DRUGS, PREGNANCY, AND LACTATION

Pregnancy Registries

BY GERALD G. BRIGGS, B. PHARM., FCCP

Pregnancy registries are valuable sources of information, and for many drugs and vaccines, they are the primary source of human pregnancy experience.

The strengths of these registries are their prospective nature—women are enrolled before the outcome is known—and enrollment is over a wide geographical area. Typically, two types of pregnancy outcomes are obtained: outcomes with birth defects and outcomes without known birth defects. The latter comprises live births, fetal deaths, and spontaneous abortions.

Registries can identify early signals of teratogenicity, but they have several limitations. They depend on voluntary reporting, which results in selection bias, and they are not representative of target populations. Pregnancies that are lost to follow-up may have had different outcomes than those with documented outcomes. Furthermore, registries lack details on elective terminations and fetal deaths without birth defects, and all spontaneous abortions. Finally, with some exceptions, they usually lack control groups.

Because the total number of exposed pregnancies is unknown, data from a registry cannot be used to calculate prevalence of an outcome, but the data can be used to estimate the proportion of birth defects. Some registries also collect data on retrospective reports, which are less representative of the target population because they can be biased toward the reporting of more unusual and severe outcomes. However, they may be helpful in detecting unusual patterns of birth defects.

In the chart below are the pregnancy registries listed on the Food and Drug Administration Web site, which provides additional details on the registries, such as fax numbers, links to other Web sites, and mailing addresses (www.fda.gov/womens/registries).

Because the strength of a registry is based on numbers, I encourage health care professionals to enroll appropriate patients in these registries whenever possible.

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Registries/Studies

Organization of Teratology Information Specialists (OTIS)* Autoimmune Diseases Study
(877-311-8972)
Rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis
Leflunomide (Arava), etanercept (Enbrel), adalimumab (Humira), abatacept (Orencia)

OTIS Vaccinations in Pregnancy Study (877-311-8972)
Tetanus, diphtheria and pertussis, influenza, and/or meningococcal vaccines
*includes control groups and dysmorphology examinations of exposed infants

Motherisk Program* (800-670-6126)

Vaccines	Hepatitis B vaccine (includes Twinrix)
Toe and nail fungal infections	Lamisil
Weight loss	Meridia (sibutramine)
Asthma	Singulair (montelukast)

*includes control groups

Kendle International Pregnancy Registries

HIV/AIDS (800-258-4263)	Antiretroviral agents
Migraine headaches (800-336-2176)	Imitrex (sumatriptan) and Amerge (naratriptan)
Multiple sclerosis (800-478-7049)	Betaseron (interferon beta-1b)
Partial onset seizures (888-537-7734)	Keppra (levetiracetam)
Partial seizures (800-336-2176)	Lamictal (lamotrigine)
Hepatitis C (800-593-2214)	Copegus (ribavirin)
Depression (800-336-2176)	Wellbutrin and Zyban (bupropion)

Amevive Pregnancy Registry (866-834-7223)

Chronic plaque psoriasis	Amevive (alefacept)

Avonex Pregnancy Registry (800-811-0104)

Relapsing forms of multiple sclerosis	Avonex (interferon beta-1a)

Cooper Health Cancer and Childbirth Registry

Cancer medicines	(856-757-7876)

Fabry Registry (800-745-4447, ext. 15500)

Fabry disease	Fabrazyme (agalsidase beta)
Hurler-Scheie syndrome/mucopolysaccharidosis I	Aldurazyme (laronidase)

Massachusetts General Hospital* AED Pregnancy Registry (888-233-2334)
Antiepileptic drugs
*includes comparison group

Merck Pregnancy Registry Program (800-986-8999)

Chickenpox	Varivax vaccine
MMR and chickenpox	ProQuad vaccine
Herpes zoster	Zostavax vaccine
Human papilloma virus (HPV)	HPV vaccine (Gardasil)
Type 2 diabetes	Janumet (sitagliptin/metformin)
Type 2 diabetes	Januvia (sitagliptin)
Migraine headaches	Maxalt (rizatriptan)
Asthma	Singulair (montelukast)

MPS VI Clinical Surveillance Program
Maroteaux-Lamy syndrome (polydystrophic dwarfism or mucopolysaccharidosis VI [MPS VI])
Galsulfase (naglazyme)
clinicaltrials.gov/ct/show/NCT00214773?order=2

National Transplantation Pregnancy Registry
Antirejection drugs
(877-955-6877)

Raptiva Pregnancy Registry

Chronic plaque psoriasis (877-727-8482)	Efalizumab (Raptiva)

Rebif Pregnancy Registry

Multiple sclerosis (877-447-3243)	Interferon beta-1a (Rebif)

Tysabri Pregnancy Registry

Multiple sclerosis (866-831-2358)	Natalizumab (Tysabri)

Neoral Pregnancy Registry

Psoriasis and rheumatoid arthritis (888-522-5581)	Cyclosporine (Neoral)

Twinrix Pregnancy Registry

Hepatitis A & B Prevention (888-522-5581)	Hepatitis A/hepatitis B vaccine (Twinrix)

Xolair Pregnancy Registry

Asthma (866-496-5247)	Omalizumab (Xolair)

Postmarketing CellCept Data Prompt Stronger Pregnancy Alert

BY ELIZABETH MECHCATIE
Senior Writer

Postmarketing reports of an increased risk of first trimester loss and congenital malformations associated with the use of mycophenolate mofetil during pregnancy has prompted a pregnancy category label change for the immunosuppressant drug.

Mycophenolate mofetil, marketed as CellCept by Roche, is approved for preventing organ rejection in allogenic kidney, heart, or liver transplant recipients, and is used with cyclosporine and corticosteroids.

CellCept also has been used off-label to treat some dermatologic and rheumatologic conditions.

Based on postmarketing data from the U.S. National Transplantation Pregnancy Registry and other postmarketing data in women exposed to systemic CellCept during pregnancy, the pregnancy category label has been changed from a category C, in which the risk of fetal harm cannot be ruled out, to category D, in which there is positive evidence of fetal risk.

Exposure to CellCept during pregnancy has been associated with an increased risk of first trimester loss, and an increased risk of congenital malformations, "especially external ear and facial abnormalities, including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney," according to Roche and the Food and Drug Administration.

The pregnancy category change was announced on the FDA's MedWatch site, and in a letter to health care professionals issued by Roche.

The letter refers to the December 2006 publication of reports from the transplant registry of 33 pregnancies in 24 female transplant patients exposed to regimens containing CellCept. Of the 33 cases, there were 15 spontaneous abortions (45%). Of the 18 live-born infants, 4 (22%) had structural malformations. There were also postmarketing reports, collected between 1995 and 2007, of 77 women exposed to systemic CellCept during pregnancy, of whom 25 (33%) had spontaneous abortions and 14 (18%) had a malformed infant or fetus.

The Roche letter advised that women of childbearing potential—including pubescent girls and perimenopausal women—should have a negative serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL 1 week before starting treatment and they should receive contraceptive counseling. Unless abstinence is chosen, women in this category should start using two contraceptive methods 4 weeks before starting treatment with CellCept, and should continue using those two methods for 6 weeks after stopping treatment. CellCept should not be used in a woman who plans to become pregnant "unless she cannot be successfully treated with other immunosuppressant drugs," according to the letter.

Roche encourages health care professionals to register pregnant women exposed to CellCept in the transplant registry by calling 877-955-6877. ■

For the MedWatch announcement, Roche letter, and revised label, go to: www.fda.gov/medwatch/safety/2007/safety07.htm#CellCept2. Report adverse reactions to CellCept to Roche at 800-526-6367, or to the FDA at 800-332-1088 or www.fda.gov/medwatch.

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