



# World of Drug Information

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## Opioid Therapy for Chronic Nonmalignant Pain

CURRENT CLINICAL ISSUES

**Goal:** To increase awareness of the appropriate use of opioids for chronic pain and address concerns of equianalgesic dosing and drug addiction potential.

### Objectives:

1. List the categories of pain and an example of each.
2. Describe the Joint Commission on-Accreditation of Healthcare Organizations (JCAHO) 2001 Pain Standards goals for healthcare professionals.
3. Explain the mechanism of action and side effects of the opioids.
4. Explain the challenges in equianalgesic opioid dose conversions.
5. Describe the differences between drug tolerance, drug dependence and drug addiction and their relevance to opioid use in chronic pain.

### Introduction:

Chronic pain is a worldwide problem affecting millions of people. It affects an individual's daily functioning and quality of life. A 1998 World Health Organization (WHO) survey of approximately 26,000 primary care patients on five continents found that 22% of those surveyed had experienced chronic pain in the past year. (Gurejo, 1998) Patients experiencing chronic pain are five times more likely to utilize health care services than patients without chronic pain. A recent survey found that 58% of patients with chronic pain also had coexisting symptoms of depression or anxiety that influenced their need for health care services. (Becker, 1997)

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or is described in terms of such damage" according to the International Association for the Study of Pain. (Mersky, 1994) Pain is classified as acute, chronic or pain due to malignancy. These three types of pain differ physiologically, neurologically, pathologically and in therapeutic management. Acute pain is a natural response to tissue damage and its duration is dependent on resolution of the healing of the injured tissue. Chronic pain is defined as pain that persists beyond the healing of tissue damage or in the absence of an ongoing illness.

Chronic pain has a more comprehensive effect on the patient's life compared to acute pain. It is often associated with insomnia, depression and decreased overall quality of life. Cancer pain is either related to the primary or secondary malignancy or is due to treatment with chemotherapy or radiation.

Pain can also be categorized as nociceptive, neuropathic or idiopathic. Nociceptive pain is caused by damage to soft or bony tissue symptomatically presenting as a localized sharp or aching pain. Pain due to arthritis, blunt trauma or cancer are examples of nociceptive pain.

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Peripheral or central nervous system damage, not tissue injury or inflammation, cause neuropathic pain. Trigeminal neuralgia and phantom pain are examples of neuropathic pain. Idiopathic pain lacks an underlying diagnostic condition causing the pain. (Asburn, 1999) and (Shimp, 1998).

Chronic pain, the focus of this article, is not a homogenous condition. Chronic pain has many possible underlying etiologies that require medical treatment in addition to the symptom of pain. A total care approach includes complementary therapies in conjunction with pharmacological intervention. Chronic pain therapy requires an integrated multidisciplinary approach involving physicians, pharmacists, nurses, physical and occupational therapists, as well as social and psychological services to address all the patient's needs. Pharmacists serve an important role on the pain management team.

To address the special needs for pain management JCAHO developed pain management guidelines that were approved in March 1999 and implemented in January 2001. The guideline goals are for the healthcare team to become proficient in pain assessment, therapeutic management and patient follow-up to ensure optimum patient care. Pain assessment determines the patient's pain intensity, location, duration, onset, alleviating factors, present pain management, pain management history and quality of life with current pain management. The 0-10 intensity pain scale, Wong-Baker FACES Pain Rating Scale (smile – frown), and the Verbal descriptor scale are recommended. Adult patients are encouraged to use the 1-10 pain intensity scale. If they can not understand or are not willing to use it, the smile-frown or verbal scale is used. The verbal descriptor scale uses adjectives such as none, mild, moderate, bearable, uncomfortable, etc. to explain the pain intensity. The goal of therapy requires a thorough pain assessment, as well as individualized care for each patient's specific needs and monitored follow-up for continuation of good quality care.

JCAHO sees the need for a multi-disciplinary committee approach to fully meet the patient's needs. The pharmacist has an integral role in the healthcare team to ensure optimum drug therapy management. This role requires basic competence in pain assessment, knowledge of analgesics and the ability to evaluate the effectiveness of the pain management. The pharmacist may provide education for healthcare clinicians and patients on the potential for drug dependence or addiction to opioids. Concern about analgesic dependence and addiction, has been known to result in drug underutilization and incomplete pain control. In the community setting, the pharmacist is the first healthcare professional with whom the patient has contact after drug

management is established and is in a position to provide drug therapy follow-up.

## Treatment:

The goal of therapy is to control the pain and improve the patient's quality of life. A critical first step in pain management is careful comprehensive assessment of the patient, including the patient's general medical condition and the possible causes of pain. Individualization of therapy and reevaluation on an ongoing basis are required for optimum results. Nonpharmacological therapies and special therapies including intraspinal analgesia or neuroablative therapies may be necessary for optimal treatment of select patients, but will not be discussed in this article. (Ferrell, 1998) Pharmacotherapy for pain treatment typically involves three types of analgesics: the nonsteroidal anti-inflammatory agents (NSAIDs), (including the salicylates), "adjuvant analgesics" and opioids. "Adjuvant analgesics" are agents whose primary indication is not analgesia, but they confer pain relief under special circumstances. The most commonly used adjuvant therapies are corticosteroids, antidepressants, anticonvulsants, and antihistamines. Chronic pain can present as intermittent flares or constant persistent pain. NSAIDs, aspirin, acetaminophen, antidepressants and selected anticonvulsants are effective for acute pain flares, but are used cautiously for chronic pain due to side effect and efficacy concerns. (Marcus, 2000) Chronic use of NSAIDs is associated with gastrointestinal bleeding and ulcers. End-stage renal failure has been found in 2 of every 1000 patients with daily NSAID use for five or more years. (Bach, 1998) NSAIDs used on a daily basis are also associated with drug interactions with beta-adrenergic blockers, ACE inhibitors, diuretics and sulfonyleureas. (Marcus, 2000) Chronic use of acetaminophen has been associated with hepatotoxicity and coagulopathy. (Bach, 1998)

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Opioids are used in a step approach to treat cancer pain and should also be part of the armamentarium of therapy options for patients with chronic pain. WHO uses a three-step analgesic ladder to guide drug therapy based on pain intensity. (Levy, 1996)

The use of opioids for the treatment of chronic pain is controversial for both healthcare professionals and patients due to concerns involving side effects, drug tolerance and drug addiction.

Opioid receptors reside in the central nervous system, gastrointestinal tract and in the periphery. Exogenous opioids produce their analgesic effect by acting on the receptors in the central nervous system, mimicking the endogenous opioids (endorphins, enkephalins, and dynorphins) to elicit the analgesic response. The opioid receptors are classified as mu, delta and kappa receptors. The opioids, based on receptor activity, fall into three classes: full agonists, partial agonists and mixed agonist-antagonist. Full agonists act at the mu receptor. Partial agonists

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occupy less of the mu receptor and produce a lesser analgesic response. Mixed agonist-antagonists act at the kappa receptor and are neutral at the mu receptor. (Reisine, 1996)

Morphine, the standard opioid to which all others are compared, is a full agonist and acts at the mu receptor to elicit its effect. Morphine is often prescribed in the sustained release oral formulation for the treatment of chronic pain. (Moulin, 1996) Morphine, like most opioids, has variable oral bioavailability due to first pass hepatic metabolism. (Reisine, 1996) The metabolic path for morphine is conjugation with glucuronic acid to produce the major metabolite, morphine-6-glucuronide. This metabolite has analgesic activity and is primarily excreted by the kidney. Patients with renal failure may require dose alterations due to decreased urinary excretion of the metabolite. Morphine is effective in treating nociceptive pain, but its efficacy in neuropathic pain requires further research.

However, Zenz and colleagues evaluated 100 patients with neuropathic (n=53) or nociceptive pain (n=47) treated with 0.4-3.2 mg buprenorphine, 20-2000 mg sustained-release morphine or 60-540 mg sustained-release dihydrocodeine. Good pain relief was reported in 51 percent of patients, partial pain relief in 28 percent and improved function in all patients. In the neuropathic patient subgroup 43 percent reported good pain relief. The authors concluded the opioids tested were effective in nociceptive and neuropathic pain. (Zenz, 1992)

Side effects commonly experienced by opioid naive patients are sedation, dizziness, nausea, vomiting, urticaria, and constipation. Respiratory depression is rare in patients receiving chronic opioid therapy. (Shimp, 1998) Mild cognitive impairment and myoclonus may occur, but tend to be transient. (Moulin, 1996) Moulin and colleagues did a randomized 6-week study with 83.5 mg oral morphine or 1.7 mg bupropion (active placebo) in 46 patients with chronic non-malignant pain. The side effects reported in this study were nausea (18), dizziness (17) and constipation (19). By six weeks most patients became tolerant to the side effects of nausea, dizziness and sedation. The time to reach drug side effect tolerance for the subjects was not given. Patients did not become tolerant to the constipation. Most patients taking opioids on a chronic basis should be encouraged to engage in physical activity, drink plenty of fluids and use a stimulant laxative such as senna or bisacodyl. The osmotic and saline laxatives often are not effective due to the reduced peristalsis caused by activation of the opioid receptors in the gastrointestinal tract. Bulk forming laxatives should be avoided because they may cause pressure and not aid peristalsis. (Gloth, 2001) Severe constipation due to morphine may affect the patient's quality of life more than pain itself.

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Fentanyl, in a transdermal controlled release formulation, has shown analgesic efficacy in cancer pain. It can provide continuous analgesic relief, less constipation and can be used in patients allergic to morphine. (Allan, 2001) Allan and colleagues recently conducted a randomized trial comparing transdermal fentanyl and sustained release morphine for treating chronic pain. Of the 212 patients, 138 (65%) preferred fentanyl, whereas 59 (28%) preferred morphine and 15 (7%) expressed no preference. The incidence of side effects was similar in both treatment groups; however, more patients had constipation with morphine compared to fentanyl (48% vs 29%). The authors concluded that the main reason for the larger preference of fentanyl was due to better pain control with less constipation and enhanced quality of life.

## Equianalgesic Dosing:

Patients experiencing unacceptable side effects, poor analgesic control or drug tolerance may require opioid rotation. Rotation requires determination of an approximate equianalgesic conversion. Most equianalgesic conversion tables are based on comparing opioid potency to 10 mg subcutaneous morphine sulfate. (Reisine, 1996) A recent chart review (Quang-Cantagrel, 2000) looked at the efficacy of opioid rotation for significant side effects or drug tolerance in 87 outpatients on long acting opioids. After initial pain relief failure, the second opioid provided pain relief in 31% of patients. In the third, fourth and fifth rotations the efficacy success rates were 40%, 56% and 14% respectively. The authors concluded that the cumulative percentage of efficacy increases with each new opioid tested and that failure of one opioid can not predict the patient's response to another.

Bruera and co-workers 1996, did a retrospective dose ratio study of 113 patients treated with oral morphine sulfate or subcutaneous hydromorphone (n= 48) compared to subcutaneous hydromorphone or oral methadone (n=65). The dose ratio between morphine and subcutaneous hydromorphone was 5.33 (close to published equianalgesic table results). The subcutaneous hydromorphone to methadone ratio was 1.14:1 (5 to 10 times higher than equianalgesic table predictions).

The manufacturer of transdermal fentanyl provides a conversion table, but it is very broad, making direct comparisons of opioids difficult. According to the manufacturer's conversion table, the dose ratio of oral morphine to transdermal fentanyl ranges from 75-225 mg morphine to one mg fentanyl for the 25 mcg/hour patch. Donner and colleagues 1996, in a multicenter study of 98 cancer patients, found the direct conversion ratio of oral sustained release morphine to transdermal fentanyl to be 100 mg:1 mg. This is in the range of the manufacturers' information, but it emphasizes the challenges in opioid direct dose conversion.

Many equianalgesic tables have been published to aid the clinician in converting among opioids: Foley, 1985;

Levy,1996; Anderson, 2001; Gloth, 2001; Khouzam, 2000. Discrepancies between the conversion table doses and clinical experience have resulted in drug under or overdosing. (Anderson, 2001) Variation can exist in a patient based on previous drug exposure or other variables. Equianalgesic conversion tables should be used as guides for an initial dose for an individual patient. It is recommended that dosing be on a regularly scheduled daily basis and determined through titration based on accurately documented regular pain assessments. The recommended starting dose is 50% of the conversion dose, titrated to effect. (Anderson, 2001)

## Concerns for Opioid Use:

Addiction or dependence is a major concern of clinicians using opioids in the management of chronic pain. A lack of understanding of these issues can result in opioids being underutilized and drug addiction being over emphasized. Drug tolerance refers to a phenomenon in which exposure to a drug results in a decreased effect or the need for a higher dose to maintain the desired effect. Tolerance to the opioids would result in a shortened duration of action, decreased intensity of the analgesic effect and other effects caused by the depression of the central nervous system. Research has been done on drug tolerance for opioids in the treatment of cancer pain. The reports have not shown the development of tolerance to be a clinical problem. (Collett, 1998) Most patients with chronic pain reach an effective dose after titration and remain stable for long time periods and become tolerant to the side effects of nausea, sedation, and dizziness.

Drug physical dependence is defined as “the potential for an abstinence syndrome, or withdrawal, after abrupt dose reduction of the drug or administration of an antagonist drug.” (O’Brein, 1996) Patients who have received a therapeutic dose of an opioid for one to two weeks will have only a mild withdrawal period. In chronic pain using opioid treatment, tapering the dose down over a week or more is recommended to avoid a withdrawal syndrome. (Collett, 1998) The tapering schedule is based on the opioids half-life and elimination rate. (O’Brein, 1996)

Addiction is defined as “a behavioral pattern of drug use, characterized by overwhelming involvement with the use of a drug (compulsive use), the securing of its supply, and the high tendency to relapse after withdrawal”. (O’Brein, 1996) Fortunately, research indicates that addiction is rare in patients with chronic pain. The Boston Collaborative Drug Surveillance Program found only four cases of documented addiction in 11,882 hospitalized patients without a previous history of drug addiction, who were receiving opioids for various

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indications (Porter, 1980) A survey of over 10,000 burn patients on chronic opioids found no addiction. (Perry, 1982) Drug addiction is characterized by drug seeking behavior. Patients on opioids for chronic pain may be asking for more pain medication and may appear to be drug seeking. In reality these patients may be experiencing “pseudoaddiction”. The American Society of Addiction Medicine 1997 public policy statement identified this condition as behavior changes similar to those seen in true addiction that results due to inadequate pain management. When a clinician has a concern about addictive behavior in a patient on opioids, it is important for the healthcare team to discuss this with the patient. Dose adjustment with careful follow-up to continue efficacy assessment is usually needed.

## Conclusion:

Chronic pain is a widespread healthcare concern affecting millions of lives and requiring an integrated healthcare team approach for optimum patient care. When indicated, opioids should be used to provide adequate pain relief and improve the patient’s daily functioning. Healthcare practitioners and patients share a concern about the addiction potential of the opioids, often resulting in underutilization of the drugs and inadequate pain relief. Clinical evidence shows a low drug addiction potential in chronic pain patients on long-term opioid therapy with documented pain assessments. Pharmacists can provide both patient and physician addiction education. The patient should also be counseled on opioid side effects and their treatment. Pharmacists serve a key role in pain management follow-up to ensure optimum pain relief and improve the quality of their patient’s lives.



## Accreditation Information

The University of Iowa College of Pharmacy is approved by the American Council on Pharmaceutical Education as a provider of continuing pharmaceutical education. The ACPE program number is 020-000-01-024-H01. The University of Iowa will award 1 contact hour (0.1 CEU) of continuing pharmacy education for satisfactory completion of this monograph.

To earn continuing education credit, complete the assessment exercise, CE registration form and program evaluation, and return to Iowa Drug Information Service with a \$5.00 check for the processing fee, made out to the College of Pharmacy. A certificate will be awarded upon achieving a passing grade of 70% or better. Pharmacists must complete this program by October 1, 2002 to receive credit.

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## New Descriptor for Transdermal Administration

A new descriptor for transdermal administration will be added to the IDIS database starting with the September 2001 update. Previously, transdermal administration of drugs had been included under the descriptor for topical administration. The new term, **159 ADM TRANSDERMAL**, is defined as follows:

Administration of a drug through the skin using an adhesive patch, (e.g. estrogen, testosterone, nicotine or fentanyl patch), or topical application of a drug for systemic absorption (e.g. nitroglycerin or dimethyl sulfoxide). This also includes inadvertent transdermal absorption with resultant systemic absorption.

Descriptor **159 ADM TRANSDERMAL** will be listed under the major category class THERAPEUTIC in the subcategory Administration. The index records for previously indexed articles have been updated to include the new term if the index record contained the descriptor for topical administration in combination with estrogen, estrogens conjugated, estradiol, testosterone, nicotine, nitroglycerin, clonidine, scopolamine, dimethyl sulfoxide, or hormone replacement (HRT). This addition will affect approximately 2,500 database records.

## Assessment Questions:

Circle the most appropriate answer:

- Which is **NOT** a category of pain?
  - nociceptive
  - temporal
  - idiopathic
  - neuropathic
- Arthritis is an example of which type of pain?
  - neuropathic pain
  - acute pain
  - idiopathic pain
  - nociceptive pain
- Chronic pain patients treated with opioids do not become tolerant to which side effect?
  - nausea
  - urticaria
  - constipation
  - myoclonus
- Which of the following statements about morphine is correct?
  - Morphine undergoes conjugation to produce the major metabolite, morphine-5-glucuronide.
  - Morphine is a full agonist and acts at the delta receptor to elicit its effect.
  - Morphine is primarily excreted by the kidney and may require dose alterations in renal failure patients.
  - Morphine is more effective in treating idiopathic pain compared to nociceptive or neuropathic pain.
- Most equianalgesic tables compare the drug potency to which of the following morphine doses?
  - 1 mg subcutaneous morphine sulfate
  - 5 mg subcutaneous morphine sulfate
  - 10 mg subcutaneous morphine sulfate
  - 20 mg subcutaneous morphine sulfate
- Which of the following is an important concern in equianalgesic opioid dose conversion?
  - Determining the dose that provides an equal therapeutic effect.
  - Determining the analgesic dosage that develops drug dependence.
  - Availability of information sources to determine equivalence.
  - Overcoming the patients concerns about opioid addiction potential.
- Which of the following is an example of drug tolerance?
  - The initial drug, when discontinued, causes a withdrawal effect.
  - The initial drug dosage no longer provides effective pain control.
  - Patients begin to have compulsive use of the treatment drug.
  - Patients begin drug seeking behavior.
- Pseudo addiction in pain management is characterized as which of the following:
  - The patient denies ( his/her) addiction.
  - The patient is psychologically addicted to the drug.
  - The patient is experiencing inadequate pain management.
  - The patient has an unrecognized addiction.
- The goals for the healthcare team established by the JCAHO 2001 Pain Standards includes proficiency in all of the following **EXCEPT**?
  - pain assessment
  - cost containment
  - therapeutic management
  - management follow-up
- Which of the following is true regarding recommendations by the JCAHO 2001 Pain Standards for healthcare professionals?
  - No pain scale was recommended for pain assessment.
  - The goal of therapy requires a thorough pain assessment, as well as individualized care and monitored follow-up.
  - Patient education should include a warning about the severe addiction potential of opioids in chronic pain management.
  - A thorough pain assessment only includes the patient's pain intensity, duration and location.

### Directions

Select the most appropriate answer for each of the following questions and circle the corresponding letter on the answer sheet.

To receive one hour of continuing education credit (0.1 CEU) for successful completion of this program, you must:

- Complete the answer sheet.
- Print or type your name, address, social security number and pharmacy license number(s) in the space provided on the CE registration form.
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**ANSWER SHEET**

- |    |   |   |   |   |     |   |   |   |   |
|----|---|---|---|---|-----|---|---|---|---|
| 1. | a | b | c | d | 6.  | a | b | c | d |
| 2. | a | b | c | d | 7.  | a | b | c | d |
| 3. | a | b | c | d | 8.  | a | b | c | d |
| 4. | a | b | c | d | 9.  | a | b | c | d |
| 5. | a | b | c | d | 10. | a | b | c | d |

**CE REGISTRATION**

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**PROGRAM EVALUATION**

	Excellent				Poor
Overall quality	5	4	3	2	1
Relevance to practice	5	4	3	2	1
Value of content	5	4	3	2	1
	Agree				Disagree
Important to pharmacists	5	4	3	2	1
Increased my knowledge	5	4	3	2	1
Achieved stated objectives	5	4	3	2	1
Was educational and not promotional	5	4	3	2	1

It took me \_\_\_\_\_ hours and \_\_\_\_\_ minutes to read this article and complete the assessment questions.

## Individual FDA Drug or Biologic Approval Packages Now Available For Purchase

In response to outside requests for FDA Approval Packages [formerly Summary Basis of Approval Equivalents (SBAs)], we are now accepting orders for individual FDA drug or biologic Approval Packages. The Approval Packages contain clinical information on recently approved drugs or biologics that is often not published elsewhere. We organize each Approval Package into a standardized format, by creating a Table of Contents, identifying the pivotal studies and preparing abstracts of the pivotal studies.

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### A few thoughts . . .

As this issue of the *World of Drug Information* goes to press, we are reeling from the events of September 11<sup>th</sup>. The following message comes from University of Iowa President Coleman. I would like to share the message with you as it distills and represents this Division's guiding principles in providing drug information to an international community. These sentiments have served us well for the past 35 years and will continue to light our future.

—Hazel Seaba, Director  
Division of Drug Information

### THE UNIVERSITY OF IOWA

"Dear Friends:



Today many of our fellow citizens are suffering. Our hearts go out to them, and to their families. At this difficult time, all members of our wider community need to support each other and to work together to foster an atmosphere of mutual trust and caring. One of our collective core values is to offer a supportive and humane environment in which people from a wide variety of backgrounds and traditions may encounter each other in a spirit of cooperation, openness and respect for difference and diversity. Today, let us rededicate ourselves to our mission of building bridges and advancing a community in which all people can work together."

—Mary Sue Coleman, President, University of Iowa

# IDIS Disease Terms for Pain

## INDEXING NOTES

Pain is one of the cardinal manifestations of a disease. Pain is present in ninety percent of all diseases. Pain is a universal and complex symptom that constitutes the most frequent complaint encountered by health professionals. Pain can be classified by its intensity, length and location, but presumed pathophysiology can also be used to differentiate different pain types and subtypes. Pain management is a therapeutic and economical challenge to health care professionals.

### What are the *IDIS* disease terms for pain?

A search conducted in the *IDIS* Thesaurus with <*pain\** and *di*> yields almost 200 entries (August 2001 Update). Word terminations such as *-algia*, *-ache* or *-ynia* retrieve over one hundred additional entries.

Examples:

Cervical Pain

See *CERVICALGIA 723.1*

Colpospasm

See *PAIN, FEMALE GENITAL NEC 625*.

Mastalgia

See *MASTODYNIA 611.71*

*PAIN, ANAL OR RECTAL 569.42*

Pain, Breast

See *MASTODYNIA 611.71*

Pain, Ear

See *OTALGIA 388.7*

Pain, Head

See *HEADACHE NEC 784.0*

### How are *IDIS* disease terms organized?

*IDIS* valid disease terms are arranged numerically into categories such as operation and procedure, disease state and injury. Within each category they are sub-classified by organ system. For example, earache is cross referenced to *OTALGIA*. The corresponding code for otalgia, 388.7, belongs within the ICD-9-CM code classification range for diseases of the nervous system and sense organs. The following table gives some examples of valid terms and their cross references used in indexing pain management articles.

Organ System	ICD-9-CM Range	<i>IDIS</i> Code	<i>IDIS</i> Term	Cross-Term	Some Cross Terms Examples found in <i>IDIS</i>	Hits (08/01)
Nervous System & Sense Organs	320. - 389.9	388.7	OTALGIA	6	Earache, Unspecified; Otogenic Pain; Pain, Mastoid; <i>Otalgia</i> ; Pain, Ear, etc.	7
Genitourinary System	580. - 629.	625.	PAIN, FEMALE GENITAL NEC	12	Pain, Round Ligament, Uterus; Pain, Perineal, Female; Pain, Adnexa Uteri; Vulvodynia, etc.	123
Musculoskeletal System and Connective Tissue	710. - 737.3	719.4	PAIN, JOINT	13	Arthralgia; Pain, Joint, Ankle; Pain, Joint, Metacarpophalangeal; Pain, Joint, Pelvic Region; Pain, Joint, Multiple Sites, etc.	139
		729.5	PAIN, LIMB	11	Pain, Hand; Pain, Extremity, Lower; Pain, Leg, etc.	199
Symptoms, Signs & Ill-defined Conditions	780. - 799.4	780.91	PAIN NEC	15	Pain, Paradoxical; Cancer Pain; Pain, Post-Operative; Pain, Neurogenic; Neuropathic Pain, etc.	6855
		786.5	PAIN, CHEST	17	Discomfort, Chest; Pain, Costochondral; Pain, Intercostal Muscles; Pain, Diaphragm; Pain, Rib, etc.	300
		786.51	PAIN, PRECORDIAL	5	Pain, Anginoid, Non-Psychogenic; Pain, Pericardial, Non-Psychogenic, etc.	9
		789.0	PAIN, ABDOMINAL	13	Pain, Caecum; Infantile Colic; Pain, Epigastrium; Pain, Flank, etc.	269

The valid disease term for pain is a single entity but it may also be combined with other valid disease terms to provide better retrieval of pain management articles. For example, the combination of valid terms “PAIN NEC 780.91”, and “NEOP, MGN- NEC 199.” yields over 700 articles related to the treatment of non specific pain in unspecified cancer patients.

*IDIS* is a controlled vocabulary database with numerous cross reference terms for pain. The use of the *IDIS* thesaurus is therefore crucial in finding pertinent articles pertaining to pain, an ill-defined, and complex yet frequently found condition in the clinical setting.





# Iowa Drug Information Network Appoints New Director

**Ron Herman** has joined the College of Pharmacy's Division of Drug Information Service as Director, Iowa Drug Information Network. He is replacing Kevin Moores, Pharm.D. who has taken a position at Creighton University School of Pharmacy and Allied Health Professions. As Director of the Iowa Drug Information Network, Dr. Herman will lead the management and further development of IDIN's professional service and educational missions. He currently is a member of the Clinical and Administrative Pharmacy (CAP) Division of the College of Pharmacy and will continue to teach in the CAP Division — participating in drug information and literature evaluation teaching activities.

Dr. Herman brings more than 25 years of pharmacy experience to the position. An alumnus of The University of Iowa, he graduated with a B.S. in pharmacy, M.S. in clinical pharmacy and Ph.D. with a pharmacokinetics major from the College of Pharmacy. He also completed a pharmacy residency at the Iowa City Veterans Administration Hospital. Dr. Herman spent six years in South Africa providing pharmacy and drug information consulting services to the South African Department of Health and Social Welfare. His prior assignment in the College of Pharmacy included teaching in the areas of fluids, electrolytes, nutrition and the pharmacotherapy of burns. He taught in the clinical pharmacokinetics and advanced pharmacokinetics/pharmacodynamic courses. In the clinical setting, he provided consultative pharmacy services to the patients of the Burn Treatment Center at The University of Iowa Hospitals and Clinics. In this capacity he applied and investigated the altered pharmacokinetics of drugs in the hypermetabolic burn population using various computational tools. He has been on the forefront of using technology in teaching and patient care. His abilities and experience in informatics will strengthen the Division's use of technology to improve health professional's access and use of drug information.

## FDA DRUG/BIOLOGIC APPROVALS

Generic Name (FDA Therapeutic Classification) Trade Name	Sponsor (Approval Date)	Valid IDIS Drug Term Drug Number (IDIS Citations)*	Indication/Use	Valid IDIS Disease Term Modified ICD-9-CM Number
<b>Drospirenone/ Ethinyl Estradiol</b> (1,4S)** <i>Yasmin</i>	Berlex Labs (June 7)	DROSPIRENONE 68320028 ETHINYL ESTRADIOL 68160008 (1 citation)	For contraception.	Contraceptive Management V25.
<b>Nesiritide Citrate</b> (1S) <i>Natrecor</i>	SCIOS Inc. (Aug 10)	NESIRITIDE 24080103 (23 citations)	For the intravenous treatment of patients with acutely decompensated congestive heart failure who have dyspnea at rest or with minimal activity.	Failure, Heart, Congestive 428.0
<b>Perflutren Lipid Microspheres</b> (1S) <i>Definity</i>	Dupont Pharm (July 31)	PERFLUTREN 36000039 (14 citations)	For the treatment patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border.	Ultrasound, Diagnostic 88.7

\* Through August 2001 Update. Complete bibliographic citations will be provided upon request.

\*\* New molecular entity given standard review by FDA.

# New Drug Selected Bibliography

This new drug selected bibliography provides a selection of key clinical studies and reviews of new drugs approved by the FDA May 11 through August 10, 2001. *IDIS/CD-ROM* was searched to retrieve key articles relevant to the new drugs and their approved uses.

## Nesiritide Citrate

Colucci WS, Elkayam U, Horton DP et al. Intravenous nesiritide, a natriuretic peptide, in the treatment of decompensated congestive heart failure. *N Engl J Med* 2000;343:246-53. (*IDIS* Article Number 450037) ***To determine the clinical value of nesiritide, investigators conducted two randomized studies involving 432 patients with decompensated congestive heart failure; one study to determine the short-term efficacy with regard to hemodynamic measures and symptoms, and the other to compare nesiritide with standard intravenous agents.***

Burger AJ, Elkayam U, Neibaur MT et al. Comparison of the occurrence of ventricular arrhythmias in patients with acutely decompensated congestive heart failure receiving dobutamine versus nesiritide therapy. *Am J Cardiol* 2001;88:35-9. (*IDIS* Article Number 466476). ***In a randomized study, investigators compared the occurrence of ventricular arrhythmias in 305 patients with decompensated congestive heart failure who received either intravenous standard dobutamine therapy or nesiritide (0.015 microgram/kg/min or 0.030 microgram/kg/min), in addition to assessing the efficacy of nesiritide compared to dobutamine therapy.***

Dunn A, Chow MS and Kluger J. Nesiritide; a natriuretic peptide with hemodynamic benefits in patients with acute decompensated CHF. *Formulary* 1999;34:123-131. (*IDIS* Article Number 424367). ***This article is a comprehensive review of the synthetically prepared brain natriuretic peptide, nesiritide.***

## Perflutren Lipid Microspheres

Kitzman DW, Goldman ME, Gillam LD et al. Efficacy and safety of the novel ultrasound contrast agent perflutren (Definity) in patients with suboptimal baseline left ventricular echocardiographic images. *Am J Cardiol* 2000;86:669-674. (*IDIS* Article Number 452894). ***Investigators conducted a prospective, multicenter, double-blind, placebo-controlled trial to assess the safety and efficacy of perflutren for left ventricular cavity opacification and endocardial border delineation in 211 patients with suboptimal baseline echocardiograms.***

Weissman NJ, Cohen MC, Hack TC, et al. Infusion versus bolus contrast echocardiography: a multicenter, open-label, crossover trial. *Am Heart J* 2000;139:399-404, (*IDIS* Article Number 444996). ***In a multicenter, randomized, controlled, crossover study, investigators compared the usefulness of 2 single "slow" bolus injections of 10 microliters/kg to an infusion (1.3 mL in 50 mL normal saline at 4.0 mL/min) of perflutren for contrast echocardiography in 64 patients with suboptimal echocardiographic images.***

Cohen JL, Cheirif J, Segar DS et al. Improved left ventricular endocardial border delineation and opacification with Optison (FS069), a new echocardiographic contrast agent: results of a phase III multicenter trial. *J Am Coll Cardiol* 1998;32:746-52 (*IDIS* Article Number 414603). ***In 203 patients with inadequate noncontrast echocardiograms, investigators compared the efficacy and safety of Albunex (0.8 and 0.22 mL/kg) to Optison (0.2, 0.5, 3.0, and 5.0 mL) on separate days 48 hours apart.***



Ruth Calloway, R.Ph., M.S.

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Visit our booth at the upcoming professional meetings:

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(ACCP)**

**Booth #117**

Annual Meeting  
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October 21 - 24,  
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**American Society  
of Health-System  
Pharmacists  
(ASHP)**

Midyear Clinical  
Meeting (MCM)  
New Orleans, LA  
December 2 - 6,  
2001

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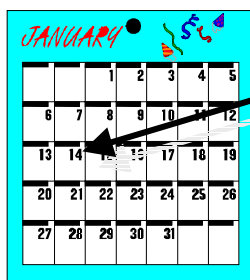
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## ERRATUM

Two errors occurred in an article that appeared in the June 2001 issue in the 'Perspective from an *IDIS* Subscriber' section Re: amiodarone (Cordarone TM) associated pulmonary disease. On page 11 under **DAT**: The Liver Function Tests should read – within normal limits except **Alkaline Phosphatase** 1.2 x ULN (not Anterior-posterior). In the last sentence of the first paragraph on page 13, an incorrect dosage of amiodarone is listed. The correct dosage is **238 mg** for 180 days (not 23 mg). Both errors have been corrected in the Volume 12, Issue 2-June 2001 newsletter found on the *IDIS* Web Site (<http://www.uiowa.edu/~idis>). We regret these errors.

## 2002 RENEWAL REMINDER



2002 *IDIS* database subscription renewal information will be sent in September. We urge you to notify us of your renewal intentions as soon as possible. To avoid interruption of service, we need to receive your renewal form by January 14, 2002. Thank you for your prompt attention to your 2002 *IDIS* subscription renewal.

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