NACDS NATIONAL ASSOCIATION OF CHAIN DRUG STORES

NACDS 75 years 1933 TO 2008

IOWA PHARMACY INFRASTRUCTURE:

There are approximately 673 pharmacies in **Iowa,** including:

- approximately **446 chain pharmacies**
- approximately 227 independent pharmacies

NACDS Members in Iowa:

Company:	Number of Pharmacies:
Costco Wholesale dba Costco Pharmacies	1
C.R. Pharmacy Service, Inc. dba CarePro Health Services	5
CVS Caremark Corporation	10
Dahl's Food Markets, Inc.	10
Hartig Drug Company, Inc.	9
Hy-Vee Inc.	118
Lewis Drugs, Inc.	6
Medicine Shoppe International, Inc.	51
Nash Finch Co.	5
NuCara Management Group, Inc.	10
Pharmacy Express Services, Inc.	2
Schnucks Markets, Inc.	1
Sears Holdings Corporation	20
Shopko Stores Operating Co.	22
Snyders Drug Stores, Inc.	4
SUPERVALU INC.	1
Target Corporation	21
Thrifty White Stores	3
Walgreen Co.	60
Wal-Mart Stores, Inc.	56
TOTAL NUMBER OF MEMBER COMPANIES: 20	

There are approximately **1,792 community pharmacists** active in the state of **Iowa**, including **1,467 chain pharmacists** with in-state addresses.

Community pharmacies **employ** approximately **36,255** full and part-time employees, including:

- **34,484 chain pharmacy employees**
- 1,771 independent pharmacy employees

* Headquartered in state

11/18/2008

Community pharmacies pay an estimated **$240,780,000** in total **taxes** to the state of **Iowa** every year, including:

- **$227,181,000 by chain pharmacies**
- $13,599,000 by independent pharmacies

The Marketplace: 78.3% Third Party 12.1% Medicaid 9.5% Cash

Seniors 65 and over make up **14.7%** of the total population in the state of **Iowa**.

* Headquartered in state

11/18/2008

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CHAIN DRUG STORES

IssueBrief

Generic Substitution of Immunosuppressant Drugs

Introduction
Pharmacist substitution of brand name drugs with FDA-approved, therapeutically equivalent[1] drugs saves money for patients, employers, and insurance carriers. It is a legal and well-established practice throughout the country. Prescribers, when issuing prescriptions to patients, indicate whether a pharmacist may engage in generic substitution. Prescribers retain the ultimate authority in this matter.

Throughout the country, legislation is emerging that would create obstacles to the existing generic substitution practices for immunosuppressant prescription drug products. These bills would prevent pharmacists from substituting immunosuppressant drugs with generically equivalent alternatives unless the pharmacist first obtains additional consents from both the prescriber and the patient. Such a mandate would adversely affect the delivery of patient care.

Prescribers Already Retain the Ultimate Authority
These bills create redundant and unnecessary recordkeeping requirements for pharmacists and prescribers. When prescribers issue prescriptions to a patient, they make the determination whether generic substitution is appropriate and indicate that decision on the face of the prescription. There is no benefit or improvement in care achieved by requiring a pharmacist to contact a prescriber to obtain additional consent; doing so only unnecessarily reconfirms the prescriber's earlier decision. The record generated by this act would essentially be a duplicate of the consent already given via the original prescription.

This Poor Use of the Prescriber's and Pharmacist's Time Would Have Negative Consequences for Patients
Mandating that a pharmacist obtain additional consent from a prescriber before dispensing an FDA-approved generically equivalent drug would create unnecessary requirements for pharmacists and physicians to perform in their already busy days. The extra time that this new process would require would detract from the ability of both to serve the needs of their patients. Pharmacists would experience severe logistical problems in attempting to obtain additional consent from prescribers. Pharmacists would not be able to reach prescribers who are treating patients, and would have to wait hours or days for a response. The likely result would be massive delays for patients waiting to have their prescriptions filled. Such delays are both an inconvenience to patients and impediments to the timely delivery of patient care. Particularly for transplant recipients who must strictly comply with their medication regime to prevent organ rejection, delays in drug therapy can have immediate and serious health consequences.

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1 http://www.fda.gov/cder/orange/obannual.pdf, page vi. A common misconception is that pharmacists are "generically" substituting a product for a brand name product. Since this language is common, it will be used throughout this Issue Brief; however, it is important to note that pharmacists are engaged in substituting a multi-source product that the FDA has determined to be therapeutically equivalent to the brand name product prescribed.

Immunosuppressant Drugs are Prescribed for Many Approved and Off-Label Uses Unrelated to Transplantation

The majority of immunosuppressant drugs have numerous FDA-approved uses beyond preventing organ rejection in transplant patients. Cyclosporine products (i.e. Neoral, Gengraf) are approved to treat both rheumatoid arthritis and psoriasis. Azathioprine products (i.e. Imuran, Azasan) are also approved for rheumatoid arthritis. Furthermore, the majority of immunosuppressant drugs prescribed to prevent organ rejection are also prescribed for various off-label uses. (When a drug has an "off-label use," the drug is being prescribed to treat conditions other than what has been approved for use by FDA. This routinely occurs.) These off label uses include acute graft versus host disease (GVHD); rheumatoid arthritis[2]; Crohn's disease; psoriasis[3]; refractory uveitis; Churg-Strauss syndrome; treatment of diffuse proliferative lupus nephritis; chronic ulcerative colitis; generalized myasthenia gravis; and Behcet's syndrome. Considering the numerous FDA-approved and off-label uses of immunosuppressant drugs, it is not possible for a pharmacist to determine based on the specific drug prescribed whether a particular patient is being prescribed a particular product to prevent organ rejection following a transplant surgery without a patient diagnosis written on a prescription. Immunosuppressant drugs are prescribed to treat numerous conditions; therefore, just because a patient is treated with an immunosuppressant drug does not mean that particular patient is an organ transplant recipient. The only way that a pharmacist could be sure that he or she is meeting the mandate would be to obtain additional consent for all immunosuppressant drugs prescribed, regardless of the patient's particular condition. This is an unworkable requirement that would cause extreme delays in the delivery of pharmacy care.

FDA Approves Generic Immunosuppressant Drugs

In an April 2007 letter to NACDS from FDA's Director of the Center for Drug Evaluation and Research Dr. Steven Galson, FDA restated its longstanding position on therapeutic equivalence between generic and innovator drug products.[4] FDA indicated that generic drugs that have met FDA's rigorous approval process are interchangeable with brand-name drugs under all approved indications and conditions of use. FDA concluded that:

- generically equivalent products do not require any additional clinical tests or examinations by the health care provider when substituted for the brand-name product;
- special precautions are not needed when a formulation and/or a manufacturing change occurs for a drug product so long as the change is approved according to applicable laws and regulations by the FDA;
- as noted in the "Orange Book," in the judgment of the FDA, products evaluated as therapeutically equivalent can be expected to have equivalent clinical effect whether the product is brand name or generic drug product; and,
- it is not necessary for the health care provider to approach any one therapeutic class of drug products differently from any other class, when there has been a determination of therapeutic equivalence by FDA for the drug products under consideration. In making this determination, FDA makes no distinction or exclusions for any specific drug class.

2, 3 Note that not all immunosuppressant drugs are approved to treat rheumatoid arthritis and psoriasis.

4 FDA previously stated its opinion on therapeutic equivalence between generic and innovator drug products in a 1998 letter to health practitioners from then Associate Commissioner for Health Affairs Dr. Stuart Nightingale.

FDA's conclusions are applicable to all generic drugs, including immunosuppressant drugs. As such, no state should enact special requirements for generic substitution that go beyond what FDA has already established is necessary.

Conflicts with Medicaid Laws

These types of bills propose requirements that conflict with Medicaid laws relating to generic substitution. Medicaid programs generally require pharmacists to automatically dispense generically equivalent products if prescribers do not expressly indicate on the prescription face that a brand product is medically necessary. In a case where a prescriber makes no indication on a prescription that a brand product is necessary, and the pharmacist is unable to obtain the required additional consent from the prescriber, the pharmacist would be forced to violate either the Medicaid requirement or violate the generic substitution laws relating to dispensing immunosuppressant drugs. Creating a law that would force pharmacists into a Hobson's choice, that would lead them to break another law, is unworkable and poor public policy.

This Proposed Process Creates Barriers to Generic Substitution that Would Ultimately Increase Costs to Patients and the Healthcare System Unnecessarily

If pharmacists were required to obtain additional consent for all prescriptions for immunosuppressant drugs, such a mandate would become a deterrent to generic substitution. Due to the logistical challenges, pharmacists would be forced to fill prescriptions with more expensive brand name products even if the patient prefers to receive the generically equivalent product. The unfortunate result of this scenario is that patients would have no choice other than to pay higher prices for the more expensive brand product.

NACDS
NATIONAL ASSOCIATION OF CHAIN DRUG STORES

IssueBrief

Generic Substitution of Drugs to Treat Epilepsy

Introduction

Pharmacist substitution of brand name drugs with FDA-approved, therapeutically equivalent[1] drugs saves money for patients, employers, and insurance carriers. It is a legal and well-established practice throughout the country. Prescribers, when issuing prescriptions to patients, indicate whether a pharmacist may engage in generic substitution. Prescribers retain the ultimate authority in this matter.

Throughout the country, legislation is emerging that would create obstacles to the existing generic substitution practices for prescription drugs used to treat epilepsy (anticonvulsants). These bills would prevent pharmacists from substituting drugs prescribed to treat epilepsy with generically equivalent alternatives unless the pharmacist first obtains additional consents from both the prescriber and the patient. Such a mandate would adversely affect the delivery of patient care.

Prescribers Already Retain the Ultimate Authority

These bills create redundant and unnecessary recordkeeping requirements for pharmacists and prescribers. When prescribers issue prescriptions to a patient, they make the determination whether generic substitution is appropriate and indicate that decision on the face of the prescription. There is no benefit or improvement in care achieved by requiring a pharmacist to contact a prescriber to obtain additional consent; doing so only unnecessarily reconfirms the prescriber's earlier decision. The record generated by this act would essentially be a duplicate of the consent already given via the original prescription.

This Poor Use of the Prescriber's and Pharmacist's Time Would Have Negative Consequences for Patients

Mandating that a pharmacist obtain additional consent from a prescriber before dispensing an FDA-approved generically equivalent drug would create unnecessary requirements for pharmacists and physicians to perform in their already busy days. The extra time that this new process would require would detract from the ability of both to serve the needs of their patients. Pharmacists would experience severe logistical problems in attempting to obtain additional consent from prescribers. Pharmacists would not be able to reach prescribers who are treating patients, and would have to wait hours or days for a response. The likely result would be massive delays for patients waiting to have their prescriptions filled. Such delays are both an inconvenience to patients and impediments to the timely delivery of patient care. Particularly for epileptics who must strictly comply with their medication regime, delays in drug therapy can have immediate and serious health consequences.

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1 http://www.fda.gov/cder/orange/obannual.pdf, page vi. A common misconception is that pharmacists are "generically" substituting a product for a brand name product. Since this language is common, it will be used throughout this Issue Brief, however, it is important to note that pharmacists are engaged in substituting a multi-source product that the FDA has determined to be therapeutically equivalent to the brand name product prescribed.

Epilepsy Drugs are Commonly Used for Off-Label Purposes

The common practice of prescribing drugs for off-label uses further complicates the issue of obtaining additional consent to generically substitute drugs for treatment of epilepsy (anticonvulsants). (When a drug has an "off-label use," the drug is being prescribed to treat conditions other than what has been approved for use by FDA. This routinely occurs.) A study of the 2001 IMS Health National Disease and Therapeutic Index (NDTI) to define prescribing patterns by diagnosis for 160 commonly prescribed drugs indicated that some of the highest rates of off-label prescribing are for anticonvulsants.[2] One *New York Times* article quoted Pfizer, the maker of Neurontin, an anticonvulsant frequently prescribed for off-label uses, as stating that ***78 percent*** of Neurontin prescriptions in the year 2000 were to treat conditions other than epilepsy;[3] such off-label uses accounted for nearly ***90 percent*** of Neurontin's sales in recent years.[4] Studies have shown that Neurontin and its generic equivalents are prescribed for off-label uses ***83 percent*** of the time, making it the most frequently prescribed drug (of all drugs) for off-label uses.[5] As a class of drugs, anticonvulsants are prescribed for off-label uses ***46 percent*** of the time.[6] Figures reported by states to CMS also illustrate the high rate of off-label use of anticonvulsant drugs, reaching four to five percent of expenditures in some states. Neurontin is frequently prescribed for migraines, Depakote for treating bi-polar disorder, and Topamax for conditions that include alcoholism, sleep disorders, eating disorders, and bi-polar disorder.

Since off-label prescribing is common, and can exceed prescribing for FDA-approved uses, it is not possible for a pharmacist to determine based on the specific drug prescribed whether a particular patient is an epileptic or not without a patient diagnosis written on a prescription. Some anticonvulsant drugs are prescribed to treat conditions other than epilepsy; therefore, just because a patient is treated with an anticonvulsant drug does not mean that particular patient is epileptic. The only way that a pharmacist could be sure that he or she is meeting the mandate would be to obtain additional consent for all anticonvulsants prescribed and any other drug that could potentially be used to treat epilepsy, regardless of whether the patient is actually epileptic. This is an unworkable requirement that would cause extreme delays in the delivery of pharmacy care.

Anticonvulsants are frequently prescribed for non FDA-approved uses. Such prescribing practices are lucrative for drug manufacturers. Many anticonvulsant drugs have recently lost patent protection, or will lose patent protection in the near future. With generic substitution threatening brand name drug sales, we question the motives of legislation that erects artificial barriers to generic substitution.

2Radley, David, et. al., "Off-label Prescribing Among Office-Based Physicians," *Archives of Internal Medicine*, 166 (2006), p. 1022.

3 "Documents Show Effort to Promote Unproven Drug," by Melody Peterson, *New York Times,* October 29, 2002. Pfizer acquired Neurontin's manufacturer, Warner-Lambert, in 2000.

4 "Pfizer to Pay $430 Million Over Promoting Drug to Doctors," by Gardiner Harris, *New York Times,* May 14, 2004.

5 Radley, David, et. al., "Off-label Prescribing Among Office-Based Physicians," *Archives of Internal Medicine*, 166 (2006), p. 1021, 1023.

6 *Ibid. at 1022.*

FDA Approves Generic Drugs to Treat Epilepsy

In an April 2007 letter to NACDS from FDA's Director of the Center for Drug Evaluation and Research Dr. Steven Galson, FDA restated its longstanding position on therapeutic equivalence between generic and innovator drug products.[7] FDA indicated that generic drugs that have met FDA's rigorous approval process are interchangeable with brand-name drugs under all approved indications and conditions of use. FDA concluded that:

- generically equivalent products do not require any additional clinical tests or examinations by the health care provider when substituted for the brand-name product;
- special precautions are not needed when a formulation and/or a manufacturing change occurs for a drug product so long as the change is approved according to applicable laws and regulations by the FDA;
- as noted in the "Orange Book," in the judgment of the FDA, products evaluated as therapeutically equivalent can be expected to have equivalent clinical effect whether the product is brand name or generic drug product; and,
- it is not necessary for the health care provider to approach any one therapeutic class of drug products differently from any other class, when there has been a determination of therapeutic equivalence by FDA for the drug products under consideration. In making this determination, FDA makes no distinction or exclusions for any specific drug class.

FDA's conclusions are applicable to all generic drugs, including drugs approved to treat epilepsy. As such, no state should enact special requirements for generic substitution that go beyond what FDA has already established is necessary.

Conflicts with Medicaid Laws

These types of bills propose requirements that conflict with Medicaid laws relating to generic substitution. Medicaid programs generally require pharmacists to automatically dispense generically equivalent products if prescribers do not expressly indicate on the prescription face that a brand product is medically necessary. In a case where a prescriber makes no indication on a prescription that a brand product is necessary, and the pharmacist is unable to obtain the required additional consent from the prescriber, the pharmacist would be forced to violate either the Medicaid requirement or violate the generic substitution laws relating to dispensing drugs for treatment of epilepsy. Creating a law that would force pharmacists into a Hobson's choice, that would lead them to break another law, is unworkable and poor public policy.

This Proposed Process Creates Barriers to Generic Substitution that Would Ultimately Increase Costs to Patients and the Healthcare System Unnecessarily

If pharmacists were required to obtain additional consent for all prescriptions for drugs approved or used to treat epilepsy that could potentially be substituted with a generically equivalent drug, such a mandate would become a deterrent to generic substitution. Due to the logistical challenges, pharmacists would be forced to fill prescriptions with more expensive brand name products even if the patient prefers to receive the generically equivalent product. The unfortunate result of this scenario is that patients would have no choice other than to pay higher prices for the more expensive brand product.

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7 FDA previously stated its opinion on therapeutic equivalence between generic and innovator drug products in a 1998 letter to health practitioners from then Associate Commissioner for Health Affairs Dr. Stuart Nightingale.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

April 16, 2007

National Association of
Chain Drug Stores
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This is in reply to your letter dated March 15, 2007 requesting that the FDA restate its policy regarding the bioequivalence and substitutability of drugs that are listed in the FDA's "Orange Book" or *Approved Drug Products with Therapeutic Equivalence Evaluations*.

The FDA has many years of experience in the review of generic drugs, and has great confidence in the quality and equivalence of generic drug products. FDA works with pharmaceutical companies to assure that all drugs marketed in the U.S., both brand-name and generic, meet specifications for identity, strength, quality, purity and potency. In approving a generic drug product, the FDA requires many rigorous tests and procedures to assure that the generic drug is interchangeable with the brand-name drug under all approved indications and conditions of use. As noted in the Preface to the Orange Book (27th Edition).

> FDA classifies as therapeutically equivalent those products that meet the following criteria: (1) they are approved as safe and effective; (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the same active drug ingredient in the same dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent; (4) they are adequately labeled; (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations.
>
> FDA considers drug products to be therapeutically equivalent if they meet the criteria outlined above, even though they may differ in certain other characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time and other minor aspects of labeling (e.g., the presence of specific pharmacokinetic information) and storage conditions. When such differences are important in the care of a particular patient, it may be appropriate for the prescribing physician to require that a particular brand be dispensed as a medical necessity. With this limitation, however, FDA believes that products classified as therapeutically equivalent will produce the same clinical effect and safety profile as the prescribed product.

If FDA has determined a generic to be therapeutically equivalent to the innovator product, FDA continues to believe, as stated in a letter dated January 28, 1998, to Health Practitioners, that:

- Additional clinical tests or examinations by the health care provider are not needed when a generic drug product is substituted for the brand-name product.
- Special precautions are not needed when a formulation and/or manufacturing change occurs for a drug product provided that the change is approved according to applicable laws and regulations by the FDA.
- As noted in the "Orange Book," in the judgment of the FDA, products evaluated as therapeutically equivalent can be expected to have equivalent clinical effect whether the product is a brand-name or generic drug product.
- It is not necessary for the health care provider to approach any one therapeutic class of drug products differently from any other class, when there has been a determination of therapeutic equivalence by FDA for the drug products under consideration.

We continue to monitor and, if indicated, investigate reports of potential inequivalence. The FDA is committed to approving high quality generic drug products that can be used with confidence by the American public.

Sincerely,

Steven Galson

Steven Galson, M.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

January 11, 2008

Ms. Nicole Schultz
Iowa Pharmacy Association
8515 Douglas Avenue, Suite 16
Des Moines, IA 50322

Dear Ms. Schultz:

This is in reply to your correspondence dated November 6, 2007, directed to Ms. Susan Winckler requesting that the FDA provide a statement regarding generic substitution, particularly with respect to anti-epilepsy drugs. It was forwarded to the Office of Generic Drugs for a reply.

The FDA has many years of experience in the review of generic drugs and assures the quality and equivalence of approved generic drug products. FDA works with pharmaceutical companies to assure that all drugs marketed in the U.S., both brand-name and generic, meet specifications for identity, strength, quality, purity and potency. In approving a generic drug product, the FDA requires that the proposed generic product is demonstrated to be equivalent to the brand-name drug in both the rate and extent of absorption. As noted in the Preface to the *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") (27th Edition),

> FDA classifies as therapeutically equivalent those products that meet the following criteria: (1) they are approved as safe and effective; (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the same active drug ingredient in the same dosage form and route of administration, and, (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent; (4) they are adequately labeled; (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations.
>
> FDA considers drug products to be therapeutically equivalent if they meet the criteria outlined above, even though they may differ in certain other characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time and other minor aspects of labeling (e.g., the presence of specific pharmacokinetic information) and storage conditions. When such differences are important in the care of a particular patient, it may be appropriate for the prescribing physician to require that a particular brand be dispensed as a medical necessity. With this limitation, however, FDA believes that products classified as therapeutically equivalent will produce the same clinical effect and safety profile as the prescribed product.

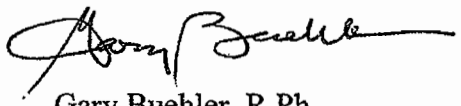
FDA is aware that certain individuals and groups have expressed particular concern about the switching of anti-epileptic drug products. To date, we have no scientific evidence that demonstrates a particular problem with this group of products. Further, there are frequently circumstances other than the switch that may cause untoward responses. We continue to follow-up such reports and interact with those concerned.

If FDA has determined a generic to be therapeutically equivalent to the innovator product, FDA continues to believe that:

- Additional clinical tests or examinations by the healthcare provider are not needed when a generic drug product is substituted for the brand-name product or vice-versa.
- Special precautions are not needed when a formulation or manufacturing change occurs for a drug product provided the change is approved according to applicable laws and regulations by the FDA.
- As noted in the "Orange Book," in the judgment of the FDA, products evaluated as therapeutically equivalent can be expected to have equivalent clinical effects whether the products are brand-name or generic.
- It is not necessary for the healthcare provider to approach any one therapeutic class of drug products differently from any other class when there has been a determination of therapeutic equivalence by FDA for the drug products under consideration.

We continue to monitor, take seriously, and, if indicated, investigate reports of potential inequivalence of all generic drugs. The FDA is committed to approving high-quality generic drug products that can be used with confidence by the American public.

Sincerely,



Gary Buehler, R.Ph.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
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cc: S. Winckler
C. Jung