

IDIS/Web Search Strategies: Epilepsy in Pregnancy

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In the United States, it is estimated that 500,000 women who suffer from epilepsy are of childbearing age.¹ Clinicians treating women with epilepsy face the unique challenge of maintaining seizure control and attempting to minimize teratogenic risk potential when their patients become pregnant. Unfortunately, discontinuing anticonvulsants prior to conception, or early in pregnancy, is not a viable option for the majority of women with epilepsy.² Convulsive seizures during pregnancy are harmful to the expectant mother and her developing fetus. A recent prospective study found that convulsive seizures during the first trimester were associated with congenital malformations in 7.4 % of pregnancies.³ The risk of congenital malformations is higher in women with epilepsy. A Finnish study⁴ compared the risk of major fetal malformation in women with epilepsy. The study found that major congenital malformations occurred in 4.6% of women treated with antiepileptic drugs (AEDs) compared to 2.8% for untreated patients, odds ratio 1.7 (95% CI 1.05-2.81). It is essential that the healthcare team caring for a pregnant woman with epilepsy is aware of the current literature and therapy recommendations to maintain the delicate balance between seizure control and potential teratogenic risks.

The pharmacists working in the Division of Drug Information Service at the University of Iowa have gathered and indexed information from several types of sources that are useful in assisting the clinician in obtaining the primary literature necessary to answer questions related to AED use in pregnancy. Examples of how you can best use *IDIS*/Web for these types of questions are presented here.

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Maternal Use of Anticonvulsants and Effects on the Neonate

A general search can be done to find all articles that focus on maternal use of anticonvulsants during pregnancy and potential teratogenic risks. The search can be constructed combining the disease term for epilepsy, EPILEPSY NEC 345., and the population tag for pregnancy, PREGNANCY NEC V22., in the Disease field. To search for articles containing both disease terms you must manually change the Boolean operator within the disease field from “or” to “and” before performing the search. Note the default Boolean operator within the Disease field is “or” and will automatically be used in the search unless it is changed manually.

The search strategy can include all anticonvulsants by using the truncated drug class code 2812* in the Drug field. The drug class of anticonvulsants is searched in the Thesaurus and retrieves the following entry:

(DR) ANTICONVULSANTS 28120000
Search 2812* to include all drugs in this category

The screenshot shows the IDIS search interface. The search criteria are as follows:

- All Fields: (empty)
- Drug: 2812*
- Disease: "EPILEPSY NEC 345." and "PREGNANCY NEC V22." (Boolean operator: and)
- Descriptor: "SIDE EF FETAL EFFECT 48" (Boolean operator: and)
- Title: (empty)
- Author: (empty)
- Abstract: (empty)
- Journal: (empty)
- Volume: (empty)
- Issue: (empty)
- Page: (empty)
- Year: (empty)
- Article Number: (empty)
- Sequence Number: (empty)

Additional options include: "Only search records with abstracts" (unchecked), and search buttons for "search" and "clear".

Figure 1

For more information about searching by drug class, consult the June 1999 issue of *World of Drug Information*, <http://www.uiowa.edu/~idris/wodjun99.htm#search.tip>. When the Thesaurus is searched for the appropriate descriptor term for congenital malformation the results show the correct term is SIDE EF FETAL EFFECT 48. Note: In the Thesaurus descriptor terms include (DE) after the valid term; disease terms (DI) and drug terms (DR). The search retrieved several articles that may be relevant. If you want to search for a specific type of epilepsy, consult the Thesaurus for the appropriate valid disease term. To view a complete search template for this search strategy see Figure 1.

The screenshot shows the IDIS search interface with the following search criteria:

- All Fields: (empty)
- Drug: "VALPROIC ACID 28122015" (Boolean operator: and)
- Disease: "EXPOSURE, PRENATAL V89." (Boolean operator: and)
- Descriptor: (empty)
- Title: (empty)
- Author: (empty)
- Abstract: (empty)
- Journal: (empty)
- Volume: (empty)
- Issue: (empty)
- Page: (empty)
- Year: (empty)
- Article Number: (empty)
- Sequence Number: (empty)

Additional options include: "Only search records with abstracts" (unchecked), and search buttons for "search" and "clear".

Figure 2

In IDIS/Web it is also possible to do a more specific search for congenital malformations induced by in-utero exposure. This type of search would focus on the neonate and a specific drug such as valproic acid. In IDIS/Web, in-utero contact or exposure to a chemical or therapeutic substance is found in the Thesaurus as EXPOSURE, PRENATAL V89. A search can be conducted using the term “EXPOSURE, PRENATAL V89” in the Disease field and "VALPROIC ACID 28122015" can be selected for the Drug field using either the Thesaurus or Drug Look Up. To view a complete search template for this search strategy see Figure 2.

The searches presented here are some examples of the valuable drug therapy information that can be easily accessed using the *IDIS*/Web database to assist you in answering drug information questions. In addition to these resources, the pharmacists at IDIS may be contacted by e-mail or telephone to offer assistance in formulating a search.

References

1. Hirtz D, Thurman DJ, Gwinn-Hardy K, et al. How common are the “common” neurologic disorders? *Neurology*. 2007;68:326-37.
2. Sethi NK, Wasterlain A, Harden CL. Pregnancy and epilepsy—when you’re managing both. *J Fam Pract*. 2010;59:675-9.
3. Sachdeo R. The evidence-based rationale for monotherapy in appropriate patients with epilepsy. *Neurology*. 2007;69(Suppl 3):S1-2. (*IDIS* Article Number 588371)
4. Artama M, Auvinen A, Raudaskosi T, et al. Antiepileptic drug use of women with epilepsy and congenital malformations in offspring. *Neurology*. 2005;64:1874-8. (*IDIS* Article Number 536738)
5. Sarrazin N. Searching with drug classes. *World of Drug Info*. 1999; 10(2). Available from: <http://www.uiowa.edu/~idis/wodjun99.htm>. Accessed: 2-15-2011.

2011 Iowa Drug Information Service Exhibit Schedule

Please join us:

American Association of Colleges
of Pharmacy (ACCP)
July 9 — July 12, 2011
San Antonio, Texas
USA

71st World Congress of
Pharmacy & Pharmaceutical
Sciences 2011 (FIP)
September 2 — September 8, 2011
Hyderabad
India

New Molecular Entities & Biologicals

FDA Approvals
December 2010 - March 2011

An *IDIS* search retrieved articles relevant to the new drugs and their approved uses. These articles provide a selection of key critical studies and reviews. Additional information on these newly approved drugs will be available in the FDA Approval Package (an official United States Food and Drug Administration [FDA] document) that is compiled for new drugs following approval. The FDA Approval Package includes reviews of the pivotal and supportive clinical studies conducted during the approval process. These studies are often not published elsewhere. FDA Approval Packages are selectively indexed and included as part of the *IDIS* database as they become available. Use the descriptor 155 FDA APPROVAL PACKAGE in combination with the valid drug term to retrieve these documents from the *IDIS* database.

For some newly approved drugs the FDA Approval Package may not yet be available. If the medication has been reviewed by one of the FDA Advisory Committees, you may still access data from pivotal studies, even those that have not been published in peer reviewed literature. These Committee reports are indexed in the *IDIS* database using the descriptor "FDA ADVISORY COMMITTEE 164". In addition to access to data from pivotal studies, these reports provide critical commentary from the Advisory Committee members, and specific, important questions related to the use and safety of the medication.

Generic Name Trade Name (FDA Review Classification)	Sponsor (Approval Date)	Valid <i>IDIS</i> Drug Term Drug Number (<i>IDIS</i> Citations)	Indication/Use Dosage Form	Valid <i>IDIS</i> Disease Term Modified ICD-9-CM Number
Azilsartan Medoxomil <i>Edarbi</i> (S)	Takeda Pharms NA (Feb. 25, 2011)	AZILSARTAN MEDOXOMIL 24080414 FDA Approved Indication (1 citation) Total (1 citation)	Hypertension. Oral Tablet.	Hypertension 401.
Belimumab <i>Benlysta</i> (BIOL)	Human Genome Sciences Inc. (Mar. 10, 2011)	BELIMUMAB 82000498 FDA Approved Indication (13 citations) Total (16 citations)	Systemic lupus erythematosus. Injection.	Lupus Erythematosus, System 710.0
Ioflupane I 123 <i>Datscan</i> (P)	GE Healthcare (Jan. 14, 2011)	IOFLUPANE I 123 36680110 FDA Approved Indication (7 citations) Total (7 citations)	SPECT imaging for detection of dopamine transporters in adult patients with suspected Parkinsonian syndromes. Injection.	Radioisotope Scan, Cerebral 92.11 Parkinson's Disease 332.
Roflumilast <i>Daliresp</i> (S)	Forest Research Institute Inc. (Feb. 28, 2011)	ROFLUMILAST 44100079 FDA Approved Indication (38 citations) Total (61 citations)	Chronic obstructive pulmonary disease (COPD). Oral Tablet.	Obstruction, Air, Chr NEC 496.
Spinosad <i>Natroba</i> (S)	Parapro Pharms (Jan. 18, 2011)	SPINOSAD 84041207 FDA Approved Indication (1 citation) Total (1 citation)	Head lice. Topical Suspension.	Pediculus, Capitis 132.0
Vilazodone Hydrochloride <i>Viibryd</i> (S)	Trovis Pharma LLC (Jan. 21, 2011)	VILAZODONE 28160496 FDA Approved Indication (1 citation) Total (1 citation)	Depression. Oral Tablet.	Disorder, Depressive NEC 311.

Review Classification:

S=Standard Review, the drug appears to have therapeutic qualities similar to those of one or more already marketed drugs

AA=Accelerated Approval

FT=Fast Track

P=Priority Review, significant improvement compared to marketed products, in the treatment, diagnosis, or prevention of a disease

BIOL=Biological

O=Orphan

Selected Bibliography

Ioflupane I 123

Anonymous. Briefing information from drug sponsor. Peripheral and Central Nervous System Advisory Committee Meeting, August 11, 2009. *FDA Advisory Committee*, 2009. (IDIS Article Numbers 623799-623804)

Data from three Phase 3 clinical studies was pooled in this post-hoc analysis to determine the sensitivity and specificity of visual interpretations of ioflupane I 123 (Datscan), and included a total of 648 patients with signs and symptoms of movement disorders or dementia. The study drug was injected at doses of 3 to 5 mCi (111 to 185 MBq) and was tested in single photon emission tomography (SPECT) cerebral imaging to detect loss of functional nigrostriatal dopaminergic neurons. Ioflupane I 123 was found to have high sensitivity and specificity, approximately 90% for each, in detecting striatal dopaminergic deficit (SDD). The study drug was also found to be safe with no serious side effects and no cocaine-like adverse effects.

Spinosad

Stough D, Shellabarger S, Quiring J, Gabrielsen AA. Efficacy and safety of spinosad and permethrin creme rinses for pediculosis capitis (head lice). *Pediatrics*. 2009; 124:E389-E395. (IDIS Article Number 624176)

Two multicenter, randomized trials compared 0.9% spinosad without nit-combing with 1% permethrin with combing in a total of 1038 patients aged ≥ 6 months. All household members with lice received the same treatment and the primary end point was the proportion of lice-free primary participants at 14 days after the last treatment. Each product was administered either once or twice in the 21-day period. Results showed that 84.6% in study 1, and 86.7% in study 2, of patients treated with spinosad were free of lice, compared with 44.9% and 42.9% of the permethrin-treated patients, ($p < 0.001$).

Vilazodone hydrochloride

Rickels K, Athanasiou M, Robinson DS, et al. Evidence for efficacy and tolerability of vilazodone in the treatment of major depressive disorder; a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry*. 2009; 70:326-333. (IDIS Article Number 614935)

This 8-week, randomized trial assessed the efficacy and tolerability of 40 mg (titrated from 10 mg to 40 mg over 2 weeks) of vilazodone in a total of 397 patients (vilazodone=198, placebo=199) with major depressive disorder. Efficacy was assessed using change from baseline to week 8 on the Montgomery-Asberg Depression Rating Scale (MADRS), the Hamilton Rating Scale for Anxiety (HAM-D-17), and the Clinical Global Impressions-Severity of Illness (CGI-S) and -Improvement (CGI-I) scales. Results showed the mean changes in MADRS and HAM-D-17 from baseline to week 8 were significantly greater with vilazodone ($p=0.001$ and $p=0.022$, respectively) compared with placebo. The CGI-S and CGI-I scores were both significantly improved at 8 weeks, ($p=0.001$ for both) compared with placebo. Side effects of vilazodone were mostly of mild to moderate intensity and included diarrhea, nausea and somnolence.



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