

CLINICAL CAPSULES

Parental Notification

Florida voters recently passed a constitutional amendment that paves the way for required parental notification before a minor can have an abortion. The state's supreme court has twice struck down parental notification laws passed by the state legislature, saying that they run contrary to the privacy clause in the state's constitution. Florida Right to Life, which supported the amendment, said it is important for parents to be involved to ensure their child is receiving proper care. But the American Civil Liberties Union of

Florida opposed the amendment, saying that mandating notification can jeopardize teens' health by causing delays that can increase risks to their physical and emotional health. Most teens who have abortions do not involve at least one parent, ACLU said, but those who do not often have good reasons for keeping the information private.

Cervical Infection Risk

Use of Depo-Provera was significantly associated with the development of cervical infections in a study of 819 women, said Charles S. Morrison, Ph.D.

Even after adjustment for sexual behavior and demographic traits, including condom use and multiple sex partners, women who used Depo-Provera (medroxyprogesterone) were more likely to develop gonorrhea or chlamydia within a year, compared both with women who used oral contraceptives and controls, said Dr. Morrison of Family Health International, a research organization in Research Triangle Park, N.C.

The use of oral contraceptives was not associated with increased risk or development of infections.

After a mean follow-up of 337 days, 45 women in the prospective cohort study

had developed at least one cervical infection. Most of the women were single (77%) and nulliparous (75%). They ranged in age from 15 to 45 years, with a median age of 22 years (Sex. Transm. Dis. 2004;31:561-7).

The researchers calculated risk based on how many women became infected within a year (woman-years) and found a rate of 13.7 infections/100 woman-years in the Depo-Provera group, significantly higher than women in the oral contraceptive group (3.9 infections/100 woman-years) and the control group (6/100 woman-years).

Off-Label Antinausea Drug

Ondansetron is increasingly prescribed off label for nausea and vomiting in pregnancy, and results of a new study suggest it is safe for this indication.

In the prospective observational study, the drug, which is typically used for treating nausea and vomiting in chemotherapy patients, was not associated with an increased risk of fetal malformations, reported Adrienne Einarson, R.N., of the University of Toronto and her colleagues (BJOG 2004;111:940-3).

The investigators studied women exposed to ondansetron (Zofran); other antiemetics, including Diclectin, metoclopramide, phenothiazines, and ginger; and/or no drugs or only drugs known to be nonteratogenic. To date, outcomes from 176 pregnancies in each group have been evaluated.

In the ondansetron group there were 169 live births, 5 miscarriages, and 2 therapeutic abortions. There were six major malformations, for a rate of 3.5%. The mean birth weight was 3,362 g. There were no statistical differences between the three groups in any of the study end points, the investigators said.

Ondansetron appears safe for the fetus, but the investigators noted that the sample size in this study is small and that many more cases would need to be studied before a definitive conclusion about the safety of the drug could be made.

Stretch Genes

Genetic factors appear to play a role in the development of striae gravidarum, rather than pregnancy weight or increases in weight during pregnancy, Anne Chang, M.D., said at the annual meeting of the Society for Investigative Dermatology in Providence, R.I.

Dr. Chang and her associates surveyed a group of 161 women who had given birth and found that 55% had striae gravidarum (SG), which arose on average at a gestational age of 25 weeks. Ninety percent of the women who reported having SG said that they developed them during their first pregnancy, while 10% said that SG first developed during their second pregnancy.

Women were significantly more likely to develop SG if their mother or other family members had SG, if they had a personal history of breast or thigh striae, or if they were nonwhite. The genetic risk factors identified in the study suggest that an intrinsic dysregulation of elastic fibers may make women prone to developing SG, said Dr. Chang, a dermatology fellow at Stanford (Calif.) University.

—From staff reports

References: 1. Data on file. Pfizer Inc., New York, NY. 2. IMS Health Inc.; May 2004.

LIPITOR® (Atorvastatin Calcium) Tablets

Brief Summary of Prescribing Information

CONTRAINDICATIONS: Active liver disease or unexplained persistent elevations of serum transaminases. Hypersensitivity to any component of this medication. **Atherosclerosis** is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components of fetal development, including synthesis of steroids and cell membranes. Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant females. Hypersensitivity reactions are contraindicated during pregnancy and in nursing mothers. **ATORVASTATIN SHOULD BE ADMINISTERED TO WOMEN OF CHILDBEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEIVE AND HAVE BEEN INFORMED OF THE EXTENT OF THE CONTRAINDICATIONS. If a patient becomes pregnant while taking this drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.**

WARNINGS: Liver Dysfunction—HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Persistent elevations (>3 times the upper limit of normal ALT) occurring on 2 or more occasions in 0.7% of patients who received atorvastatin in clinical trials. The incidence of these abnormalities was 0.2%, 0.2%, 0.8%, and 2.3% for 10, 20, 40, and 80 mg, respectively. One patient in clinical trials developed jaundice. Increases in liver function tests (LFT) in other patients were not associated with jaundice or other clinical signs or symptoms. Upon dose reduction, drug interruption, or discontinuation, transaminase levels returned to or near pretreatment levels without sequelae. Eighteen of 30 patients with persistent LFT elevations continued treatment with a reduced dose of atorvastatin. It is recommended that liver function tests be performed prior to and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (eg, semiannually) thereafter. Liver enzyme changes generally occur in the first 3 months of treatment with atorvastatin. Patients who develop a history of liver disease, active liver disease or unexplained persistent transaminase elevations are contraindications to the use of atorvastatin (see CONTRAINDICATIONS). **Skeletal Muscle**—Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported in atorvastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aches or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values >10 times ULN, should be considered in any patient with myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. Atorvastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. The risk of myopathy during treatment with drugs in this class is increased with concurrent administration of cyclosporine, fibrin acid derivatives, erythromycin, niacin, orazole antifungals. Physicians considering concurrent therapy with atorvastatin and fibrates, including gemfibrozil, should be aware of increased risk of myopathy. Atorvastatin and fibrates, including gemfibrozil, should not be administered to patients taking other drugs metabolized via the same cytochrome isozymes are not expected. **Colistepol**: Plasma concentrations of atorvastatin decreased approximately 25% when colistepol and atorvastatin were administered. However, LDL-C reduction was greater when atorvastatin and colistepol were administered than when either drug was given alone. **Cimetidine**: Atorvastatin plasma concentrations and LDL-C reduction were not altered by coadministration of cimetidine. **Digoxin**: When multiple doses of atorvastatin and digoxin were administered, steady state plasma digoxin concentrations were decreased. Physicians prescribing digoxin should be monitored appropriately. **Erythromycin**: In healthy individuals, plasma concentrations of atorvastatin increased approximately 40% with coadministration of atorvastatin and erythromycin, a known inhibitor of cytochrome P-450 3A4 (see WARNINGS, Skeletal Muscle).

PREGAUCIONS: **General**—Before instituting therapy with atorvastatin, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, and weight reduction in obese patients, and to treat other underlying medical problems (see INDICATIONS AND USAGE, and full prescribing information). **Information for Patients**—Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. **Drug Interactions**—The risk of myopathy during treatment with drugs in this class is increased with concurrent administration of cyclosporine, fibrin acid derivatives, niacin, orazole antifungals, and fibrates (see WARNINGS, Skeletal Muscle, and Atorvastatin and Maalox®). **Interactions with Alcohol**: Administration of atorvastatin to patients taking alcohol resulted in decreased plasma concentrations of atorvastatin and increased plasma concentrations of atorvastatin metabolites. **Other Drugs**: Administration of atorvastatin and digoxin were administered. **Other Drugs**: Administration of atorvastatin and digoxin were administered. **Other Drugs**: Administration of atorvastatin and digoxin were administered.

USE AND DOSAGE: Atorvastatin is a statin. It is used to reduce the risk of stroke and heart disease in patients with hypercholesterolemia. It is also used to reduce the risk of heart disease in patients with heart disease. The recommended dose is 20 mg once daily. The maximum recommended dose is 80 mg once daily. The drug should be taken once daily with or without food. The drug should be taken for at least 4 weeks before laboratory tests are performed.

ADVERSE REACTIONS: In clinical trials, the most common adverse reactions were headache, myalgia, and upper respiratory tract infections. Other adverse reactions included nausea, constipation, and diarrhea. In patients taking atorvastatin with other lipid-lowering drugs, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with fibrates, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with niacin, the most common adverse reactions were flushing and rash. In patients taking atorvastatin with cyclosporine, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with azole antifungals, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with erythromycin, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with cimetidine, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with colistepol, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with digoxin, the most common adverse reactions were myalgia, muscle pain, and weakness. In patients taking atorvastatin with other drugs metabolized via the same cytochrome isozymes, the most common adverse reactions were myalgia, muscle pain, and weakness.

development was delayed (rotator performance at 100 mg/kg/day and acoustic startle at 225 mg/kg/day; pinnae detachment and eye opening at 225 mg/kg/day). These doses correspond to 100 mg/kg and 225 mg/kg (225 mg/kg) the human AUC at 80 mg/day. Rare reports of congenital anomalies have been received following intrathecal exposure to HMG-CoA reductase inhibitors. There has been one report of severe congenital bony deformity, tracheo-esophageal fistula, and anal atresia (VATER association) in a baby born to a woman who took lovastatin with dexamethasone sulfate during the first trimester of pregnancy. LIPITOR should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking LIPITOR, it should be discontinued and the patient advised again as to the potential hazards to the fetus. **Nursing Mothers**—During rat pups had plasma and liver drug levels of 50% and 40%, respectively, of that in their mother's milk. Because of the potential for adverse reactions in nursing infants, women taking LIPITOR should not breast-feed (see CONTRAINDICATIONS). **Pediatric Use**—Safety and effectiveness in patients 10-17 years of age with heterozygous familial hypercholesterolemia have been evaluated in a controlled clinical trial of 6 months duration in adolescent boys and postmenstrual girls. Patients treated with LIPITOR had an adverse experience profile generally similar to that of patients treated with placebo, the most common adverse experiences observed in both groups, regardless of causality assessment, were infections. **Doses greater than 20 mg have not been studied in this patient population.** In this limited controlled study, there was no detectable effect on growth or sexual maturation in boys or on menstrual cycle length in girls. **USE AND DOSAGE:** Atorvastatin is a statin. It is used to reduce the risk of stroke and heart disease in patients with hypercholesterolemia. It is also used to reduce the risk of heart disease in patients with heart disease. The recommended dose is 20 mg once daily. The maximum recommended dose is 80 mg once daily. The drug should be taken once daily with or without food. The drug should be taken for at least 4 weeks before laboratory tests are performed.

Body System	Placebo	Atorvastatin 10 mg	Atorvastatin 20 mg	Atorvastatin 40 mg	Atorvastatin 80 mg
Adverse Event	N = 270	N = 863	N = 36	N = 79	N = 94
BODY AS A WHOLE					
Infection	10.0	10.3	2.8	10.1	7.4
Headache	7.0	5.4	16.7	2.5	6.4
Accidental Injury	3.7	4.2	0.0	1.3	3.2
Flu Syndrome	1.9	2.2	0.0	2.5	3.2
Abdominal Pain	0.7	2.8	0.0	0.0	2.1
Back Pain	3.0	2.0	0.0	3.8	1.1
Allergic Reaction	2.6	0.9	2.8	1.3	0.0
Asthenia	1.9	2.2	0.0	3.8	0.0
DIGESTIVE SYSTEM					
Constipation	1.8	2.1	0.0	2.5	1.1
Diarrhea	0.5	0.4	0.0	1.3	5.3
Dyspepsia	4.1	2.3	2.8	1.2	2.1
Flatulence	3.3	2.1	2.8	1.3	1.1
RESPIRATORY SYSTEM					
Sinusitis	2.6	2.8	0.0	2.5	6.4
Pharyngitis	1.5	2.5	0.0	1.3	2.1
SKIN AND APPENDAGES					
Rash	0.7	3.9	2.8	3.8	1.1
MUSCULOSKELETAL SYSTEM					
Arthralgia	1.5	2.0	0.0	5.1	0.0
Myalgia	1.1	3.2	5.6	1.3	0.0

Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)—In ASCOT (see CLINICAL PHARMACOLOGY, Clinical Studies) a full prescribing information) involving 10,255 participants treated with LIPITOR 10 mg daily (n=5,188) or placebo (n=5,137), the safety and tolerability profile of the drug treated with LIPITOR was comparable to that of the group treated with placebo during a median of 3.3 years of follow-up.

The following adverse events were reported, regardless of causality assessment in patients treated with atorvastatin in clinical trials. The events in italics occurred in >2% of patients and the events in plain type occurred in <2% of patients.

Body as a Whole: Chest pain, face edema, fever, neck rigidity, malaise, photosensitivity reaction, generalised edema. **Digestive System:** Nausea, gastroenteritis, liver function tests abnormal, colitis, vomiting, gastritis, dry mouth, rectal hemorrhage, esophagitis, stricture, glossitis, mouth ulceration, anorexia, increased appetite, stomatitis, biliary pain, chills, duodenal ulcer, dysphagia, enteritis, melena, gum hemorrhage, stomach ache, tenesmus, ulcerative stomatitis, hepatitis, parotiditis, cholestatic jaundice. **Respiratory System:** Bronchitis, pharyngitis, pneumonia, dyspnea, asthma, epistaxis. **Nervous System:** Insomnia, dizziness, paresthesia, somnolence, amnesia, abnormal dreams, libido decreased, emotional lability, incoordination, peripheral neuropathy, torticollis, facial paralysis, hyperkinesia, depression, hyposthesia, hypertension, vertigo, leg cramps, bursitis, tenosynovitis, myasthenia, tendinous contracture, myositis, skin and appendages: Pruritus, contact dermatitis, alopecia, dry skin, sweating, acne, urticaria, eczema, seborrhea, skin ulcer. **Urogenital System:** Urinary tract infection, urinary frequency, cystitis, hematuria, impotence, dysuria, kidney calculus, nocturia, epididymitis, fibrocystic breast, vaginal hemorrhage, albuminuria, breast enlargement, metrorrhagia, nephritis, urinary incontinence, urinary retention, urinary urgency, abnormal ejaculation, uterine hemorrhage. **Special Senses:** Amblyopia, tinnitus, dry eyes, refraction disorder, eye hemorrhage, deafness, glaucoma, parosmia, taste loss, taste perversion. **Cardiovascular System:** Palpitation, vasodilatation, syncope, migraine, postural hypotension, phlebitis, arhythmia, angina pectoris, hypertension. **Metabolic and Nutritional Disorders:** Peripheral edema, hyperglycemia, creatine phosphokinase increased, gout, weight gain, hypoglycemia. **Hemic and Lymphatic System:** Echinocystis, anemia, lymphadenopathy, thrombocytopenia, petechia. **Postinfection Reactions:** Adverse events associated with LIPITOR therapy reported since market introduction, that are not listed above, regardless of causality assessment, include the following: myalgias, angioedemous edema, bullous rash (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), and rhabdomyolysis. **Pediatric Patients (10-17 years)** In a 26-week controlled study in boys and postmenstrual girls (n=140), the safety and tolerability profile of LIPITOR 10 mg daily was generally similar to that of placebo (see CLINICAL PHARMACOLOGY, Clinical Studies section in full prescribing information and PRECAUTIONS, Pediatric Use).

ORIGIN: There is no specific treatment for atorvastatin overdose. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance atorvastatin clearance.

Please see full prescribing information for additional information about LIPITOR.

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