AdvancePCS

health improvement REPORT

Improving Patient Safety

Results From a Year of Drug Safety Interventions

Improving patient safety is a concern shared by all in the health care industry. Studies in recent years have revealed that adverse drug events (ADEs) – caused by clinically inappropriate prescribing, drug interactions, and drug-induced health complications – are among the leading threats to patient safety in this country.

According to a January 2000 report by the Institute of Medicine, approximately 44,000 to 98,000 deaths can be attributed to medical errors per year, with 7,000 deaths resulting from ADEs.[1] Other studies conducted in hospital settings have estimated that ADEs account for more than 100,000 deaths annually, making ADEs the 4th leading cause of death in the United States[2] and costing as much as $136 billion annually – more than the total cost of cardiovascular or diabetic care in the United States[3].

As a result of these findings, the government has called for improved drug packaging, communication and timely access to data via information technology.

AdvancePCS – Applying Solutions Today

As the nation's largest pharmacy benefit management and health improvement company – administering pharmacy care benefits for 75 million, or one in four Americans – AdvancePCS is uniquely positioned to positively impact pharmaceutical safety in this country.

Processing prescription claims electronically for hundreds of thousands of plan members per day, AdvancePCS' point-of-service drug utilization review (DUR) system plays a crucial role in improving pharmaceutical care safety. The system delivers important value by flagging potentially harmful drug interactions based on a patient's active prescription history across all provider pharmacies. Although some pharmacies may employ similar DUR electronic alert systems, their systems are limited to considering only the patient's prescription history filled within their own pharmacy or pharmacy chain.

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AdvancePCS reviews prescriptions for clinical safety at 59,000 retail pharmacies across the country, as well as within AdvancePCS' own mail service pharmacies.

AdvancePCS recently quantified the impact its system has on preventing ADEs in the millions of members it serves. This report summarizes those findings for 2001, covering an entire year of DUR alert activity throughout the AdvancePCS network encompassing virtually all pharmacies in the United States. These results show that AdvancePCS' online DUR alert system, in partnership with participating pharmacies, prevents millions of potential drug interactions and adverse drug events per year.

What's Inside

This Health Improvement Report details results from 12 months of activity by the AdvancePCS online DUR alert system. These DUR alerts were issued to improve the pharmaceutical care for 75 million individuals covered by AdvancePCS pharmacy benefit plans during 2001.

In addition to quantifying the number and type of DUR alerts that resulted in safer pharmaceutical care for millions of patients, this report highlights a few examples of important drug-drug interactions as well as adverse drug events in various therapeutic review categories, such as Drug-Age (drugs that should be used with caution due to the patient's age), Drug-Allergy (drugs to which a patient may have cross-sensitivities), and Drug-Pregnancy (drugs that should not be used during pregnancy).

Finally, this report looks beyond the online DUR system and explores other ways in which AdvancePCS supports safe pharmaceutical care for its plan members. These methods involve communicating with physicians, pharmacists and patients to encourage safe and appropriate pharmaceutical care throughout the entire health care continuum. AdvancePCS' commitment to these efforts stems from its belief that safe pharmaceutical care not only leads to improved patient outcomes, but also lowers health care costs for both members and plans.

Key Findings

The full-year analysis of activity resulting from AdvancePCS' DUR alert system revealed the following significant results:

- In 2001, AdvancePCS issued DUR safety-related alerts for more than 32 million prescriptions, or 7.2% of all claims. Of this number, 2.9 million prescriptions were "reversed", meaning the pharmacist dispensed a safer alternative in consultation with the prescribing physician. Consequently, the AdvancePCS DUR system, in partnership with contracted pharmacies across the country, may have prevented millions of adverse drug reactions, injuries or deaths, and continues to do so.
- "Out-of-chain" DUR alerts – meaning drug alerts based on potential drug-drug interactions involving prescriptions filled at other pharmacies – accounted for 22% of all reversals in the Drug-Drug Interaction category, 10% of reversals in the Overuse category, and 25% of reversals in the Ingredient/Therapeutic Duplication category. These numbers are significant because they represent therapeutic changes that would not have occurred without AdvancePCS' review of a patient's active prescriptions filled at all provider pharmacies.

[1] Committee on Quality of Health Care in America: Institute of Medicine. To err is human: building a safer health system. Washington, D.C.: National Academy Press; 2000.

[2] Lazarou J, Pomeranz B, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA. 1998; 279:1200–1205.

[3] Johnson JA, Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Arch Intern Med. 1995; 155: 1949–1956.

- In the Drug-Drug Interaction category, alerts resulted in therapeutic changes in 10% of all claims for five clinically important drug-drug interactions recently identified by the University of Arizona and the AdvancePCS Center for Healthier Aging, with support from the Centers for Disease Control and Prevention (CDC). An average of 14.5% of these reversals occurred in AdvancePCS' "outside of pharmacy chain" review, resulting in therapeutic changes that would not have occurred otherwise.

AdvancePCS' Online DUR Alert System

AdvancePCS plays a critical role in identifying the potential for harmful drug interactions at the "point of fulfillment" – the pharmacy. A real-time alert system is employed at approximately 59,000 retail pharmacies as well as within AdvancePCS' own mail service pharmacies.

The DUR Alert process begins with a pharmacist entering a prescription into the pharmacy's computer system, which is then relayed to the AdvancePCS claim adjudication system. The AdvancePCS system receives the claim, identifies the patient, verifies the price, assesses eligibility, and provides payment terms. Concurrently, the system checks the patient's prescription against any other active medications on file (filled within the latest three months) for conditions that warrant a DUR safety check. The system notifies the pharmacy of any conflicts identified within the following DUR edit categories:

1. Drug-Drug Interaction
2. Drug-Age Conflict
3. Drug-Disease Conflict
4. Drug-Allergy Conflict
5. Drug-Gender Issue
6. Drug-Pregnancy Warning
7. Excessive Controlled Substance Utilization
8. Overuse/Excessive Duration
9. High Dose Warning
10. Ingredient Duplication
11. Therapeutic Duplication

In the event that an edit is triggered, the pharmacist has the option to verify the information in consultation with the physician and patient, and make an appropriate adjustment to dispense a safer alternative or cancel the prescription.

The real-time alert system checks prescriptions against a number of potential drug and health conflicts to help ensure patient safety.

AdvancePCS drug alerts, in partnership with provider pharmacies, resulted in nearly 3 million prescriptions being changed or cancelled in 2001.

Improving Patient Safety – A Year of Data

DUR Safety Alerts and Reversals in 2001

AdvancePCS conducted a comprehensive analysis of its online DUR safety alerts for a full year of prescription fulfillment activity. This study reviewed 447 million claims fulfilled during calendar year 2001.

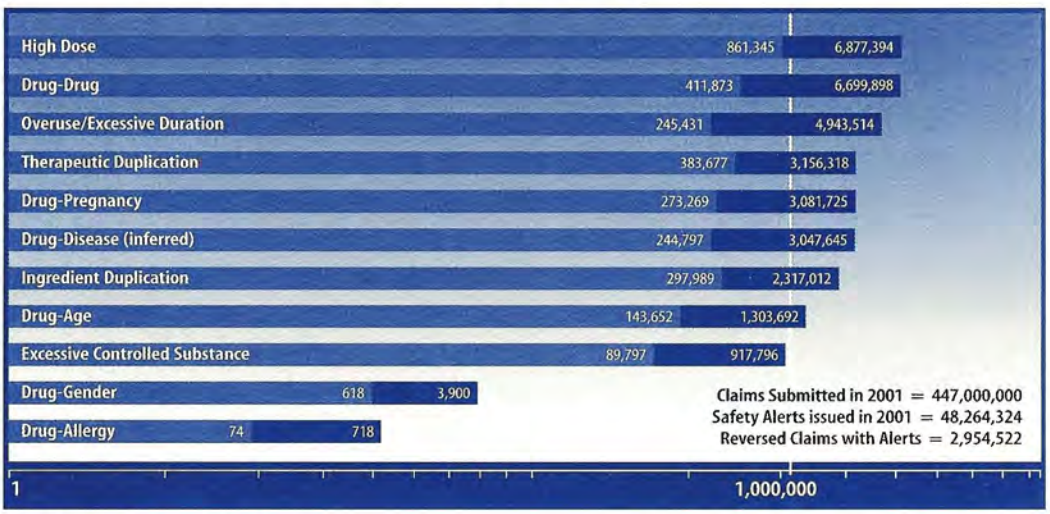
Table 1 lists the number of alerts and reversals by DUR category. A claim "reversed" is a prescription that was cancelled or changed due to pharmacist intervention.

Table 1 – Breakdown of Safety-Related Alerts By DUR Category

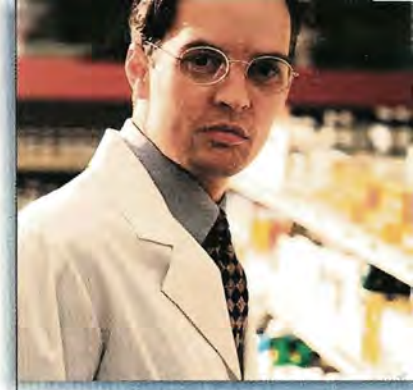
DUR Alert Category	Number of Claims Alerted	Number (%) of Claims Reversed
High Dose Warning	6,877,394	861,345 (12.5%)
Drug-Drug Interaction	6,699,898	411,873 (6.1%)
Overuse/Excessive Duration	4,943,514	245,431 (5.0%)
Therapeutic Duplication	3,156,318	383,677 (12.2%)
Drug-Pregnancy Warning	3,081,725	273,269 (8.9%)
Drug-Disease Conflict	3,047,645	244,797 (8.0%)
Ingredient Duplication	2,317,012	297,989 (12.9%)
Drug-Age Conflict	1,303,692	143,652 (11.0%)
Excessive Controlled Substance	917,796	89,797 (9.8%)
Drug-Gender Issue	3,900	618 (15.8%)
*Drug-Allergy Conflict	718	74 (10.3%)
Total of All Claims	**32,349,324**	**2,943,788 (9.1%)**

* Drug-allergy conflicts are more effectively alerted by pharmacy DUR systems due to eligibility information provided to AdvancePCS often excluding patient allergy information.

DUR Alerts Issued During 2001 By Category



Reversed Claims are shown on a logarithmic scale.

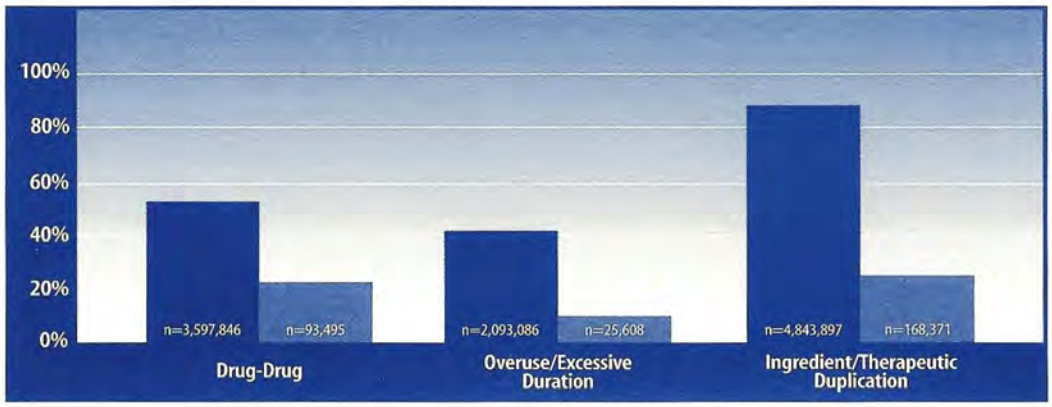


Outside of Pharmacy Chain Alerts & Reversals

Alerts Delivered Solely by the AdvancePCS System

Table 2 lists significant numbers of "out of pharmacy chain" reversals that occurred **solely because of AdvancePCS' review of prescriptions filled at all provider pharmacies.** Generally, pharmacies have a system that reviews only prescriptions filled within their own pharmacy or pharmacy chain. In the DUR categories of Drug-Drug Interaction, Overuse/Excessive Duration and Ingredient/Therapeutic Duplication, the AdvancePCS system was responsible for 62% of all the claims alerted in these catagories. Of those claims reversed, 21% can be attributed to AdvancePCS' active prescription review across all provider pharmacies.

Table 2 – Outside of Pharmacy Chain Alerts & Reversals
(Alerts Delivered Solely by the AdvancePCS System)



● **Alerts** (Scale reflects percentage of all alerts)
● **Reversed Claims** (Scale reflects percentage of all reversals)

AdvancePCS minimizes the potential for drug-drug interactions by checking plan members' new prescriptions against all other active prescriptions filled at any of the 59,000 provider pharmacies in the country.

Studies indicate that dosing errors are the most common type of prescription error that leads to adverse drug events.

Therapeutic Category Definitions & Examples

Following are definitions of the various DUR edits through which prescriptions are checked by the AdvancePCS system. Examples of some of the leading drugs alerted under each category are also listed.

High Dose Alert

High dose DUR interventions are critical for monitoring member utilization of appropriate dosage regimens. This DUR may protect members from the adverse events associated with high dosage regimens, such as increased side effects. Studies indicate that dosing errors are the most common type of prescription error that leads to ADEs, causing excessive drug dosage for the patient's age, weight, underlying condition, and renal function[4].

In 2001, AdvancePCS issued high dose alerts on 6.9 million prescriptions, 861,345 (12.5%) of which resulted in reversals due to pharmacist intervention in consultation with the prescribing physician.

Table 3 – 2001 Sample High Dose Alerts

High Dose Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
warfarin	744,430	33,144 (4.4%)
potassium chloride	18,000	1,809 (10.0%)

- Warfarin (brand name example: Coumadin®) is a blood thinner used for the treatment and prevention of blood clots. Inappropriate dosing can lead to internal bleeding and other complications.
- Potassium chloride is a supplement used to treat patients who have low potassium blood levels as a result of a particular disease state or the use of certain medications. High doses of potassium chloride can complicate other medical conditions or lead to serious cardiac complications.

Overuse/Excessive Duration

Over-utilization interventions can protect patients from adverse events associated with using a prescribed medication beyond the recommended timeframe. Consequences of over-utilization can include drug overdose, toxicity and increased side effects. This DUR also helps ensure that members are not overutilizing potentially addictive medications.

In 2001, AdvancePCS issued overuse alerts for 4.9 million prescriptions, 245,431 (5%) of which resulted in pharmacist intervention in consultation with the prescribing physician. A total of 118,009 (22%) of these interventions can be attributed to AdvancePCS' review of prescriptions filled across all provider pharmacies.

[4] Classen DC, Pestotnik SL, Evans RS, et al. Adverse drug events in hospitalized patients. JAMA, 1997;277:301-6; and Evans RS, Pestotnik SL, Classen DC, et al. Prevention of adverse drug events through computerized surveillance. Proc Annu Symp Comput Appl Med Care, 1992:437-41.

Table 4 – 2001 Sample Overuse Alerts

Overuse Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
amoxicillin	7,420	1,452 (19.6%)
hydrocodone with acetaminophen	4,477	492 (11%)

- Amoxicillin (brand name example: Amoxil®) is an antibiotic commonly used to treat ear, skin, and respiratory tract infections. As with many antibiotics, the main concern is to effectively treat an infection in a timely manner and avoid the potential for bacterial resistance against the antibiotic. Resistance may develop against amoxicillin if it is overutilized. Overutilization can cause simple bacterial infections that were once easily curable with amoxicillin to become very difficult to cure, raising the cost of treatment by requiring more potent and costly antibiotics.
- Hydrocodone with acetaminophen (brand name example: Vicodin® and Lortab®) is a combination narcotic analgesic used to relieve moderate to moderately severe pain. Patients should take this drug only for as long as it is prescribed because of the risk of addiction associated with long-term use of this therapy.

Drug utilization reviews for overuse and excessive duration can prevent drug overdose, toxicity, increased side effects, and the potential for addiction.

Therapeutic Duplication

Therapeutic duplication interventions can prevent duplication of medications prescribed in the same therapeutic class. This DUR can protect patients from unfavorable consequences, including the potential for overdose and increased side effects.

In 2001, AdvancePCS issued therapeutic duplication alerts for 3.2 million prescriptions, 383,677 (12%) of which resulted in pharmacist intervention in consultation with the prescribing physician.

Table 5 – 2001 Sample Therapeutic Duplication Alerts

Therapeutic Duplication Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
nonsteroidal anti-inflammatory drugs (NSAIDs)	86,243	10,384 (12%)
beta-blockers	66,284	7,955 (12%)

- Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (brand name example: Motrin®) and naproxen sodium (brand name example Naprosyn®) are commonly prescribed to relieve pain or inflammation. Therapeutic duplication of NSAIDs may result in adverse events such as a perforated ulcer, which could be life-threatening.
- Beta-blockers such as atenolol (brand name example: Tenormin®), propranolol (brand name example: Inderal®), and metoprolol (brand name example: Lopressor®) are commonly prescribed to lower high blood pressure. Therapeutic duplication of beta-blockers may result in adverse events such as significant decreases in heart rate or blood pressure.

Approximately 25% of ingredient duplication interventions (more than 74,000) occurred because of AdvancePCS' review of prescriptions filled across all provider pharmacies.

Ingredient Duplication

Ingredient duplication interventions can prevent excessive utilization of medications prescribed with the same active chemical component. This DUR can protect patients from adverse events, including the potential for overdose.

In 2001, AdvancePCS issued ingredient duplication alerts on 2.3 million prescriptions, 297,989 (12.9%) of which resulted in pharmacist intervention in consultation with the prescribing physician. A total of 297,987 (24.9%) of these interventions can be attributed to AdvancePCS' review of prescriptions filled across all provider pharmacies.

Table 6 – 2001 Sample Ingredient Duplication Alerts

Ingredient Duplication Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
fluoxetine	476,840	30,947 (6.0%)
lisinopril	432,062	7,002 (1.6%)

- Fluoxetine (brand name examples: Prozac® and Sarafem®) is a popular antidepressant in a class of medications called selective serotonin reuptake inhibitors (SSRIs) used to treat depression, compulsive disorders and other related conditions. Sarafem® is an example of a drug in this class used only to treat premenstrual dysphoric disorder (PMDD). Ingredient duplication of fluoxetine can result in increased heart rate or seizures.
- Lisinopril (brand name examples: Prinivil® and Zestril®) is an anti-hypertensive in a class of medications called angiotensin-converting enzyme (ACE) inhibitors. Ingredient duplication of lisinopril can result in dizziness or a detrimental drop in blood pressure.

Drug-Pregnancy Warning

Drug-pregnancy interventions are crucial to protect the health of the fetus, as some medications are known to harm the fetus. Drug-pregnancy DUR is an important safety measure to help ensure fetal and maternal safety.

In 2001, AdvancePCS issued drug-pregnancy alerts for more than 3 million prescriptions, 273,269 (8.9%) of which resulted in cancellation or an appropriate change in therapy by the pharmacist.

Table 7 – 2001 Sample Drug-Pregnancy Alerts

Drug–Pregnancy Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
warfarin sodium	101,756	3,728 (3.6 %)
estradiol	426,919	15,985 (3.7%)

- Warfarin sodium (brand name example: Coumadin®), commonly used to treat and prevent blood clots, can pose significant risks to the fetus, including fetal abnormalities. Caution should be applied to pregnant women or those who plan to become pregnant because the drug can cause bleeding in the fetus while in the uterus.
- Estradiol is a commonly prescribed estrogen supplement used to treat conditions such as menopause and vaginal atrophy. When used in pregnant women, however, estrogen therapy can increase the risk of birth defects in the reproductive organs of the developing fetus.

Drug-Disease Conflict

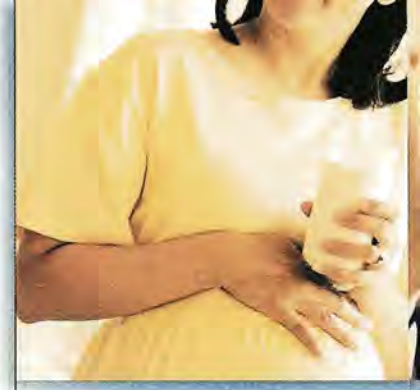
Patients who are treated for more than one disease state can experience side effects that augment or, conversely, conceal symptoms. The result can be negative health outcomes and increased medical costs.

In 2001, AdvancePCS issued drug-disease alerts on more than 3 million prescriptions, 244,797 (8%) of which resulted in cancellation or an appropriate change in therapy by the pharmacist after consultation with the prescribing physician.

Table 8 – 2001 Sample Drug-Disease Alerts

Drug–Disease Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
metformin hydrochloride	3,961	147 (3.7%)
propranolol hydrochloride	232,147	8,199 (3.5%)

- Metformin hydrochloride (brand name example: Glucophage®) is commonly used to treat diabetes. However, patients with kidney disease or heart failure should avoid taking this medication to minimize their risk of developing lactic acidosis, which can be fatal.
- Propranolol hydrochloride (brand name example: Inderal®) is a non-selective beta-blocker used to treat high blood pressure and chest pain, and prevent migraine headaches. Although propranolol is a commonly prescribed medication, it should be used cautiously in patients with asthma and other respiratory disorders such as chronic obstructive pulmonary disease because it can trigger a bronchospasm.



Patients who are treated for more than one disease state can experience side effects that augment or conceal symptoms. The drug-disease check reviews a patient's prescription history to minimize any multi-disease therapy conflicts.

Drug-age interventions are essential to protect children and the elderly from potentially negative health outcomes due to heightened drug sensitivity.

Drug-Age Conflict

Drug-age interventions are essential to protect members from medications that are not indicated for a particular age group due to heightened sensitivity and potentially negative health outcomes, in particular with children and the elderly.

In 2001, AdvancePCS issued drug–age alerts for more than 1.3 million prescriptions. Pharmacist consultation with physicians and patients resulted in 143,652 (11%) of these prescriptions being changed or cancelled.

Table 9 – 2001 Sample Drug-Age Alerts

Drug–Age Alerts	Number of Claims Alerted	Number (%) of Claims Reversed
tetracycline	12,501	3,681 (29.4%)
diazepam	330,465	17,659 (5.3%)

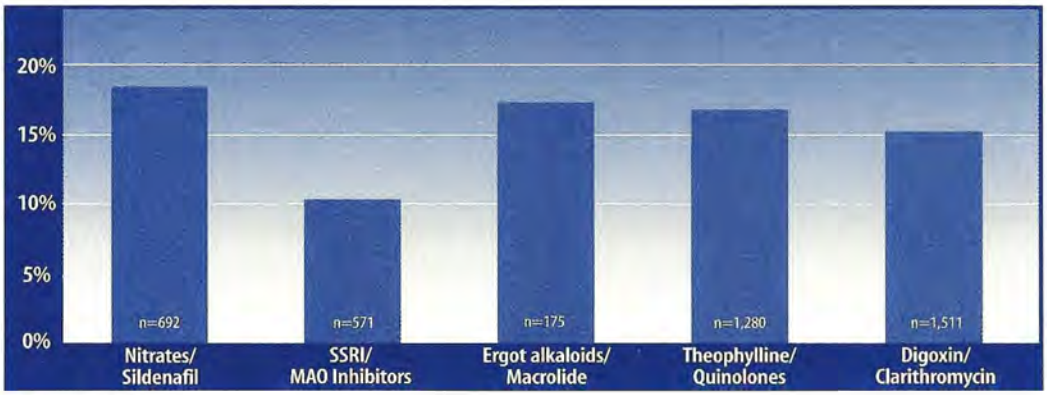
- Tetracycline and its derivatives are commonly used antibiotics that should not be used by young children because its use may permanently discolor their teeth.
- Diazepam, a benzodiazepine often used for anxiety, has a long half-life in the elderly. As a result, it can build up in the body and produce prolonged sedation, increasing the risk of falls and fractures. If a benzodiazepine is required for an elderly patient, one with a shorter half-life should be used.

Preventing Clinically Significant Drug-Drug Interactions

The AdvancePCS Center for Healthier Aging and the University of Arizona, with funding from the CDC, have recently identified a list of the top 25 clinically significant drug-drug interactions based on an extensive review of literature and input from an expert panel of physicians and pharmacists. These drug-drug interactions have the potential to produce significant adverse effects or even cause death. Therefore, monitoring and prevention of these drug combinations is critical to ensuring patient safety. Table 10 details DUR alerts and reversals for five of the 25 drug-drug interactions identified by AdvancePCS and the University of Arizona project. The AdvancePCS Center for Healthier Aging is working with the CDC and its academic and health plan partners to highlight those drug-drug interactions where prevention is most possible and is developing strategies to prevent clinically significant drug-drug interactions. Following are descriptions of these drug-drug interactions and their potentially harmful consequences.

The AdvancePCS Center for Healthier Aging is working with the CDC and its academic and health plan partners to develop strategies that prevent clinically significant drug-drug interactions.

Table 10 – Outside of Pharmacy Chain Reversals for Five Clinically Significant Drug-Drug Interactions



These percentages represent the share of claim reversals from drug-drug interaction alerts prompted by the AdvancePCS system across all provider pharmacies in 2001. These conflicts would not have been captured by retail pharmacy drug review systems that focus only on prescriptions filled by a single pharmacy or pharmacy chain.

AdvanceRx.com offers patients an online drug interaction checker that enables individuals to investigate potential drug conflicts themselves.

Sildenafil and Nitrates

Sildenafil (brand name example: Viagra®) is used for the treatment of erectile dysfunction. Nitrates (brand name example: Nitro-Dur®) are a class of medications indicated for prevention of chest pain due to coronary artery disease. When nitrates are used concurrently with sildenafil, the blood pressure lowering properties of nitrates are intensified and could lead to serious cardiovascular events. In 2001, AdvancePCS issued a total of 5,165 alerts for this interaction.

SSRI and MAO Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) (brand name example: Celexa®) and monoamine oxidase (MAO) inhibitors (brand name example: Nardil®) are two classes of medications indicated for the treatment of depression. When these two classes of medications are used concurrently, or in rapid succession of each other, the risk of a rapid rise in blood pressure or "hypertensive crisis" increases significantly. This can result in seizures, fever, marked sweating, excitation, tremors, coma, or even death.

Ergot Alkaloids and Macrolides

Ergot alkaloids (brand name example: Migranal®) are commonly used to treat conditions such as migraine headaches and Parkinson's disease. Macrolides (brand name example: Biaxin®) are a class of antibiotic medications effective in fighting a wide spectrum of infections. The concurrent use of ergot alkaloids and macrolide antibiotics may result in a severe reaction known as ergotism, which is characterized by muscle spasms of the fingers and toes, most often accompanied by pain, swelling, and bluish discoloration.

Theophylline and Quinolones

Theophylline (brand name example: Theo-24) is a drug prescribed for respiratory conditions such as asthma and chronic obstructive pulmonary disease that helps dilate or open the airways. Quinolones (brand name example: Cipro®) are a class of antibiotic medications used to treat a wide spectrum of infections. The concurrent use of theophylline and quinolone antibiotics is specifically contraindicated. Quinolone antibiotics can decrease the rate at which theophylline is eliminated from the body, resulting in an accumulation of theophylline. High theophylline levels can lead to severe seizures or fatal heart rhythms.

Digoxin and Clarithromycin

Digoxin (brand name example: Lanoxin®) is commonly used to treat mild to moderate heart failure as well as to treat some arrhythmias. Clarithromycin (brand name example: Biaxin®) a commonly prescribed antibiotic, is used for the treatment of many bacterial infections. The concurrent use of clarithromycin and digoxin can result in increased blood levels of digoxin, which can lead to heart rhythm abnormalities.

Cost Impacts of ADEs – An Ounce of Prevention is Well Worth the Savings

There is no question that ADEs contribute significantly to medical costs. Ensuring safe pharmaceutical care is well worth the investment to avoid negative patient health outcomes and increased medical costs.

A Harvard Medical Practice study on the financial impact of ADEs estimated that overall costs average $5.6 million per year per hospital, adding up to a national total of $4 billion in hospital costs associated with ADEs – $2 billion of which are associated with preventable ADEs.[5] Another study estimated the cost of drug-related death and injury to be $136 billion annually.[6] Clearly, ADEs are costly, and interventions to reduce their frequency can be justified from both an economic and quality-of-care perspective.

The good news is the fact that the more serious ADEs are preventable. Studies in hospital settings have determined that approximately one-third of ADEs are preventable, and that these account for half of all ADE-related medical costs.[7] AdvancePCS has documented that 9% of potential ADEs can be prevented through online DUR safety checks that occur at the point of dispensing. In addition, many negative health consequences can be prevented through clinical programs designed to improve the quality of care across the health care spectrum.

Injury and death associated with adverse drug events is estimated to cost the country as much as $136 billion annually.

[5] Bates DW, Cullen D, Laird N, et al. The costs of adverse drug events in hospitalized patients. JAMA. 1997; 274(4): 307-311.

[6] Johnson JA, Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Arch Intern Med. 1995; 155: 1949-1956.

[7] Bates DW, Cullen D, Laird N, et al. The costs of adverse drug events in hospitalized patients. JAMA. 1997; 274(4): 307-311.

AdvancePCS employs an array of clinical programs designed to influence appropriate and safe prescribing throughout a patient's course of treatment.

Improving Drug Safety Across the Health Care Continuum

AdvancePCS believes that maximizing pharmaceutical care safety involves more than alerting pharmacists to a potential drug issue at the point of fulfillment. That is why we employ an array of clinical programs designed to influence appropriate and safe prescribing throughout a patient's course of treatment.

Our new Pharmaceutical Care Consultations program links together clinical activities that encourage safe, appropriate and cost-saving drug care throughout the health care continuum. These activities facilitate communication between physicians, pharmacists and patients to improve patient care. For example, our Clinical Consulting program involves registered pharmacists providing one-on-one clinical support to physicians. This support includes running a monthly Patient Safety Report that details possible prescribing conflicts with other prescribers about which a doctor may be unaware. A patient's drug history from all provider pharmacies is available to physicians from no other source.

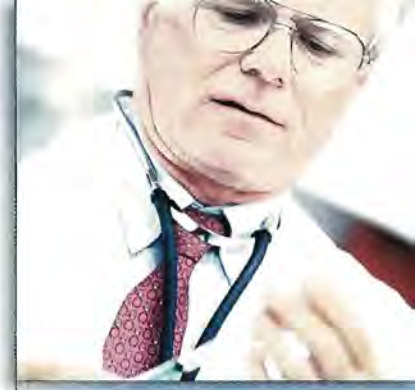
The AdvancePCS Center for Healthier Aging promotes safe medication use in seniors as part of its Healthier Aging Campaign, which aims to improve health outcomes and reduce pharmacy costs by decreasing the occurrence of ADEs. The campaign supports the Center's mission of encouraging appropriate use of medications, effective management of chronic conditions, and functional independence among the aging American population (defined as age 55 and above).

Other programs and services supporting patient safety include:

- An online drug-drug interaction checker on the AdvanceRx.com website for members to review their own medication histories.
- Patient Profiling, which entails a retrospective evaluation of patients' pharmaceutical claims each quarter. Patients whose files fall into a 'warning category' are re-examined individually by a clinical pharmacist. If there is evidence of clinical risk, a letter is sent to that member's physician to address appropriate patient care issues.
- Targeted DUR interventions that employ retrospective claims analysis to identify patients at risk in certain therapeutic categories, such as antidepressant therapy, asthma, diabetes, and controlled substance utilization. Reports are provided to physicians.
- Patient advisory letters, which are provided with prescriptions filled by AdvancePCS mail service facilities. These letters provide important information pertaining to the use of the medication, possible side effects, and remaining refills.
- Drug safety communications sent to clients and physicians to alert them of an urgent drug issue, such as a safety warning or recall.

- The AdvancePCS SpecialtyRx program, which provides physicians and members with advanced clinical support to deliver safe specialty pharmacy drug care for chronic, high-cost conditions such as multiple sclerosis, rheumatoid arthritis, hemophilia, and other life-threatening diseases. These drugs often are complicated to administer, potentially resulting in adverse drug reactions and noncompliance.

Additionally, physician connectivity will continue to play a valuable role in enhancing patient safety. AdvancePCS has begun to offer physicians online DUR and real-time access to their patients' complete prescription histories and formulary information, enabling doctors to make better informed prescribing decisions. This technology and data access significantly reduces the occurrence of conflicting prescriptions, resulting in a safer and more efficient pharmaceutical care delivery system. AdvancePCS is a founding partner in building the technology infrastructure that will create a consistent industry-wide platform for electronic data communication between pharmacy benefit managers, physicians, pharmacies and health plans. Known by name as RxHub, this technological joint venture is expected to dramatically improve patient safety across the entire health care industry.



Physician connectivity will continue to play a valuable role in enhancing patient safety.

We believe that health plan sponsors can simultaneously improve health outcomes and reduce costs through safe and effective pharmaceutical care.

Conclusion

As the U.S. population ages and the pharmaceutical industry continues to make advances in treating disease, the trend of prescription drug utilization will continue to increase. Left unchecked, adverse medical events and drug-related problems are also likely to grow. Consequences include increased risks of injury and death in patients as well as an enormous financial burden. The cost of unnecessary hospitalizations, complicated medical conditions and lost productivity related to ADEs has already reached billions of dollars per year nationally.

AdvancePCS' DUR alert system, together with pharmacy intervention, is making a significant contribution toward improving pharmaceutical care safety in this country. In 2001, this system prompted pharmacists to dispense safer alternatives for close to 3 million prescriptions. By reviewing prescription claims across all provider pharmacies, AdvancePCS is able to identify potential safety problems that a single pharmacy chain's system is not able to detect.

From these facts, it is clear that AdvancePCS plays a valuable role in managing the pharmaceutical care of the 75 million Americans we serve. In addition, our clinical programs arming physicians with patient-specific information encourage safe pharmaceutical care early in the health care continuum, prior to making prescribing choices.

AdvancePCS' technology and clinical management that enhance patient safety are a natural part of doing business as a health improvement leader. AdvancePCS is proud to be continually advancing the health care system with innovative technology and clinical programs to deliver the highest level of pharmaceutical care and safety for our clients and members. We believe that health plan sponsors can simultaneously improve health outcomes and reduce costs through safe and effective pharmaceutical care.

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The Health Improvement Company

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