

Cost Comparison

Medication/Dose	Cost*		
	Rite Aid	Kroger	CVS
Viread® (tenofovir DF) 300 mg tablet QD **nucleotide analogue	459.99	506.09	443.99
Nucleoside analogues**can be used in place of Viread®			
Zerit® (stavudine, d4T) 40 mg capsule BID	356.99	397.09	397.99
Retrovir® (zidovudine, AZT) 300 mg tablet BID	362.99	423.09	389.99
Epivir® (lamivudine, 3TC) 300 mg tablet QD	364.99	361.89	351.99
Ziagen® (abacavir) 300mg tablet BID	470.99	485.69	442.99
Videx EC® (didanosine, ddl) 400 mg tablet QD	331.99	358.29	347.99

* Cost to patient for a 30 day supply at average doses used.

Precautions

Fat redistribution: Fat redistribution such as central obesity, dorsocervical fat enlargement (“buffalo hump”), breast enlargement, peripheral wasting and facial wasting has been noted.

Bone abnormalities: it is not known if long term administration (>1year) of tenofovir DF will cause bone abnormalities. If bone abnormalities are suspected, appropriate consultation should be obtained.

Contraindications

Tenofovir DF is contraindicated in patients who are known to have a hypersensitivity to tenofovir or any of its components.

Special Populations

Gender, Race and Age: Tenofovir DF pharmacokinetics in the elderly (>65yo) have not been determined. There are no gender differences noted in tenofovir DF. Differences between different racial and ethnic groups are undetermined due to insufficient number of patients.

Renal disease: Tenofovir DF should not be administered to patients with creatinine clearance of less than 60 mL/min. Dosage adjustment is recommended in renal impairment. No specific dose alterations have been determined.

Hepatic Insufficiency: Hepatic impairment and pharmacokinetics of tenofovir DF have not been studied . Because tenofovir DF is not entirely renally excreted (70-80%), tenofovir DF pharmacokinetics can be altered with hepatic insufficiency. Tenofovir DF does not inhibit the metabolism of CYP3A4, CYP2D6, CYP2C9 or CYP2E1. There is a 6% reduction in metabolism of CYP1A substrates.

Pediatrics: Safety and effectiveness in pediatric patients have not been established.

Pregnancy: Pregnancy category B. There has been no evidence of impaired fertility or harm to fetus due to tenofovir DF in rats or rabbits. No studies have been conducted in humans, however.

Antiretroviral Pregnancy Registry. To monitor maternal-fetal outcomes of pregnant women exposed to tenofovir DF an antiretroviral Pregnancy Registry has been established. To register a patient dial 1-800-258-4263.

Lactation: The Centers for Disease Control (CDC) recommend that HIV-infected mothers NOT breast-feed their infants to avoid the risk of transmitting the virus. It is not known if tenofovir DF is secreted in breast milk. To avoid the risk of transmitting HIV to the infant and causing potential adverse reactions to the nursing baby, it is recommended that mothers not breast-feed if they are receiving tenofovir DF.

Drug Interactions

Tenofovir DF can increase didanosine levels in the blood (increasing both C_{max} and AUC) by as much as 60%, increasing the risk of side effects that can be caused by didanosine such as pancreatitis and peripheral neuropathy. Tenofovir DF should be administered two hours before or one hour after administration of di-



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danosine. Many would also empirically decrease the average daily didanosine (Videx EC[®]) dose to 250mg.

Co-administration of tenofovir DF with drugs that reduce renal function or compete for tubular secretion can increase serum concentrations of tenofovir DF. Examples include, but are not limited to, cidofovir, acyclovir, ganciclovir, and valganciclovir.

Adverse Effects

Tenofovir DF is generally well tolerated. The most common adverse effects are moderate gastrointestinal events including nausea, vomiting, diarrhea and flatulence. Other effects include asthenia, headache, abdominal pain and anorexia.

Pharmacology

Mechanism of Action: Tenofovir DF is a prodrug of tenofovir. Tenofovir DF requires diester hydrolysis for conversion to tenofovir diphosphate. Tenofovir inhibits HIV reverse transcriptase by DNA incorporation and chain termination.

Absorption/Distribution: The oral bioavailability in fasted patients is 25% following single 300 mg dose. Administration of tenofovir DF following a high fat meal (~700-1000 kcal containing 40-50% fat) increases oral bioavailability. The AUC increases 40% and the C_{max} increases 14% following multiple 300 mg qd dosing.

Metabolism/Excretion: Tenofovir DF is not a substrate of CYP450 enzymes. Tenofovir is eliminated by a combination of tubular secretion and glomerular filtration. Seventy to eighty percent of the IV dose is recovered in urine as unchanged tenofovir DF. Tenofovir DF should not be administered to patients with creatinine clearance of less than 60 mL/min. Dosage adjustment is recommended in renal impairment. No specific dose alterations have been determined.

Patient Information

1. Viread[®] (tenofovir DF) helps block HIV reverse transcriptase which is needed for HIV to multiply. Tenofovir DF lowers the amount of HIV in the blood and can help to increase T-cells. Lowering HIV in blood lowers the chances of death when the immune system is challenged; therefore it is necessary to take this medication exactly as prescribed by the physician. **Do not change the dose or stop taking the medication without talking to your physician. If the medication isn't taken every day exactly as prescribed resistance can develop.**
2. If you are taking didanosine, take tenofovir DF two hours before or one hour after didanosine.
3. Take tenofovir DF once daily with food.

4. Let your prescriber and pharmacist know of all medications you are taking (both prescription and non prescription—including herbals) and of all of your medical conditions.
5. Tenofovir DF does not cure HIV or AIDS. Tenofovir doesn't decrease the risk of passing HIV to others through sexual contact or blood. Practice safe sex and do not share needles.

References

1. Viread[®] prescribing information. Gilead Sciences. Foster City, California. October 2001.
2. Deeks SG et. al. Phase I/II trial of the pharmacokinetics, safety, and antiretroviral activity of tenofovir disoproxil fumarate in human immunodeficiency virus-infected adults. *Antimicrob Chemother* 2001 Oct; 45(10):2733-9.
3. www.AIDSmeds.

Strattera[®] (atomoxetine hydrochloride)

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Introduction

Strattera[®] [atomoxetine (ay-**TOE**-mox-it-teen)] is a methylphenoxy-benzene propanamine derivative that selectively inhibits presynaptic norepinephrine reuptake. It was approved by the FDA on November 26, 2002 for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children at least 6 years of age and adults.

Therapeutic Recommendation

When atomoxetine and methylphenidate were compared for the treatment of ADHD, no statistically significant differences were observed in the ADHD-IV rating scale. Parents and investigators noted marked improvement in inattentive, hyperactive, and impulsive symptoms with both agents.

It is unlikely that atomoxetine will have the abuse potential seen with stimulant ADHD therapies. A study comparing the subjective, psychomotor, and physiological effects of methylphenidate and atomoxetine showed that atomoxetine had “unpleasant” subjective effects as determined by the Visual Analog Scale (VAS) and Addiction Research Center Inventory (ARCI), while methylphenidate showed abuse potential through increases in the stimulant portions of the VAS and Adjective .

Rating Scale (ARS) and in multiple components of the ARCI. The lack of stimulatory properties seen in atomoxetine is attributed to its unique mechanism of action.

Atomoxetine has therapeutic effects comparable to that of methylphenidate without the potential for abuse.

Dosing and Administration

Atomoxetine is available in 10, 18, 25, 40, and 60 mg capsules. Therapy should be initiated in children and adolescents weighing up to 70 kg at 0.5 mg/kg for a minimum of 3 days, and then increased to the target dose 1.2 mg/kg/day. Doses can be given as a single daily dose in the morning or as equal divided doses in the morning and late afternoon or early evening. The maximum daily dose is the lesser of 1.4 mg/kg or 100 mg, although no additional benefit has been observed in doses in excess of 1.2 mg/kg.

Children and adolescents weighing over 70 kg and adults should be initially dosed at 40 mg/day, and after 3 days, titrated up to target daily dose of 80 mg/day administered as a single dose in the morning or divided into equal doses in the morning and late afternoon or early evening. If the desired response has not been achieved in 2 to 4 additional weeks, a maximum dose of 100 mg may be given. No additional benefit has been observed in higher doses.

Doses may be administered without regards to food. Atomoxetine therapy may be discontinued without tapering.

Warnings/Precautions

- Allergic reactions (urticaria, rash, angioneurotic edema) are uncommon.
- Growth rate may be slowed. Monitor during treatment.
- Weight loss or a reduction in the rate of weight gain may occur.
- Caution should be used in patients with hypertension, tachycardia, or cardiovascular or cerebrovascular disease. Blood pressure and heart rate can increase during treatment and should be monitored.
- Use caution in patients who are at risk for hypotension. Orthostatic hypotension has been reported.
- Use caution in poor metabolizers; dose may need to be adjusted. Some individuals are poor metabolizers of CYP2D6, meaning the activity of this metabolic pathway is reduced compared to that of extensive or normal metabolizers. Poor metabolizers lack the gene for CYP2D6 and subsequently have difficulty metabolizing its substrates. Atomoxetine exposure and plasma concentrations increase

while the elimination rate decreases. Dosage adjustment may be necessary when atomoxetine is administered with drugs that inhibit the CYP2D6 pathway such as fluoxetine, paroxetine, and quinidine.

Cost Comparison

Medication/Dose	Cost*		
	CVS	K-Mart	RiteAid
Strattera® (atomoxetine) 25, 40, or 60 mg QD	104.99	97.97	90.99
Ritalin® (brand methylphenidate)			
5 mg BID	41.19	38.97	76.97
10 mg BID	56.99	51.97	95.97
20 mg BID	79.99	143.97	124.97
Methylphenidate (generic Ritalin®)			
5 mg BID	22.69	20.99	24.98
10 mg BID	27.59	26.99	30.98
20 mg BID	40.89	38.29	40.98

*Cost reflects price to patient for a 30 day supply at average daily dose.

Contraindications

Patients with a hypersensitivity to atomoxetine or any other component of the product.

Patients who are taking, or who have taken, Monoamine Oxidase Inhibitors (MAOI) within the past 2 weeks.

Patients with narrow angle glaucoma.

Special Populations

Hepatic Insufficiency: Initial and target doses should be reduced to 50% of the normal dose in patients with moderate hepatic insufficiency (Child-Pugh Class B) and to 25% in patients with severe hepatic insufficiency (Child-Pugh Class C). Exposure to atomoxetine is increased 2-fold in patients with normal metabolic function (extensive metabolizers) who have moderate hepatic insufficiency and 4-fold in those with severe hepatic insufficiency.

Renal Insufficiency: No dosing adjustment is needed for patients with renal insufficiency/failure.

Pediatric: Atomoxetine has not been studied in children under age 6. Pharmacokinetics in children, adolescents, and adults appear to be similar.

Geriatric: The pharmacokinetics of atomoxetine in geriatric patients have not been studied.

Gender: The pharmacokinetics of atomoxetine were unaffected by gender.

Ethnicity: The pharmacokinetics of atomoxetine were unaffected by ethnicity. Approximately 7% of Caucasians and 2% of African Americans are poor metabolizers of cytochrome P450 2D6.

Pregnancy: Atomoxetine is a pregnancy category C agent. Doses exceeding the maximum human dose resulted in decreased pup weight and survival in rats and fewer live births in rabbits. Structural abnormalities were noted in the offspring of both species. Because there are no well-controlled studies in pregnant humans, it is recommended that atomoxetine be given to pregnant women only when the benefit clearly outweighs the risk to the fetus.

Lactation: Atomoxetine and its metabolites are excreted in the milk of rats. It is not known whether the drug is excreted in human milk. Use caution in nursing mothers.

Drug Interactions

CYP2D6 inhibitors: Dosage adjustment may be necessary when coadministered with CYP2D6 inhibitors, such as fluoxetine, paroxetine, and quinidine, as plasma concentrations of atomoxetine in extensive metabolizers can be increased to that seen in poor metabolizers. Studies do not support the occurrence of this drug interaction in poor metabolizers.

CYP2D6 substrates: Drugs metabolized by CYP2D6, including desipramine, do not require dosage adjustment. Atomoxetine does not significantly induce or inhibit CYP450 enzymes.

Albuterol: Additive increases in blood pressure and heart rate were observed in the coadministration of albuterol and atomoxetine.

Alcohol: No interaction noted.

Methylphenidate: No additive cardiovascular effects observed.

Midazolam: Coadministration resulted in a 15% increase in the AUC of midazolam, a substrate of CYP3A4. Drugs metabolized by CYP3A4 do not require dosage adjustment.

Drugs highly bound to plasma protein: Binding was unaffected between atomoxetine and warfarin, aspirin, phenytoin, and diazepam.

Drugs that affect gastric pH: No effect on bioavailability was observed when coadministered with magnesium/aluminum hydroxide and omeprazole.

Adverse Effects

The most common adverse effects in children and adolescents were fatigue, dyspepsia, decreased ap-

petite, dizziness, mood swings, insomnia, nausea, and vomiting. Adults most often experienced constipation, dry mouth, decreased appetite, dizziness, insomnia, decreased libido, ejaculatory problems, impotence, urinary hesitation/retention, and dysmenorrhea.

Pharmacology

Mechanism of Action: Although its exact mechanism of action is unknown, atomoxetine is thought to act by selectively inhibiting presynaptic norepinephrine reuptake, thus enhancing noradrenergic function. Catecholamine levels are increased in the prefrontal cortex, an area that regulates attention and memory. Little-to-no affinity is observed between muscarinic, histaminic, dopaminergic, serotonergic, and alpha-adrenergic receptors and atomoxetine. The lack of drug abuse potential in atomoxetine is hypothesized to result from its lack of effect on dopamine in striatum or nucleus accumbens, unlike methylphenidate.

Absorption/Distribution: Atomoxetine has rapid oral absorption that occurs 1 to 2 hours after dosing. Absolute bioavailability is 63% in extensive metabolizers and 94% in poor metabolizers. In adults, administration of atomoxetine with a high-fat meal resulted in a 37% lower C_{max} and a 3-hour delay in T_{max} . C_{max} was 9% lower in children and adolescents when given with food. Though its absorption rate is slowed when administered with food, the extent of absorption remains unaffected so that the product can be given without regard to food. Serum protein binding is about 98%, primarily to albumin. Volume of distribution is 0.85 L/kg, distributing mainly into total body water.

Metabolism/Excretion: Atomoxetine is metabolized by the liver through CYP450. The main metabolic pathway is oxidation by CYP2D6 with subsequent glucuronidation. The major active metabolite of atomoxetine, 4-hydroxyatomoxetine, is equipotent to its parent compound, but is present in low concentrations of the plasma (1% in extensive metabolizers and 0.1% in poor metabolizers). N-Desmethylatomoxetine, the product of metabolism by CYP2C9 and other CYP450 enzymes, circulates at low plasma concentrations (5% in extensive metabolizers and 45% in poor metabolizers) and has much less pharmacological activity than atomoxetine.

The AUC of atomoxetine is increased 10-fold, peak plasma concentration is increased 5-fold, and elimination rate is slowed in poor metabolizers of CYP2D6. Atomoxetine is a substrate of CYP2D6, but does not induce or inhibit other drugs in the pathway.

The mean clearance and half-life of atomoxetine are 0.35 L/hr/kg and 5.2 hours, respectively, in extensive metabolizers, and 0.03 L/hr/kg and 21.6 hours, respectively, in poor metabolizers. More than 80% of an atomoxetine dose is excreted in the urine, less than 17% in the feces, and less than 3% is excreted unchanged.

Patient Information

1. Take with or without food.
2. Take on the regular schedule prescribed by the physician. Do not take more or less than prescribed.
3. Use caution when driving a car or operating hazardous machinery until you know if your performance is affected by the drug.
4. Atomoxetine is not associated with stimulant or euphoric properties, so its abuse potential is low.
5. Atomoxetine is not a controlled substance; physicians can call in prescriptions and refills to the pharmacy.

iameter of 54 mm and a cross-section of 4 mm. The ring can easily be inserted and removed by the female. When compared to oral forms of hormonal contraception in studies, ease of insertion and compliance were much higher. Because of the high level of compliance, fewer pregnancies were seen while taking this medication (6 out of 100 women). The compliance is partly due to the sustained release action of this hormonal contraceptive. After insertion, the ring is left inside the vagina for three weeks and then removed for a one week interval. Another positive aspect of NuvaRing is the fact that it can be removed during sexual intercourse for up to three hours. Though removal can be accomplished with little to no risk, only 10% of patients chose to remove the ring during the treatment period. Adverse reactions are low; however, when compared to oral methods of contraception, "spotting" was a very common event, occurring in 98% of the women. Pricing and efficacy of NuvaRing are comparable to other methods of contraception; however the thought or fear of an object remaining in the vagina for a three week period of time may worry some women, causing this form of hormonal contraception to become less popular.

Dosing and Administration

NuvaRing is available as a combination progestin and estrogen vaginal ring. The ring is inserted into the vagina by the woman herself. NuvaRing is to be inserted between day 1 and 5 of the current menstrual period, even if bleeding has not finished. Proper insertion is accomplished by the female choosing any position which is comfortable for her, such as standing, squatting or lying down. Holding the ring between the thumb and index finger, compress the ring and gently push the folded ring into the vagina. The exact position of the vaginal ring is not critical for it to function. NuvaRing is to be left inside the vagina for three consecutive weeks and removed three weeks later on the same day of the week as insertion.

The ring is removed by hooking the index finger under the forward rim or by grasping the ring between the thumb and index finger and pulling it out. **DO NOT** flush the used vaginal ring in the toilet.

If the contraceptive ring has been temporarily taken out during the three week use period, rinse it with cool water and reinsert as soon as possible, **at the latest, within three hours**. If the ring has been out for greater than three hours, contraceptive effectiveness may be reduced. An extra form of birth control must be used until the contraceptive vaginal ring has been in place for at least **seven** days in a row.

If the contraceptive ring has been left in the vagina for

References

1. Crismon ML. Atomoxetine Created Excitement in ADHD Community. *American Pharmaceutical Association Drug Info Line*. 2002 Dec; 3(12):1.
2. Bymaster FP, Katner JS, Nelson DL, et al. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. *Neuropsychopharmacology* 2002 Nov; 27(5): 699-711.
3. Heil SH, Holmes HW, Bickel WK, et al. Comparison of the subjective, physiological, and psychomotor effects of atomoxetine and methylphenidate in light drug users. *Drug Alcohol Depend* 2002 Jul; 67(2): 149-56.
4. Kratochvil CJ, Heiligenstein JH, Dittmann R, et al. Atomoxetine and methylphenidate treatment in children with ADHD: a prospective, randomized, open-label trial. *J Am Acad Child Adolesc Psychiatry*. 2002 Jul; 41(7): 776-84.
5. Strattera™ (atomoxetine hydrochloride) prescribing information. Eli Lilly and Company. Indianapolis, IN. December 2002.

NuvaRing[®] (etonogestrel/ethinyl estradiol vaginal ring)

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Introduction

NuvaRing (etonogestrel/ethinyl estradiol) is a new form of contraception that was FDA approved in October 2001. NuvaRing itself is a flexible combined hormonal contraceptive vaginal ring.

Therapeutic Recommendation

NuvaRing is a flexible vaginal ring with a outer di-

NEW DRUG UPDATE

up to one extra week, remove it and insert a new ring after a 1-week ring free interval. Rule out pregnancy if the ring has been left in place greater than four weeks.

Cost Comparison

Medication/Dose	Cost**		
	CVS	Kroger	RiteAid
NuvaRing (vaginal ring) (etonogestrel/ethinyl estradiol)	43.99	46.17	38.99
Ortho-Evra (patch) (norelgestromin/ethinyl estradiol)	34.99	37.17	35.99
Depo-Provera** (injection) (medroxyprogesterone)	62.59	62.97	75.99
Ortho-Tricycline (oral) (norgestimate/ethinyl estradiol)	34.99	29.99	35.99
Yasmin (oral) (drospirenone/ethinyl estradiol)	34.29	28.59	29.99

** All medications for one month supply, except **Depo-Provera—3 month supply.**

Contraindications/Precautions

NuvaRing should not be used in patients currently with or with a past medical history significant for thrombophlebitis or thromboembolic disorders; coronary artery disease (CAD); valvular heart disease with complications; severe hypertension; diabetes with vascular involvement; headache with focal neurological symptoms; major surgery with prolonged immobilization; known or suspected breast or endometrial cancer; undiagnosed abnormal vaginal bleeding; cholestatic jaundice of pregnancy; active liver disease; known or suspected pregnancy; heavy smoking (≥ 15 cigarettes/day); > 35 years of age; and, hypersensitivity to any component of the vaginal ring.

Special Populations

Geriatrics: This medication has not been studied in women ≥ 65 years of age and is not indicated in this population.

Pregnancy: Teratology studies have been performed in animals using the oral route of administration with the vaginal ring dosages and have revealed no harm to the fetus due to etonogestrel. *Pregnancy Category X.*

Lactation: The effects of the contraceptive ring in nursing mothers has not been evaluated. Advise women who are breast-feeding not to use the contraceptive ring but to use other forms of birth control until the child is weaned.

Children: Safety and efficacy have been established in

women of reproductive age. Although studies have not been conducted, safety and efficacy is expected to be the same for postpubertal adolescents < 16 years of age and those ≥ 16 years of age. Use of this product before menarche is not indicated.

Drug Interactions

Drug interactions that may occur while using NuvaRing remain the same as with oral forms of hormonal contraception. Although there are numerous potential interactions with hormonal contraceptives, the following is a partial list: Co-administration with acetaminophen may result in an increased ethinyl estradiol level and a decreased acetaminophen level. Administration of the contraceptive ring with certain antibiotics may also alter drug levels, such as griseofulvin, penicillins and tetracyclines, which decrease the amount of hormonal blood levels. Atorvastatin and ascorbic acid may also increase the level of ethinyl estradiol. CYP 3A4 inhibitors appear to increase plasma hormone levels. Protease Inhibitors and Saint Johns Wort when given with contraceptives may decrease the effectiveness. Due to the sensitive nature (and liability issues) associated with drug interactions in birth control, always check before prescribing or dispensing new medications.

Adverse Effects

The most common adverse events reported in clinical trials are vaginitis (13.7%); headache (11.8%); upper respiratory tract infection(s) (3.2%); leukorrhea (5.9%); sinusitis (3.8%); weight gain (3%); and nausea (4.5%).

Pharmacology

Mechanism of Action: NuvaRing acts as other combination hormonal contraceptives do, which is by suppression of gonadotropins. The primary effect of this agent is inhibition of ovulation, however other alterations occur such as changes in the cervical mucus and the endometrium, inhibiting sperm entry and implantation, respectively.

Absorption/Distribution: Etonogestrel released by the vaginal ring is rapidly absorbed, with bioavailability after vaginal administration being 100%. The ethinyl estradiol component of the contraceptive ring is also rapidly absorbed, however the bioavailability of this component is 55.6%, comparable to that of oral ethinyl estradiol. The agent is 32% bound to sex hormone binding globulin (SHBG) and 60% bound to albumin in the blood. The ethinyl estradiol component is highly, yet not completely, bound to serum albumin (98.5%). This binding induces an increase in the serum levels of SHBG.

Metabolism/Excretion: Both components of NuvaR-

ing are metabolized in the liver by cytochrome P450 3A4 isoenzymes. Both etonogestrel and ethinyl estradiol are eliminated via urine, bile, and feces.

Patient Information

1. This product does not protect against HIV infection (AIDS) or any other sexually transmitted diseases.
2. See detailed package instructions for proper vaginal insertion.
3. Although refrigerated prior to dispensing, the vaginal ring may be stored at room temperature for up to four months. Avoid storing in direct sunlight.
4. NuvaRing can be removed during sexual intercourse for up to a three hour period. For reinsertion, run the ring under cool water and insert as normal.
5. Call your health care provider right away if any uncommon side effects are experienced, such as sharp chest pain, coughing up blood, shortness of breath, pain in the calf, etc. Any severe symptoms such as these may indicate serious medical problems.
6. To avoid adverse effects or accidental pregnancy, be sure to speak to your doctor or pharmacist about potential drug interactions.

7. If dosages are missed or if the vaginal ring has been left in too long, be sure to use alternate forms of contraception, such as male condoms and/or spermicide, until a new vaginal ring has been in place for at least seven days. In the event of a missed menstrual period, rule out pregnancy.

References

1. NuvaRing® Etonogestrel/Ethinyl Estradiol Vaginal Ring. Product information. Organon, Inc. West Orange, NJ. October 2001.
2. Roumen FJ, Apter D, et al. Efficacy, tolerability and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinyl estradiol. *Hormone Reproduction*. 2001 (16). 469 - 475.
3. Mulders T, Dieben T. Use of the novel combined contraceptive vaginal ring NuvaRing for ovulation inhibition. *Fertility and Sterility*. May 2001 (75). 865 - 870.



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