

# LDI

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# Specialty Drug News

## Off-Label Prescribing

**Off-label prescribing is the physician practice of prescribing a drug for a purpose different from the indications for which the product was approved by the Food and Drug Administration.**

Given a drug's painstaking path to approval in even a single disease, many Americans are surprised to learn that once a new drug enters the U.S. market, doctors are legally free to prescribe it off-label for any condition. The practice is widespread and can pose a real challenge when trying to determine coverage under a benefit plan.

Once a drug is approved and is in widespread use, it may show signs of benefit in treating other ailments. But drug manufacturers typically are not willing to spend additional money to seek FDA approval for new indications, especially if it would yield little extra revenue. While there is no hard data, estimates of off-label prescribing run as high as 60% of all drugs prescribed in the U.S. in any given year, including a large portion for chemotherapy. Prescribing can range from one extreme to another. For example, aspirin, approved by the FDA as a pain killer, was used

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to reduce the mortality rate among heart attack victims for years before the FDA sanctioned that use of it. Antibiotics, approved for bacterial infection are commonly prescribed for viral illness. Among oncologists, who are willing to accept the risks of unapproved treatments when their patients are running out of options, off-label prescribing is a common practice.

Since off-label use is often regarded as appropriate or "state-of-the-art" treatment, an important question is whether health insurance plans that provide coverage for drugs will cover them for off-label use. Most plans often deny coverage on the basis that the use, being unapproved, is "experimental", and therefore does not meet the coverage criteria set forth in the plan document. A number of states have passed laws requiring insurers to pay for off-label use of approved drugs however these laws



Avandia  
Safety  
Alert



Drug  
Spending  
in the US  
Increases  
more than  
2.5 times  
in 8 years



2007 1st  
Quarter  
Specialty  
Drug  
Pipeline  
Report



Drug  
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tion

## Off Label Prescribing Continued -

do not apply to pharmacy benefits provided by self-insured health plans.

The following Clinical Guidance is utilized by several fully-insured plans when determining medically necessary use of off-label drugs. *Note that this guidance is provided as a means to determine if off-label use is medically appropriate and is not meant to be construed as a covered benefit under a plan. Benefits for medically necessary use of off-label medications are determined by plan language.*

Off-label drug use is considered medically necessary when all of the following conditions are met:

- The drug is approved by the FDA;
- The prescribed drug use is supported in one of the following established standard reference compendia
  - The Food and Drug Administration (including listing on the FDA Orphan Drug Approval web site);
  - The American Hospital Formulary Service Drug Information,
  - The U.S. Pharmacopoeia Dispensing Information, Vol.I.
- Alternatively, in the absence of being listed in the above named sources, if the following support is available:
  - Two articles from major scientific or medical peer-reviewed journals (excluding case reports, letters, posters, and abstracts), or

- Published studies having validated and uncontested data, which supports the proposed use for the specific medical condition as safe and effective (The number of patients in study will vary with prevalence of condition)

- Accepted journals include, but are not limited to, Journal of American Medical Association, New England Journal of Medicine, and Lancet.

- Accepted study designs include, but are not limited to, randomized, double blind, placebo controlled clinical trials.

- The drug is medically necessary to treat the specific condition, including life-threatening conditions or chronic and seriously debilitating conditions.

This guideline shall not be construed to require coverage for any drug when the FDA has determined its use to be contraindicated.

The guideline shall not be construed to require coverage for any drug when the benefit plan excludes drug coverage.

The guideline shall not be construed to require coverage for any drug when the benefit plan includes drug benefit limitations based on a formulary and the off-label drug is not part of the formulary.

For questions regarding off-label drug use please feel free to contact the LDI Specialty Clinical Department at (800) 654-6176 or [smh@ldipbm.com](mailto:smh@ldipbm.com).

*\*Source: FDA, The Doctor Will See You Now, the San Francisco Chronicle, The Independent Review*

# Avandia Safety Alert

**The Food and Drug Administration is aware of a potential safety issue related to Avandia, a drug approved to treat type 2 diabetes. Safety data from controlled clinical trials have shown that there is a potentially significant increase in the risk of heart attack and heart-related deaths in patients taking Avandia.**

However, other published and unpublished data from long-term clinical trials of Avandia, provide contradictory evidence about risks in patients treated with Avandia.

Patients who are taking Avandia, especially those who are known to have underlying heart disease or who are at high risk of heart attack should talk to their doctors about this new information as they evaluate the available treatment options for their type 2 diabetes.

FDA's analysis of all available data is ongoing. FDA has not confirmed the clinical significance of the reported increased risk in the context of other studies. Furthermore, there is inherent risk associated with switching patients with diabetes from one

treatment to another even in the absence of specific risks associated with particular treatments. For these reasons, FDA is not asking GlaxoSmithKline, the drug's sponsor, to take any specific action at this time.

providing emerging information to patients, individual-

ment decision

“FDA is committed to ensuring that patients have the latest information available to make treatment use decisions. In this case, FDA is carefully weighing several complex sources of data, some of which show conflicting results, related to the risk of heart attack and heart-related deaths in patients treated with Avandia,” said Steven Galson, M.D., M.P.H., director of FDA's Center for Drug Evaluation and Research. “We will complete our analyses and make the results available as soon as possible. FDA will take the issue of cardiovascular risk associated with Avandia and other drugs in this class to an Advisory Committee as soon as one can be convened”.

**Patients who are taking Avandia, especially those who are known to have underlying heart disease or who are at high risk of heart attack should talk to their doctors about this new information as they evaluate the available treatment options for their type 2 diabetes.**

FDA is providing this information and their can make informed treatment decisions.

mainstream doctors have the information to make and medication use decisions.

# Drug Spending in U.S. Increases More than 2.5 Times in Eight Years

Spending for medications prescribed in outpatient settings increased from 72 billion dollars in 1997 to 191 billion dollars in 2004, according to the latest News and Numbers from the Agency for Healthcare Research and Quality (AHRQ). The data covers spending by people who live in the community and were not in institutions such as nursing homes.

- During the period of 1997-2004, the average annual expenditure for prescription drugs for people age 65 and older increased 130 percent – rising from \$819 in 1997 to \$1,914 in 2004. The average out-of-pocket cost more than doubled for this group, increasing from \$483 in 1997 to \$1,027 in 2004.

- The average annual amount spent on prescription drugs by people under age 65 who purchased prescription medications rose 140 percent from 1997 to 2004 – climbing from \$347 in 1997 to \$838 in 2004. From 1997 to 2004, the average annual amount this group spent out of pocket on prescription drugs rose from \$143 to \$304.

- From 1997 to 2004, total purchases of outpatient prescription drugs increased from approximately 2 billion to nearly 3 billions prescriptions. This increase was fueled in part by a rise in the average number of prescription drug purchases per year by the elderly

age 65 and older, which increased from 22 to 31 purchases per year.

**From 1997 to 2004, total purchases of outpatient prescription drugs increased from approximately 2 billion to nearly 3 billions prescriptions.**

- In the same time frame, younger consumers also bought more prescription drugs on average. People under age 65 who purchased prescription medications, purchased 9 prescriptions a year on average. In 2004, this number rose to 13 prescriptions per year.

AHRQ, a part of the U.S. Department of Health and Human Services, works in improve the quality, safety, efficiency, and effectiveness of health care in the United States. The data in this AHRQ News and Numbers comes from the Agency's Medical Expenditure Panel Survey, a highly detailed source of information on the health services that Americans use, how frequently they use them, the cost of these services and how they are paid. [www.ahrq.gov](http://www.ahrq.gov)

*\*Source: Medical New*

## Specialty Drug Pipeline Report

### New Route of Administration in Pipeline

Drug Name	Indication	Current Route of Administration	Investigational Route of Administration	Comments
Cayston (aztreonam lysine)	Treatment of cystic fibrosis lung infections	IV injection	Inhalation	Orphan drug
Mylinax® (cladribine)	Treatment of relapsing forms of MS	IV infusion	Oral	FDA granted fast track status

*For more information regarding LDI's Specialty Newsletter, please contact us:*

**local** 314 / 652-2121 x189  
**toll free** 800 / 652-9550 x189  
**email** [vsb@ldipbm.com](mailto:vsb@ldipbm.com)

*Specialty Drug Pipeline Report, continued:*

*Pipeline Drugs in Phase III Clinical Trials, pages 4-6*  
*New Route of Administration in Pipeline, page 7*

# Specialty Drug Pipeline Report, continued:

## Pipeline Drugs in Phase III Clinical Trials

Drug Name	Indication	Route of Administration	Comments
Tykerb® (lapatinib)	Treatment of advanced or metastatic HER2 positive breast cancer in combination with Xeloda® in women who have received prior therapy, including Herceptin®	Oral	Approved April 2007. Also being investigated for solid tumors and lung cancer.
(atamestane)	First-line treatment of hormone-dependent breast cancer in combination with Fareston®	Oral	Phase III trial ongoing
Virulizin®	First-line treatment of advanced pancreatic cancer in combination with Gemzar®	Oral	Orphan drug-fast track status
(phenoxodiol)	Treatment of hormone-refractory prostate cancer in Taxotere® non-responders and recurrent chemo-resistant late stage ovarian cancer	IV injection/Oral	FDA granted fast track status
Saforis (glutamine in UpTec)	Prevention and treatment of chemo-induced oral mucositis	Oral	FDA granted priority review status.
Xerecept® (corticotropin)	Treatment of peritumoral cerebral edema	SC injection	Orphan Drug
Tasigna® (nilotinib)	Treatment of Ph + CML in patients who do not respond or are resistant to Gleevec®	Oral	Orphan drug – fast track status
(vatalanib)	Treatment of metastatic colorectal cancer in combination with oxaliplatin, 5-FU and lecovorin	Oral	NDA filing planned for 2007
Voraxaze (glucarpidase)	Adjunctive therapy for cancer patients undergoing chemo who are at risk of methotrexate toxicity	IV injection	Orphan drug-fast track status. Available on a compassionate use basis from distributor.

## Pipeline Drugs in Phase III Clinical Trials, continued:

Drug Name	Indication	Route of Administration	Comments
Somatuline® Autogel® (lanreotide)	Treatment of acromegaly	SC injection	Response expected by August 2007
(ferumoxytol)	Treatment of anemia due to chronic kidney disease	IV injection	NDA filing planned for mid-2007
(senicapoc)	Sickle cell disease	Oral	Orphan drug – fast track status
Mircera® (erythropoietin)	Treatment of anemia due to chronic kidney disease, including dialysis	SC or IV injection	FDA accepted additional data and granted 3-month extension to the December 2006 review period
(alfimeprase)	Treatment of acute peripheral arterial occlusion and central venous catheter occlusion	IV injection	Orphan drug-fast track status. Phase III trials did not meet primary endpoints. Temporarily suspended as of December 2006.
(denufosol) Inhalation	Treatment of cystic fibrosis	Inhalation	Orphan drug-fast track status. Phase III trials initiated July 2006, complete enrollment expected by the end 2007
Viramidine® (taribavirin)	Treatment of chronic Hepatitis C in combination with pegylated interferon alfa	Oral	A higher dose of Viramidine will be studied in a Phase II trial. Manufacturer will decide whether to begin a third phase III study at a higher dose.
Refacto® AF (antihemophilic factor)	Treatment of hemophilia A	Infusion	Launch anticipated in 2008
(MK-0518)	Treatment of HIV	Oral	Available through an expanded access program
(maraviroc)	Treatment of HIV	Oral	FDA granted fast track status.
(TMC125)	Treatment of NNRTI resistant HIV infection	Oral	Studied in combination with Prezista. FDA granted fast track status.
Cimzia (certolizumab pegol)	Treatment of moderate to severe Crohn's disease, rheumatoid arthritis, psoriasis	SC injection	FDA requested more information December 2006
(fingolimod)	Treatment of relapsing-remitting MS	Oral	If approved, would be first oral agent to treat MS. Also in Phase III trials for prevention of kidney transplant rejection

## Pipeline Drugs in Phase III Clinical Trials, continued:

Drug Name	Indication	Route of Administration	Comments
(tirapazamine)	Treatment of head and neck squamous cell carcinoma and cervical cancer	IV injection	
(glufosfamide)	Second-line treatment of metastatic pancreatic cancer	IV infusion	Orphan drug-fast track status
Torisel (temsirolimus)	Treatment of RCC and mantle cell lymphoma	Oral/IV injection	Orphan drug. FDA granted priority review status December 2006
(denosumab)	Treatment of postmenopausal osteoporosis and treatment-induced bone loss	SC injection	
Preos® (parathyroid hormone)	Treatment of osteoporosis in post-menopausal women	SC injection	Submitted proposal for a new phase IIIb clinical trial to the FDA in the fourth quarter of 2006
Neupro® (rotigotine)	Treatment of early stage Parkinson's disease	Transdermal	Approval letter March 2006. Also in phase III trials for treatment of advanced-stage Parkinson's disease
Thelin (sitaxentan)	Treatment of pulmonary arterial hypertension	Oral	FDA accepted complete response to approval letter December 2006
(ambrisentan)	Treatment of pulmonary arterial hypertension	Oral	Orphan drug
Numax® (motavizumab)	Prevention of RSV in high-risk pediatric populations	IM injection	Expected to be more potent than Synagis®. Pending approval, launch anticipated during 2008-2009 RSV season
Actemra (tocilizumab)	Treatment of rheumatoid arthritis	IV infusion	
(ATG-Fresenius S)	Prevention of graft-versus-host disease lung transplantation	Injection	FDA fast track status
Certican (everolimus)	Prevention of solid organ transplant rejection in combination with Neoral®	Oral	

## New Drug Indications in Pipeline

Drug Name	Current Indication	Investigational Indication	Route of Administration	Comments
Humira® (adalimumab)	Treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis	Moderately to severely active Crohn's disease, juvenile rheumatoid arthritis and chronic plaque psoriasis	SC injection	FDA granted priority status review.
Tysabri® (natalizumab)	Treatment of relapsing forms of MS	Moderate to severe Crohn's disease	IV infusion	
Leukine® (sargramostim)	Treatment of myelogenous leukemia and bone marrow transplant	Moderate to severe Crohn's disease	SC injection	
Viread® (tenofovir)	Treatment of HIV	Treatment of chronic Hepatitis B	Oral	
Infergen® (interferon alfacon-1)	Treatment of Hepatitis C	Treatment of chronic Hepatitis C in combination with ribavirin after failure to respond to previous course of pegylated interferon alfa-2 plus ribavirin	SC injection	
Kineret® (anakinra)	Treatment of rheumatoid arthritis	Treatment of polyarticular-course chronic juvenile rheumatoid arthritis	SC injection	

## Specialty Medication Listing by Disease/Condition

### AIDS/HIV

Daunoxome  
Doxil  
Intron A  
Roferon-A  
Serostim  
Taxol  
Fuzeon

### Alpha1 - Proteinase Inhibitor Deficiency

Aralast  
Prolastin  
Zemaira

### Antihemophilic Agents

Antihemophilic Factor  
Advate  
Alphanate  
Bioclote  
Helixate FS  
Hemofil M  
Humate P  
Hyate C  
Koate DVI  
Kogenate FS  
Monarc M  
Monoclote P  
Recombinate  
ReFacto

### Anti-nausea

Aloxi  
Anzemet  
Emend  
Kytril  
Zofran

### Asthma

Xolair

### Cancer/Related

Adriamycin  
Adrucil  
Alkeran  
Aredia  
Avastin

BiCNU  
Blenoxane  
Busulfex  
Campath  
Camptosar  
Cerubidine  
Cosmegen  
Cytarabine  
Cytosan  
Depocyt  
Doxil  
DTIC-Dome  
Eligard  
Ellence  
Erbitux  
Ethyol

## Specialty Medication Listing by Disease/Condition, continued:

Faslodex  
Fludara  
Gemzar  
Gleevec  
Herceptin  
Hycamtin  
Idamycin  
IFEX  
Intron A  
Leucovorin  
Leukine  
Leustatin  
Lupron Depot  
Lupron Depot-Ped  
Mesnex  
Mustargen  
Mutamycin  
Mylotarg  
Navelbine  
Nexavar  
Nipent  
Novantrone  
Oncaspar  
Ontak  
Paraplatin  
Platinol AQ  
Proleukin  
Rituxan  
Roferon-A  
Sutent  
Tarceva  
Taxol  
Taxotere  
Temodar  
Thyrogen  
Toposar  
Trelstar Depot  
Trelstar LA  
Trisenox  
VePesid  
Vinblastine  
Vincasar  
Vumon  
Xeloda  
Zanosar  
Zoladex  
Zometa

### Contraceptives

Depo-Provera

### Crohn's Disease

Remicade

### Dystonia

Botox  
Myobloc

### Factor IX Concentrates

Alphanine SD  
Benefix  
Mononine  
Profilnine SD  
Proplex T  
Bebulin VH

### Gaucher's Disease

Ceredase  
Cerezyme  
Zavesca

### Growth Hormone Deficiency

Genotropin  
Humatrope  
Norditropin  
Nutropin  
Nutropin AQ  
Saizen

### Hematologics

Arixtra  
Aranesp  
Epogen  
Fragmin  
Innohep  
Lovenox  
Neulasta  
Neumega  
Neupogen  
Procrit

### Hepatitis C

Copegus  
Infergen  
Intron A  
Pegasys  
Peg-Intron  
Rebetron  
Roferon-A

### Hormone Deficiency

Delatestryl  
Delestrogen  
Depo-Estradiol  
Depo-Testosterone

### Hunter Syndrome

Elaprase

### Primary Immunodeficiency

Carimune NF  
Gamimune N  
Gammagard S/D  
Gammar-P  
Gamunex

Iveegam EN  
Panglobulin  
Panglobulin NF  
Polygam S/D  
Venoglobulin-S

### Miscellaneous

Alferon-N  
Milrinone  
Zincard

### Multiple Sclerosis

Avonex  
Betaseron  
Copaxone  
Novantrone  
Rebif  
Tysabri

### Osteo/ Rheumatoid/ Psoriatic Arthritis

Enbrel  
Humira  
Hyalgan  
Kineret  
Orencia  
Remicade  
Supartz  
Synvisc

### Osteoporosis

Forteo  
Miacalcin

### Psoriasis

Amevive  
Enbrel  
Raptiva  
Remicade

### Respiratory Syncytial Virus

Synagis

### Rh Hemolytic Disease

BayRho-D  
Micro-Rhogam  
Rhogam  
WinRho-SDF