogen vapor systems.

Who regulates storage of reproductive tissues?

Fertility centers are subject to oversight by many federal, state, and local agencies but regulation of storage of reproductive tissues in fertility centers is not specifically addressed. For the most part, American clinical laboratories are regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, except for the embryology component of the fertility laboratory. The Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), and the Centers for Disease Control and Prevention (CDC) have joint responsibility for the law, which empowers the government to monitor performance, conduct inspections, and enforce compliance.

Some states (Maryland, New York, Oregon, and California) license tissue banks and biorepositories, which also includes oversight of cryogenic storage of reproductive tissues.

The College of American Pathologists (CAP) has legal jurisdiction to inspect and accredit fertility laboratories. CAP inspects hundreds of fertility laboratories biennially, but their checklists include only two questions on cryogenic storage based on the American Association of Tissue Bank standards. The first question covers laboratory compliance with having a written procedure for monitoring and maintaining adequate liquid nitrogen levels with evidence of compliance as the actual written procedure and records of monitoring LN$_2$ levels at a defined frequency. The second question covers laboratory compliance with having 24-hour/day (either remote or in the laboratory) alarm monitoring and annual maintenance checks of the alarm system. Evidence of compliance is required and includes documentation of response to alarms and a written protocol for responding to alarms and taking alternative measures.

DR. ORY is Professor of Obstetrics and Gynecology, Florida International University, Miami, Florida, a Partner in IVF Florida, Margate, and a member of the Contemporary OB/GYN Editorial Board.

MS. MILLER is Scientific and Research Director at IVF Florida, Margate.

DISCLOSURES The authors report no potential conflicts of interest with regard to this article.

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Oxytocin suspect in cases with poor outcomes

Patient refuses cesarean, blames infant injury on oxytocin

A 19-year-old Florida woman brought a malpractice action following the delivery of her child by an obstetrician employed by a federally funded medical clinic. She claimed the obstetrician was negligent for failing to perform an emergency cesarean and continuing use of oxytocin despite ominous signs of fetal compromise. As a result, the child suffered a severe brain injury requiring 24-hour professional care for the rest of his life.

The obstetrician argued that the patient refused cesarean delivery multiple times, against the obstetrician’s medical advice, prior to the vaginal delivery. He noted the refusals in the medical records. He claimed he did not fall below the standard of care in administering oxytocin or using a vacuum for delivery because the patient refused the recommended cesarean delivery.

THE VERDICT The jury found in favor of the child, the patient, and the husband, including $20,965,144 for the child’s future economic damages and

$7.625 million for his non-economic damages as well as $3.3 million for the patient and $1 million to the father.

Did aggressive use of oxytocin cause uterine rupture?

A Kansas woman presented to a hospital in labor at term. The on-call obstetrician ordered oxytocin augmentation. According to protocol, dosage of the drug was to be increased by 2 MU up to 30 MU or until adequate contraction pattern was observed. Over the next few hours, the nurses increased the infusion several times. When the patient began to push, a bloody discharge from the vagina was noted and the fetal heart rate (FHR) was temporarily lost. When the FHR was found, it was down to 50 beats per minute. After a few attempts to deliver the infant by vacuum and forceps, an emergency cesarean was performed. The patient had a ruptured uterus and the infant suffered permanent brain injury.

The patient sued those involved with the delivery, alleging the health care pro-

ANALYSIS

Oxytocin is one of the most frequently used drugs during labor but it can also become a major issue in a malpractice case filed after a labor and delivery if there is an adverse outcome. If the drug is used during labor, all policies and protocols in effect at the time will be requested during discovery and will be compared to how the patient’s oxytocin dose was managed. Any deviation from the protocol will be pointed out as care falling below the standard, whether or not it had anything to do with the alleged injury. It is imperative that everyone administering oxytocin during labor is aware of what the protocol requires and documents any reason or thought process for deviating from that protocol.

FOR MORE LEGALLY SPEAKING CASES TURN TO PAGE 31

FROM THE AUTHOR - This will be my final column for Contemporary OB/GYN. I have had the privilege of writing for this magazine for many years and thank the editorial leadership and staff for that opportunity. And thanks to you, the readers, for all your comments and for making the Legally Speaking column a success. – Dawn Collins, JD

Ms Collins is an attorney specializing in medical malpractice in Long Beach, California. She can be reached at dawncfree@gmail.com.
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