

Treatment Urged for All Pregnant HIV Patients

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HOUSTON — Pregnant women should be treated for human immunodeficiency virus infections even if they are asymptomatic with normal CD4 counts and have a low viral load, said Hunter A. Hammill, M.D.

Pregnancy itself does not affect the course of the disease. The woman's condition will not become worse, but the

baby is at risk, he said at a conference on vulvovaginal diseases sponsored by Baylor College of Medicine.

"Optimum therapy should be offered to minimize vertical transmission to the infant," said Dr. Hammill of the college.

Infants of HIV-positive mothers will test positive for 6-8 weeks after birth. Without treatment, about one-third will be infected and remain positive. Breast-feeding can increase the vertical infection rate by 20%.

Studies summarized by Dr. Hammill have reported transmission rates of less than 1%-13% when various therapies were tested in pregnant women. "My series is now down to less than a tenth of a percent vertical transmission with vaginal delivery when treating with HAART [Highly Active Antiretroviral Therapy]," he said.

Dr. Hammill urged practitioners to get up to date on new antiretroviral treatments. About 30 different treatment options are available, he said, and these are

typically given in three-drug combinations.

Patients have to be monitored as some agents will have side effects. Among these, he listed unusual dreams, yellow skin, liver and renal toxicities, and nausea lasting several weeks until the patient's body adapts.

Some HAART drugs do pose special risks. He cited rash and hepatic toxicity with nevirapine (Viramune), hyperglycemia with protease inhibitors, and mitochondrial toxicity with nucleoside analogs.

His greatest concern is efavirenz (Sustiva), which is sometimes prescribed because it is considered safe in pregnancy. Because one animal study has linked it to monkey anencephaly, Dr. Hammill said he switches his patients to another drug.

"If you see an HIV patient on Sustiva, please think of birth control," he said.

Dr. Hammill also urged physicians to provide intensive counseling about the importance of complying with treatment. "The big thing in AIDS is adherence," he said. "If you don't take the drug, it doesn't work."

Maternal Morbidity Tied to Prolonged MgSO₄ Tocolysis

RENO, NEV. — Increased maternal morbidity is significantly associated with magnesium sulfate tocolysis that lasts longer than 48 hours, a retrospective study has demonstrated.

Investigators compared 78 women who received MgSO₄ tocolysis for longer than 48 hours with 77 women who received MgSO₄ tocolysis for 48 hours or less. Women who received prolonged tocolysis were significantly more likely to have at least one adverse event (56.4% vs. 28.5%).

The most common adverse events were chest tightness, pulmonary edema, and visual disturbances, investigators wrote in a poster presentation at the annual meeting of the Society for Maternal-Fetal Medicine.

Babies born to the two groups of mothers had similar Apgar scores, hypotonia, and neonatal mortality rates. But babies born to women who underwent prolonged tocolysis had significantly higher magnesium levels, averaging 3.6 mg/dL, compared with 2.8 mg/dL for babies born to control women, reported Anwar Nasar, M.D., and colleagues at the American University of Beirut (Lebanon).

In addition, three infants born to mothers who had received large amounts of MgSO₄ showed radiolucent bones and metaphyseal widening, evidence of abnormal bone mineralization.

"Given the scarcity of evidence of its effectiveness as a tocolytic and the potential of significant adverse effects on the mother and neonate, aggressive attempts at prolonging pregnancy with intravenous magnesium sulfate are unjustifiable," the investigators wrote.

—Robert Finn

BRIEF SUMMARY

NUVARING®
(etonogestrel/ethinyl estradiol vaginal ring)
delivers 0.120 mg/0.015 mg per day

Patients should be aware that this product does not protect against HIV infections (AIDS) and other sexually transmitted diseases.

Only

FOR VAGINAL USE ONLY

Read this leaflet carefully before you use NuvaRing® so that you understand the benefits and risks of using this form of birth control. The leaflet gives you information about the possible serious side effects of NuvaRing®. This leaflet will also tell you how to use NuvaRing® properly so that it will give you the best possible protection against pregnancy. Read the information you get whenever you get a new prescription or refill, because there may be new information. This information does not take the place of talking with your healthcare provider.

What is NuvaRing®?

NuvaRing® (NEW-vah-ring) is a flexible combined contraceptive vaginal ring. It is used to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases (STD's) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

NuvaRing® contains a combination of a progestin and estrogen, two kinds of female hormones. You insert the ring in your vagina and leave it there for three weeks. You then remove it for a one-week ring-free break. After the ring is inserted, it releases a continuous low dose of hormones into your body.

Contraceptives that contain both an estrogen and a progestin are called combination hormonal contraceptives. Most studies on combination contraceptives have used oral (taken by mouth) contraceptives. NuvaRing® may have the same risks that have been found for combination oral contraceptives. This leaflet will tell you about risks of taking combination oral contraceptives that may also apply to NuvaRing® users. In addition, it will tell you how to use NuvaRing® properly so that it will give you the best possible protection against pregnancy.

Who should not use NuvaRing®?

Cigarette smoking increases the risk of serious cardiovascular side effects when you use combination oral contraceptives. This risk increases even more if you are over age 35 and if you smoke 15 or more cigarettes a day. Women who use combination hormonal contraceptives, including NuvaRing®, are strongly advised not to smoke.

- Do not use NuvaRing® if you have any of the following conditions:
 - pregnancy or suspected pregnancy
 - blood clots in your legs (thrombosis), lungs (pulmonary embolism), or eyes now or in the past
 - chest pain (angina pectoris)
 - heart attack or stroke
 - severe high blood pressure
 - diabetes with complications of the kidneys, eyes, nerves, or blood vessels
 - headaches with neurological symptoms
 - known or suspected breast cancer or cancer of the lining of the uterus, cervix, or vagina (now or in the past)
 - unexplained vaginal bleeding
 - yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during past use of oral contraceptives (birth control pills)
 - liver tumors or active liver disease
 - disease of the heart valves with complications
 - need for a long period of bedrest following major surgery
 - an allergic reaction to any of the components of NuvaRing®

Tell your healthcare provider if you have ever had any of the conditions just listed. Your healthcare provider can suggest another method of birth control.

Talk with your healthcare provider about when to start NuvaRing® if you are recovering from the birth of a child or a second trimester miscarriage or abortion or if you are breastfeeding.

In addition, talk to your healthcare provider about using NuvaRing® if you have any of the following conditions. Women with any of these conditions should be checked often by their doctor or healthcare provider if they choose to use NuvaRing®.

- a family history of breast cancer
- breast nodules, fibrocystic disease, an abnormal breast x-ray, or abnormal mammogram
- diabetes
- high blood pressure
- high cholesterol or triglycerides
- headaches or epilepsy
- mental depression
- gallbladder or kidney disease
- major surgery (You may need to stop using NuvaRing® for a while to reduce your chance of getting blood clots.)
- any condition that makes the vagina get irritated easily
- prolapsed (dropped) uterus, dropped bladder (cystocele), or rectal prolapse (rectocele)
- severe constipation

How should I use NuvaRing®?

For the best protection from pregnancy, use NuvaRing® exactly as directed. Insert one NuvaRing® in the vagina and keep it in place for three weeks in a row. Remove it for a one-week break and then insert a new ring. During the one-week break, you will usually have your menstrual period. Your healthcare provider should examine you at least once a year to see if there are any signs of side effects of NuvaRing® use.

When should I start NuvaRing®?

Follow the instructions in one of the sections below to find out when to start using NuvaRing®.

If you did not use a hormonal contraceptive in the past month
Counting the first day of your menstrual period as "Day 1", insert your first NuvaRing® between Day 1 and Day 5 of the cycle, but at the latest on Day 5, even if you have not finished bleeding. During this first cycle, use an extra method of birth control, such as male condoms or spermicide, for the first seven days of ring use.

If you are switching from a combination oral contraceptive (birth control pill containing both progestin and estrogen)

Insert NuvaRing® anytime during the first seven days after the last combined (estrogen and progestin) oral contraceptive tablet and no later than the day when you would have started a new pill cycle. No extra birth control method is needed.

If you are switching from a progestin-only contraceptive (mini-pill, implant, injection, or IUD)

- When switching from a mini-pill, start using NuvaRing® on any day of the month. Do not skip days between your last pill and first day of NuvaRing® use.
- When switching from an implant, start using NuvaRing® on the same day you have your implant removed.
- When switching from an injectable contraceptive, start using NuvaRing® on the day when your next injection is due.
- When switching from a progestin-containing IUD, start using NuvaRing® on the same day you have your IUD removed.

When you are switching from a progestin-only contraceptive, use an extra method of birth control, such as male condoms or spermicide, for the first seven days after inserting NuvaRing®.

Following first trimester abortion or miscarriage

If you start using NuvaRing® within five days after a complete first trimester abortion or miscarriage, you do not need to use an extra method of contraception.

If NuvaRing® is not started within five days after a first trimester abortion or miscarriage, begin NuvaRing® at the time of your next menstrual period. Counting the first day of your menstrual period as "Day 1", insert NuvaRing® on or before Day 5 of the cycle, even if you have not finished bleeding. During this first cycle, use an extra method of birth control, such as male condoms or spermicide, for the first seven days of ring use.

When do I insert a new ring?

After a one-week ring-free break, insert a new ring on the same day of the week as it was inserted in the last cycle. For example, if NuvaRing® was inserted on a Sunday at about 10:00 PM, after the one-week break you should insert a new ring on a Sunday at about 10:00 PM.

If NuvaRing® slips out:

Rarely, NuvaRing® can slip out of the vagina if it has not been inserted properly, or while removing a tampon, moving the bowels, straining, or with severe constipation.

If NuvaRing® slips out of the vagina, and it has been out less than three hours, you should still be protected from pregnancy. NuvaRing® can be rinsed with cool to lukewarm (not hot) water and should be reinserted as soon as possible, and at the latest within three hours. If you have lost NuvaRing®, you must insert a new NuvaRing® and use it on the same schedule as you would have used the lost ring. If NuvaRing® has been out of the vagina for more than three hours, you may not be adequately protected from pregnancy. NuvaRing® can be rinsed with cool to lukewarm (not hot) water and reinserted as soon as possible. You must use an extra method of birth control, such as male condoms or spermicide, until the NuvaRing® has been in place for seven days in a row.

Women with conditions affecting the vagina, such as prolapsed (dropped) uterus, may be more likely to have NuvaRing® slip out of the vagina. If NuvaRing® slips out repeatedly, you should consult with your healthcare provider.

If NuvaRing® is in your vagina too long:

If NuvaRing® has been left in your vagina for an extra week or less (four weeks total or less), remove it and insert a new ring after a one-week ring-free break.

If NuvaRing® has been left in place for more than four weeks, you may not be adequately protected from pregnancy and you must check to be sure you are not pregnant. You must use an extra method of birth control, such as male condoms or spermicide, until the new NuvaRing® has been in place for seven days in a row.

If you miss a menstrual period:

You must check to be sure that you are not pregnant if:

- you miss a period and NuvaRing® was out of the vagina for more than three hours during the three weeks of ring use
- you miss a period and you had waited longer than one week to insert a new ring
- you have followed the instructions and you miss two periods in a row
- you have left NuvaRing® in place for longer than four weeks

Overdose

What should I avoid while using NuvaRing®?

Smoking may increase your risk of heart attack or stroke while using combination hormonal contraceptives, including NuvaRing®. The risk increases with age and number of cigarettes smoked a day.

Cigarette smoking increases the risk of serious cardiovascular side effects when you use combination oral contraceptives. This risk increases even more if you are over age 35 and if you smoke 15 or more cigarettes a day. Women who use combination hormonal contraceptives, like NuvaRing®, are strongly advised not to smoke.

Do not breast feed while using NuvaRing®. Some of the medicine may pass through the milk to the baby and could cause yellowing of the skin (jaundice) and breast enlargement. NuvaRing® could also decrease the amount and quality of your breast milk.

The hormones in NuvaRing® can interact with many other medicines and herbal supplements. Tell your healthcare provider about any medicines you are taking, including prescription medicines, over-the-counter medicines, herbal remedies, and vitamins.

The blood levels of the hormones released by NuvaRing® were increased when women used an oil-based vaginal medication (miconazole nitrate) for a yeast infection while NuvaRing® was in place. The pregnancy protection of NuvaRing® is not likely to be changed by use of these products. The blood levels of the hormones released by NuvaRing® were not changed when women used vaginal, water-based spermicides (nonoxonyl or N-9 products) along with NuvaRing®.

While using NuvaRing®, you should not rely upon a diaphragm when you need a backup method of birth control because NuvaRing® may interfere with the correct placement and position of a diaphragm.

If you are scheduled for any laboratory tests, tell your doctor or healthcare provider you are using NuvaRing®. Contraceptive hormones may change certain blood tests results.

What are the possible risks and side effects of NuvaRing®?

Blood clots

The hormones in NuvaRing® may cause changes in your blood clotting system which may allow your blood to clot more easily. If blood clots form in your legs, they can travel to the lungs and cause a sudden blockage of a vessel carrying blood to the lungs. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or other vision problems. The risk of getting blood clots may be greater with the type of progestin in NuvaRing® than with some other progestins

in certain low-dose birth control pills. It is unknown if the risk of blood clots is different with NuvaRing® use than with the use of certain birth control pills.

Heart attacks and strokes

Hormonal contraceptives may increase your risk of strokes (blockage of blood flow to the brain) or heart attacks (blockage of blood flow to the heart). Any of these conditions can cause death or serious disability. Smoking greatly increases the risk of having heart attacks and strokes. Furthermore, smoking and the use of combination hormonal contraceptives, like NuvaRing®, greatly increases the chances of developing and dying of heart disease. If you use combination hormonal contraceptives, including NuvaRing®, you should not smoke.

High blood pressure and heart disease

Combination hormonal contraceptives, including NuvaRing®, can worsen conditions like high blood pressure, diabetes, and problems with cholesterol and triglycerides.

Cancer of the breast

Various studies give conflicting reports on the relationship between breast cancer and hormonal contraceptive use. Combination hormonal contraceptives, including NuvaRing®, may slightly increase your chance of having breast cancer diagnosed. After you stop using hormonal contraceptives, the chance of having breast cancer diagnosed begins to go back down. You should have regular breast examinations by a healthcare provider and examine your own breasts monthly. Tell your healthcare provider if you have a family history of breast cancer or if you have had breast nodules or an abnormal mammogram.

Gallbladder disease

Combination hormonal contraceptive users may have a higher chance of having gallbladder disease.

Liver tumors

In rare cases, combination hormonal contraceptives, like NuvaRing®, can cause non-cancerous (benign) but dangerous liver tumors. These benign liver tumors can break and cause fatal internal bleeding. In addition, it is possible that women who use combination hormonal contraceptives, like NuvaRing®, have a higher chance of getting liver cancer. However, liver cancers are extremely rare.

The common side effects reported by NuvaRing® users are:

- vaginal infections and irritation
 - vaginal discharge (leukorrhea)
 - headache
 - weight gain
 - nausea
- In addition to the risks and side effects listed above, users of combination hormonal contraceptives have reported the following side effects:
- vomiting
 - change in appetite
 - abdominal cramps and bloating
 - breast tenderness or enlargement
 - irregular vaginal bleeding or spotting
 - changes in menstrual cycle
 - temporary infertility after treatment
 - fluid retention (edema)
 - spotty darkening of the skin, particularly on the face
 - rash
 - weight changes
 - depression
 - intolerance to contact lenses

Call your healthcare provider right away if you get any of the symptoms listed below. They may be signs of a serious problem:

- sharp chest pain, coughing blood, or sudden shortness of breath (possible clot in the lung)
- pain in the calf (back of lower leg; possible clot in the leg)
- crushing chest pain or heaviness in the chest (possible heart attack)
- sudden severe headache or vomiting, dizziness or fainting, problems with vision or speech, weakness, or numbness in an arm or leg (possible stroke)
- sudden partial or complete loss of vision (possible clot in the eye)
- yellowing of the skin or whites of the eyes (jaundice), especially with fever, tiredness, loss of appetite, dark colored urine, or light colored bowel movements (possible liver problems)
- severe pain, swelling, or tenderness in the abdomen (gallbladder or liver problems)
- breast lumps (possible breast cancer or benign breast disease)
- irregular vaginal bleeding or spotting that happens in more than one menstrual cycle or lasts for more than a few days
- swelling (edema) of your fingers or ankles
- difficulty in sleeping, weakness, lack of energy, fatigue, or a change in mood (possible severe depression)

How effective is NuvaRing®?

If NuvaRing® is used according to the directions, your chance of getting pregnant is about 1 to 2% a year. This means that, for every 100 women who use NuvaRing® for a year, about one or two will become pregnant. Your chance of getting pregnant increases if NuvaRing® is not used exactly according to the directions.

By comparison, the chances of getting pregnant in the first year of typical use (not always following directions exactly) of other methods of birth control are as follows:

No birth control method:	85%
Spermicides alone:	26%
Periodic abstinence methods (calendar, ovulation, thermometer):	25%
Withdrawal:	19%
Cervical Cap with spermicides:	20 to 40%
Vaginal sponge:	20 to 40%
Diaphragm with spermicides:	20%
Condom alone (male):	14%
Condom alone (female):	21%
Oral contraceptives:	5%
IUD:	less than 1 to 2%
Implants:	less than 1%
Injection:	less than 1%
Sterilization:	less than 1%

Other information

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use NuvaRing® for a condition for which it was not prescribed. Do not give NuvaRing® to anyone else who may want to use it.