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***IDIS*/Web Search Strategies: Breastfeeding**

The previous issue of [World of Drug Information](#) reviewed strategies for locating information about drugs during pregnancy. This issue will focus on a closely related topic – drugs during lactation. Examples of how you can best use *IDIS*/Web to obtain the literature necessary to answer questions regarding medication use during breastfeeding are presented here.

Breastfeeding-Related *IDIS*/Web Vocabulary Terms

Check Tags

There are two check tags (terms which are not International Classification of Diseases codes) that may be used when searching for information about drugs during breastfeeding. These check tags are used in the Disease field.

V24.1 – Lactating Mother – use this check tag when searching for articles in which the mother or lactation is the focus.

V24.11 – Infant, Breastfed – use this check tag when searching for articles in which the infant is the focus.

Breastfeeding-Related Disorders

There are several Disease terms in *IDIS*/Web for disorders related to breastfeeding.

611.0 – Inflammation, Breast – use this term when searching for articles about acute mastitis.

676. – Disorder, Lactat/Breast NEC – use this term when searching for articles about lactation disorders not elsewhere classified (for example, cracked nipples or postpartum breast engorgement).

676.4 – Failure, Lactation – use this term when searching for articles about suppressed lactation or lactation failure.

Drug Concentration in Breast Milk

There is a Descriptor for the concentration of a drug in breast milk.

24 – Pkin Excretion Milk

Example Searches

Search 1 – Is metformin safe during lactation?

Strategy: Locate the Drug term for metformin and the lactation check tag in the Thesaurus.

Search 1

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Drug A to Z List
Disease Hierarchy
Disease A to Z List
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search clear

All Fields [i] [] and ▾
Drug [i] "METFORMIN 68200407" and ▾ Look Up
Disease [i] "LACTATING MOTHER V24.1" and ▾ Look Up
Descriptor [i] [] and ▾ Look Up
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Search 2 – What is the risk to breastfed infants whose mothers receive duloxetine?

Strategy: Locate the Drug term for duloxetine and the breastfed infant check tag in the Thesaurus.

Search 2

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Drug [i] "DULOXETINE 28160710" and ▾ Look Up
Disease [i] "INFANT, BREASTFED V24.11" and ▾ Look Up
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Search 3 – How is mastitis due to breastfeeding treated?

Strategy: Locate the Disease term for acute mastitis and the lactation check tag in the Thesaurus. Manually change the operator between the two terms from “or” to “and” before executing the search.

Search 3

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Search 4 – Is bromocriptine useful for breast engorgement?

Strategy: Locate the Drug Term for bromocriptine and the Disease term for lactation-related breast engorgement in the Thesaurus.

Search 4

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Year From: To: 2011

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Search 5 – Are there any randomized studies of domperidone for lactation failure?

Strategy: Locate the Drug term for domperidone, the Disease term for lactation failure, and the Descriptor for randomized studies in adults in the Thesaurus.

Search 5

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Disease Hierarchy
Disease A to Z List
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search clear

All Fields and
Drug "DOMPERIDONE 56220004" and Look Up
Disease "FAILURE, LACTATION 676.4" and Look Up
Descriptor "STUDY RANDOMIZE ADULT 135" and Look Up
Title and
Author and Look Up
Abstract and
Journal and Look Up
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Article Number:
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search clear

Search 6 – How much hydrocodone is excreted in breast milk?

Search Strategy: Locate the Drug term for hydrocodone and the Descriptor for Milk excretion in the Thesaurus.

Search 6

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Drug Hierarchy
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Disease A to Z List
Descriptor Definitions
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search clear

All Fields and
Drug "HYDROCODONE 48000072" and Look Up
Disease and Look Up
Descriptor "PKIN EXCRETION MILK 24" and Look Up
Title and
Author and Look Up
Abstract and
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Vicki Kee is a 1989 graduate of the University of Alabama at Birmingham (B.A. in English) and a 1999 graduate of Samford University School of Pharmacy (Pharm.D.). She completed a drug information residency at Idaho State University College of Pharmacy in 2003 and then joined *IDIS* in 2005 she became a Board Certified Pharmacotherapy Specialist. Vicki is a contributing author to the *World of Drug Information* newsletter, assists with answering drug information inquiries made to the Iowa Drug Information Network (IDIN), teaches drug information to pharmacy students and indexes journal articles for inclusion into the *IDIS* database.

New Molecular Entities & Biologicals

FDA Approvals
March 2011-May 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 |
|--|--|--|---|---|
| Abiraterone acetate <i>Zytiga</i> (P) | Centocor Ortho. (Apr. 28, 2011) | ABIRATERONE ACETATE 10120879 FDA Approved Indication (23 citations) Total (23 citations) | Prostate cancer. Oral Tablet. | NEOP, MGN-Prostate 185. |
| Boceprevir <i>Victrelis</i> (P) | Schering (May 13, 2011) | BOCEPREVIR 8180101 FDA Approved Indication (15 citations) Total (16 citations) | Chronic hepatitis C. Oral Capsule. | Hepatitis, Viral C 070.51 |
| Fidaxomicin <i>Dificid</i> (S) | Optimer Pharma (May 27, 2011) | FIDAXOMICIN 8122950 FDA Approved Indication (14 citations) Total (14 citations) | Clostridium difficile- associated diarrhea. Oral Tablet. | Colitis, Pseudomembranous 008.45 |
| Gabapentin Enacarbil <i>Horizant</i> (S) | Glaxo Group Ltd. (Apr. 6, 2011) | GABAPENTIN ENACARBIL 28122048 FDA Approved Indication (3 citations) Total (8 citations) | Restless legs syndrome. Oral Tablet. | Syndrome, Restless Legs 333.94 |
| Gadobutrol <i>Gadavist</i> (S) | Bayer Healthcare (Mar. 14, 2011) | GADOBUTROL 36680060 FDA Approved Indication (24 citations) Total (52 citations) | Imaging agent for nervous system scans. Intravenous solution. | Magnetic Resonance Imaging 88.9 Contrast Radiogram, Brain 87.02 |
| Ipilimumab <i>Yervoy</i> (BIOL) | Bristol Myers Squibb (Mar. 25, 2011) | IPILIMUMAB 10120232 FDA Approved Indication (46 citations) Total (65 citations) | Melanoma. Injection. | Melanoma, Malignant, Skin 172. |
| Linagliptin <i>Tradjenta</i> (S) | Boehringer Ingelheim (May 2, 2011) | LINAGLIPTIN 68200025 FDA Approved Indication (1 citation) Total (3 citations) | Type 2 diabetes. Oral Tablet. | Diabetes Mellitus 250. |

| Generic Name Trade Name (FDA Review Classification) | Sponsor (Approval Date) | Valid IDIS Drug Term Drug Number (IDIS Citations) | Indication/Use Dosage Form | Valid IDIS Disease Term Modified ICD-9-CM Number |
|--|------------------------------------|---|---|---|
| Rilpivirine <i>Edurant</i> (S) | Tibotec (May 20, 2011) | RILPIVIRINE 8180874 FDA Approved Indication (7 citations) Total (7 citations) | HIV 1 Infection. Oral Tablet. | Syn-Acq Immune Deficiency 042. |
| Telaprevir <i>Incivek</i> (P) | Vertex Pharms (May 23, 2011) | TELAPREVIR 8180088 FDA Approved Indication (27 citations) Total (28 citations) | Hepatitis C. Oral Tablet. | Hepatitis, Viral C. 070.51 |
| Vandetanib <i>Vandetanib</i> (P) | IPR Pharms, Inc. (Apr. 6, 2011) | VANDETANIB 14000504 FDA Approved Indication (16 citations) Total (78 citations) | Medullary thyroid cancer. Oral Tablet. | NEOP, MGN-Thyroid 193. |

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

2011 Iowa Drug Information Service Exhibit Schedule

Please join us:

American Association of Colleges
of Pharmacy (AACP)
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

Selected Bibliography

Abiraterone acetate

Attard G, Reid AH, Yap TA, et al. Phase I clinical trial of a selective inhibitor of CYP17, abiraterone acetate, confirms that castration-resistant prostate cancer commonly remains hormone driven. *J Clin Oncol.* 2008; 26:4563-4571. (IDIS Article Number 604324)

This open-label dose-escalation study included 21 patients, in 3-patient cohorts, who were chemotherapy-naïve and who had prostate cancer resistant to hormonal therapy. Doses of oral abiraterone acetate were escalated from 250-2000 mg once daily in 28-day cycles with results showing anti-tumor activity at all doses, and a plateau in pharmacodynamic effect at doses greater than 750 mg. Side effects of hypertension, hypokalemia, and lower limb edema were attributed to syndrome of secondary mineralocorticoid excess and were successfully managed. Investigators found abiraterone acetate to be safe and effective in treating castration-resistant prostate cancer.

Boceprevir

Bacon BR, Gordon SC, Lawitz E, et al. Boceprevir for previously treated chronic HCV genotype 1 infection. *N Engl J Med.* 2011; 364:1207-1217. (IDIS Article Number 654104)

A total of 640 patients with chronic hepatitis C virus genotype 1 were randomized in a 1:2:2 ratio to one of 3 groups in this 44-week study. Dosing for all patients consisted of subcutaneous peginterferon alfa 2-b at 1.5 µg per kilogram of body weight once weekly, and ribavirin 600-1400 mg per day in divided doses based on body weight. Boceprevir treatment consisted of oral doses of 800 mg 3 times daily. During a 4-week lead-in period, peginterferon and ribavirin were given to all patients. Thereafter, the control group (group 1) received peginterferon-ribavirin plus placebo for 44 weeks, group 2 received peginterferon-ribavirin plus bocerevir for 32 weeks, and group 3 received peginterferon-ribavirin plus boceprevir for 44 weeks. Rates of sustained response were significantly higher in both boceprevir groups (group 2, 59%; group 3, 66%) compared with the control group (21%), $p < 0.001$. Anemia occurred significantly more often in the boceprevir groups than in the control group.

Fidaxomicin

Louie TJ, Miller MA, Mullane KM, et al. Fidaxomicin versus vancomycin for *Clostridium difficile* infection. *N Engl J Med.* 2011;364:422-431. (IDIS Article Number 652166)

*Safety and efficacy of fidaxomicin were compared with those of vancomycin in this Phase 3 double-blind, randomized trial. Patients with acute symptoms of *C. difficile* and a positive result on a stool toxin test were randomly assigned to oral fidaxomicin 200 mg twice daily ($n=302$) or oral vancomycin 125 mg four times daily ($n=327$) for 10 days. Clinical cure rates of fidaxomicin were found to be noninferior to vancomycin (88.2% and 85.8% respectively in the modified intention-to-treat analysis, and 92.1% and 89.8% respectively in the per-protocol analysis). Significantly fewer patients in the fidaxomicin group compared with vancomycin had infection recurrence in the modified intention-to-treat analysis (15.4% vs. 25.3%; $p=0.005$) and also in the per-protocol analysis (13.3% vs. 24.0%; $p=0.004$). Adverse events were similar in both groups with the exception of significantly more serious adverse events related to laboratory test results in the fidaxomicin group.*

Gabapentin enacarbil

Bogan RK, Bornemann MA, Kushida CA, et al. Long-term maintenance treatment of restless legs syndrome with gabapentin enacarbil: a randomized controlled study. *Mayo Clin Proc.* 2010; 85:512-521. (IDIS Article Number 638110)

This 2-phase study consisted of a single-blind treatment phase in which 327 patients with moderate to severe primary restless legs syndrome were given oral gabapentin enacarbil 1200 mg daily, or placebo, for 24 weeks. Patients who were then deemed to be responders to the study drug (patients with improvements according to the International Restless Legs Scale, were randomized to a 12-week period of oral gabapentin enacarbil 1200 mg ($n=96$) daily, or placebo ($n=98$). Investigators found that a significantly smaller portion of patients treated with gabapentin enacarbil (9/96, 9%) suffered relapse compared with those treated with placebo, (22/97, 23%), ($p=0.02$). The most common adverse events were somnolence and dizziness.

Ipilimumab

Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med.* 2010; 363:711-723. (IDIS Article Number 642632)

*A Phase 3, randomized, double-blind study assessed overall survival in a total of 676 HLA-A*0201-positive patients with unresectable stage III or IV melanoma and with disease progression while receiving therapy for metastatic disease. Patients were randomly assigned to receive intravenous ipilimumab, 3 mg per kilogram of body weight, plus 1 mg subcutaneous glycoprotein 100 (gp 100) peptide vaccine, ($n=403$), ipilimumab alone, ($n=137$), or gp 100 alone, ($n=136$), administered every 3 weeks for up to 4 treatments (induction). Reinduction therapy was given to eligible patients. Median overall survival for patients who received ipilimumab plus gp 100 was 10.0 months, compared with 6.4 months for those who received gp 100 alone (hazard ratio for death, 0.68; $p < 0.001$). Median overall survival with ipilimumab alone was 10.1 months (hazard ratio for death compared with gp 100 alone, 0.66; $p=0.003$). No difference was seen in overall survival between the 2 ipilimumab groups. Immune-related adverse events of grade 3 or 4 occurred in 10-15% of patients treated with ipilimumab and in 3% treated with gp 100. Fourteen deaths were related to the study drugs, 7 of which were associated with immune-related adverse events.*

Telaprevir

Hezode C, Forestier N, Dusheiko G, et al. Telaprevir and peginterferon with or without ribavirin for chronic HCV infection. *N Engl J Med.* 2009;360:1839-1850. (IDIS Article Number 616681)

A total of 334 treatment-naïve patients with chronic hepatitis C virus (HCV) genotype 1 infection were randomly assigned to one of four treatment groups of various combinations of telaprevir (orally, 1250 mg on day 1, then 750 mg every 8 hours), peginterferon alfa-2a (subcutaneously, 180 µg weekly), and ribavirin (orally, 1000 mg/day for body weight <75 kg, 1200 mg/day for weight ≥ 75 kg). The T12PR24 group (n=81) received telaprevir, peginterferon and ribavirin for 12 weeks, then peginterferon and ribavirin for another 12 weeks. Group T12PR12 (n=82), received telaprevir, peginterferon and ribavirin for 12 weeks. Group T12P12 (n=78) received telaprevir and peginterferon without ribavirin for 12 weeks. Group PR48 (n=82), the control group, received peginterferon and ribavirin for 48 weeks. Results showed the combined rate of sustained virologic response for the T12PR12 and T12P12 groups was 48% (77/160), compared with 46% (38/82) in the PR48 (control) group (p=0.89). The rate was 60% (49/82) in the T12PR12 group (p=0.12 compared with the control group), compared with 36% (28/78) in the T12P12 group (p=0.003; p=0.20 compared with the control group). The rate in the T12PR24 group was 69% (56/81), and was significantly higher than the control group (p=0.004). Adverse events associated with telaprevir included rash, pruritis and anemia.

Vandetanib

Anonymous. Briefing information from drug sponsor. Oncologic Drugs Advisory Committee Meeting, December 2, 2010. FDA Advisory Committee. 2010. (IDIS Article Number 650360)

An international Phase III, randomized, double-blind, placebo-controlled trial assessed clinical efficacy and safety of oral vandetanib 300 mg once daily in 331 patients with unresectable locally advanced or metastatic medullary thyroid cancer. In this pivotal study, 231 patients received vandetanib and 100 received placebo. Median duration of treatment was 1 year and 9 months at data cut-off and long-term follow-up is ongoing. Progression-free survival was the primary endpoint. Vandetanib was well tolerated and showed a robust and significant benefit.



Dr. Nicola Sarrazin is a 1984 graduate of the University of Iowa (B.A. in Anthropology and Asian Studies) and a 1997 graduate of the University of Iowa College of Pharmacy (Pharm.D.). Since that time she has been a pharmacist in the College of Pharmacy's Division of Drug Information Service. Nickie's responsibilities include indexing articles for the IDIS database, overseeing the Drug vocabulary and contributing articles for the *World of Drug Information* newsletter.

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World of Drug Information is published quarterly (March, June, September, December) by the Division of Drug Information Service.

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