Current Trends in Acute & Chronic Pain Management

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Michigan Pharmacists Association
Annual Convention & Exposition
February 27, 2009

Learning Objectives

At the end of the presentation, the participant should be able to:

- Discuss the balance between opioid abuse and the undertreatment of pain
- Describe the State & National initiatives addressing the efforts to remove barriers to effective pain management
- Summarize the role of the pharmacist in the care of a patient suffering from acute or chronic pain and formulate appropriate pharmacotherapeutic interventions

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Introduction

- Outline
  - Impact of Pain and Drug Abuse
  - National Initiatives
  - State Initiatives
  - Clinical Aspects of Pain Management
  - Summary
  - Questions

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The Impact of Pain

The Impact of Pain

- **Pain >** Diabetes + heart disease + cancer !!
- Uncontrolled pain → disability
  - ↓ Quality of life
  - Interferes with daily activities, sleep, work, & social interventions
- Estimated cost: $100 billion annually
  - Healthcare costs, lost income & productivity
- Underserved populations??

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The Pain Crisis

- Health care professionals
  - Little or no training
  - Understanding of regulatory policies?
  - Fear of scrutiny from local, state, federal authorities
- Patient
  - Not aware they can ask for treatment
  - Fears - addiction
  - Minorities, elderly, others → under-treated?
- Research → < 1% NIH budget dedicated for pain

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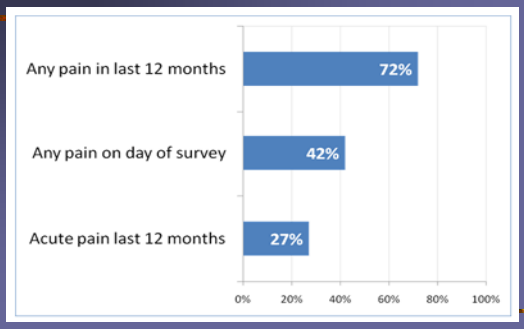
The Majority of Americans are in Pain

- National Pain Foundation
  - Harris interactive survey - December 2007
  - N = 1,484 adults (age > 18 years)
  - Measure the incidence & types of pain during the previous 12 months
  - N = 653 reported "qualifying" pain
    - Long term chronic pain, long term recurrent pain, +/or short term acute pain

7 www.nationalpainfoundation.org

Most Americans Experience Acute or Persistent Pain



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Quality of Life / Economic Impact

- Disruption in everyday activities
  - Recreational activities (65%)
  - Run errands (46%)
  - Home / chores (59%)
  - Self-care / family care (41%)
- Productivity
  - One in five (22%) – missed 1 day of work
  - At work – 48% reported lower productivity
  - $26+ billion annually lower back pain

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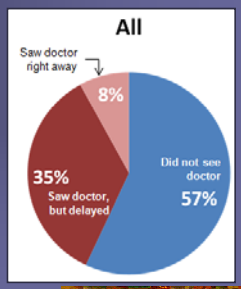
Treatment Barriers

- Reluctance to seek treatment for pain
- Myths
  - Aches & pains are normal aging process (86%)
  - Acute pain does not lead to chronic pain (26%)



10 www.nationalpainfoundation.org

Medication Related Questions

- How did you treat your pain?
  - Non-prescription (PO) 68%
  - Prescription (PO) 25%
  - Prescription (patch) 2%

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Medication Related Questions

- Why did you avoid non-prescription pain medications?

Pain would resolve on its own	Might interact with other meds
Don't like pills / capsules	Afraid of needing higher & higher doses
Don't want to be dependent	Cost too much
Avoid side effects	Upset stomach
Avoid "general" medication for pain in specific part or body	Some pain meds – sleepy & non-energetic
Not sure if medications are safe	Afraid of cardiac safety issues
Believed medication would not work well	Others…

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Medication Related Questions

- If I take a prescription pain medication, there is a good chance I may become addicted

Strongly agree	7%
Somewhat agree	30%
Somewhat disagree	36%
Strongly disagree	27%

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The Impact of Drug Abuse

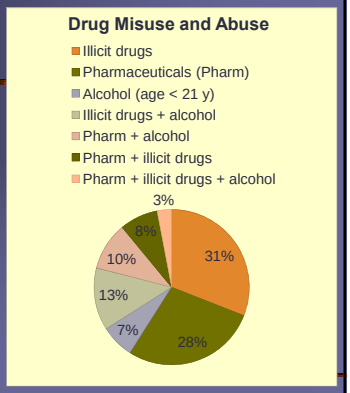
Drug Abuse Warning Network (DAWN)

- Public health surveillance system
  - Drug-related visits to emergency departments (ED's)
  - Drug-related deaths investigated by medical examiners
- Non-Federal hospitals with 24-hour ED
- Latest publication: 2006
  - N=205 hospitals
  - Michigan: Detroit Metropolitan area

15 http://dawninfo.samhsa.gov

DAWN Highlights 2006

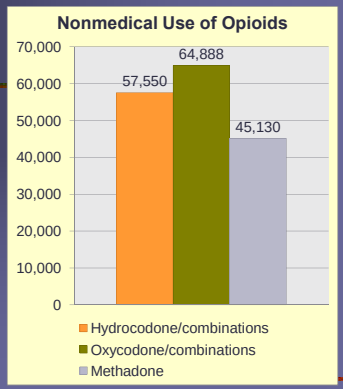
- Approximately 113 million ED visits
- Greater than 1.7 million ED visits associated with drug misuse or abuse



16 http://dawninfo.samhsa.gov

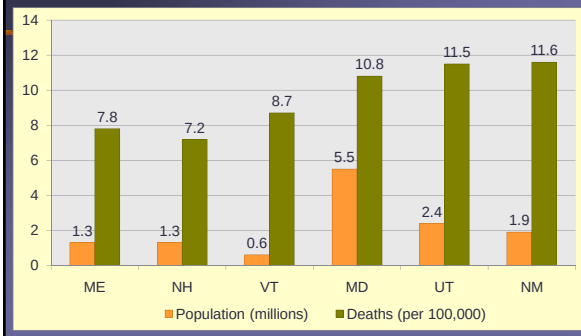
Nonmedical Use of Pharmaceuticals 2006

- Approximately 598,542 ED visits involved nonmedical use of prescription, OTC or dietary supplements
- CNS agents (51%)
  - Opioids 33%
  - Psycho-therapeutics (46%)



17 www.dawninfo.samhs.gov

Opioid-Related Drug Misuse Deaths: 2003



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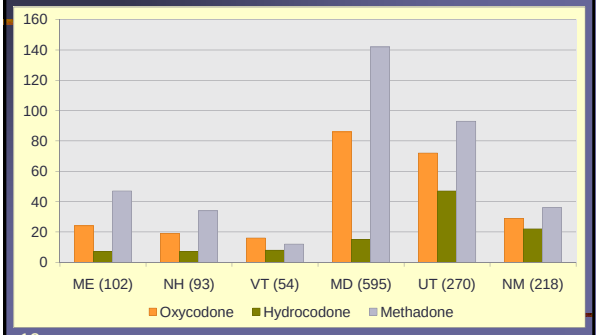
Opioid-Related Drug Misuse Deaths: 2003



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Achieving Balance

National Initiatives

State of Michigan Initiatives

Balance Between Clinical Practice & Regulatory Agencies

Clinician	Regulatory Agency
Treat Pain	Stop / Control Diversion
Avoid Contributing to Diversion	Avoid Interfering in Medicine & Patient Care

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National Initiatives

Model Policy

Prescription Monitoring Programs

Pain & Policy Studies Group

National Pain Care Policy Act of (2007) 2009

Military Pain Care Act 2008

2001-2010

Decade of Pain Control and Research

- Late 2000, Congress passed into law
- Effective January 1, 2001
- Opportunities for improved funding for pain research & education
- American Pain Society initiatives
  - Task force
    - Research
    - Professional awareness
    - Policy
    - Public awareness
  - National Pain Care Policy Act
  - Others

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Federation of State Medical Boards of the U.S. (FSMB)

- Model Policy for the Use of Controlled Substances for the Treatment of Pain
  - First publication – 1998 (Model Guidelines)
  - Latest publication - May 2004 (Model Policy)
  - Collaboration of pain experts in U.S.
  - Provide guidance to medical boards in developing pain policies & regulations
- State of MI → Medicine, nursing & pharmacy guidelines

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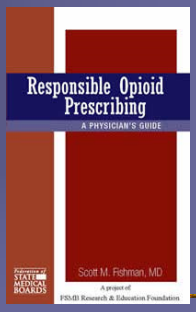
www.fsmb.org

Federation of State Medical Boards of the U.S. (FSMB)

Risk Reduction & Patient Care

- Patient evaluation, including risk assessment
- Treatment plans that incorporate functional goals
- Informed consent and prescribing agreements
- Periodic review and monitoring of patients
- Referral and patient management
- Documentation
- Compliance with state and federal law



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Prescription Monitoring Programs (PMPs)

- Monitor prescribing of controlled substances
  - Detect illicit prescribing & dispensing
  - Identify patients who are obtaining Rx from multiple sources
- N = 38 states according to Pain & Policy Studies Group (PPSG)
  - Electronic transmission of data from pharmacy
  - NY & TX → also require state-issued Rx forms
  - MI → Michigan Automated Prescription System (MAPS)

26 www.painpolicy.wisc.edu

Prescription Monitoring Programs (PMPs)

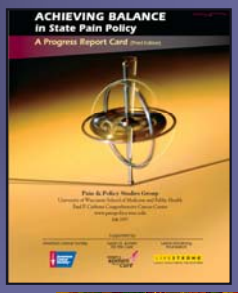
Alliance of State Pain Initiatives Statement on PMP's

- Avoid government-issued serialized Rx forms
- Include all CII – CIV + others as needed
- Program administered by agency for regulating health care vs. law enforcement
- Multidisciplinary review group – assure legitimate prescribing & dispensing are protected
- Protect patient confidentiality
- Assure healthcare professionals have access to patients' use
- Law enforcement may access with probable cause
- Develop educational programs on PMP's
- Ensure adequate communication to PMP administrators

27 www.aspi.wisc.edu

Pain & Policy Studies Group

- University of Wisconsin Pain & Policy Studies Group (PPSG)
- Assess individual state policies → Grade: A to F
- Imperative to evaluate pain policy
  - WHO, INCB, IOM, ACS, NIH
- Mission of PPSG
  - Balanced policies
  - Patient access to pain medications



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Pain & Policy Studies Group

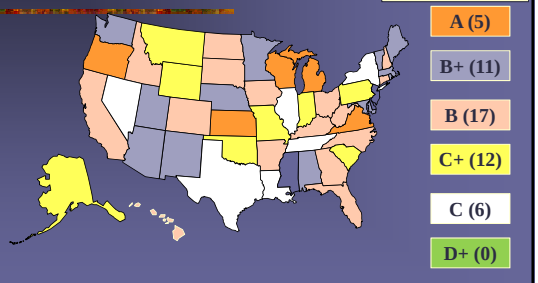
Central Principle of Balance

Medical Availability	Drug Control

•Opioids are essential drugs & necessary to relieve pain
•Opioids should be accessible to all patients requiring pain relief
•Government – ensure adequate availability of opioids
  •Empower practitioners to provide opioids in practice
  •Prescribing, dispensing, & administration according to individual patient needs
  •Ensuring sufficient supply to meet medical demand
	•When misused, opioids pose a threat to society
	•System of controls is necessary to prevent abuse, trafficking, & diversion
	  •Not intended to diminish medical usefulness of opioids
	  •Not interfere with legitimate medical uses & patient care

29 www.painpolicy.wisc.edu

How Do the States Rate in 2008?



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National Pain Care Policy Act of 2009

- Legislation to address barriers to proper pain management
- Focus
  - Improving pain care research
  - Education & training
  - Access, outreach, & care
- Introduced July 11, 2007 (HR 2994)
  - Lois Capps (D-CA) & Mike Rogers (R-MI)
- House of Representatives passed September 2008
- Re-introduced in 2009 (HR 756)

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National Pain Care Policy Act of 2009

Bill Summary (HR 756)

- Institute of Medicine conference on pain care
- Permanent authorization for the pain consortium at NIH
- Pain care education and training
- Pain management public awareness campaign

32 www.painfoundation.org

Military Pain Care Act of 2008

- American Pain Society & Pain Care Coalition
- HR 5465 introduced by David Loebsack (D-IA)
- Intended to improve pain care for armed services personnel & families
- Authorizes Department of Defense to implement a pain-care initiative

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State of Michigan Initiatives

Advisory Committee – Pain & Symptom Management
Educational DVD
MI Pharmacy Guidelines – Controlled Substances
Curriculum Guidelines – Pharmacy
MAPS
Supply of CII's in Community Pharmacies

MI Advisory Committee on Pain & Symptom Management

- Interdisciplinary committee – 1995; 1998; 2002; 2006
- Developed recommendations to balance access to pain management & improper use of controlled substances
- 17 members appointed by governor or licensing boards
- Charges
  - Address pain & symptom management issues
  - Hold a public hearing to gather information
  - Make recommendations to improve pain management in MI

35 www.michigan.gov/pm

MI Advisory Committee on Pain & Symptom Management

Completed

- Replace Official Prescription Program (OPP) → MAPS (1/02)
- Amend policy on Patient & Resident Rights & Responsibility (1/02)
- Schedule II medications (1/02)
- Pain CE requirement
- Website – launched 5/07

Pending

- Education
  - Website (on-going updates)
  - DVD
  - FSMB publication
  - Many others!
- Update model guidelines
- Curriculum guidelines
  - Adopt IASP model criteria
- Pharmacies – carry adequate supply of CII's

36 www.michigan.gov/pm

Educational DVD

- Grant obtained by the State of Michigan Controlled Substances Advisory Commission
- Topics: Pain Management & MAPS
- Projected date of completion: Mid 2008?
- Distribution: All healthcare providers who are licensed in the state of Michigan

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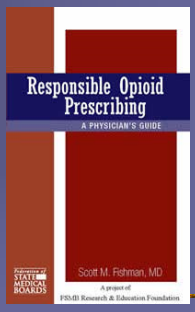
Federation of State Medical Boards of the U.S. (FSMB)

- Spring 2009
  - Customized for the State of Michigan
  - Distribution
    - Licensed physicians (N = 27,548)
    - Residents (N = 5267)



38 www.fsmb.org

MI Board of Pharmacy Guidelines for the Use of Controlled Substances for the Treatment of Pain

Preamble

"All pharmacists should become knowledgeable about effective methods of pain treatment as well as statutory requirements for prescribing and dispensing controlled substances"

39 www.michigan.gov/pm

MI Board of Pharmacy Guidelines for the Use of Controlled Substances for the Treatment of Pain

- Guidelines
  - Review of the prescription
  - Fictitious or possibly fictitious prescriptions
  - Prescription refills
  - Patient referral
- Definitions
  - Analgesic tolerance, dependence, & addiction
  - Pseudoaddiction
- Good faith
  - Dispensing of a controlled substance that in the professional judgment of the pharmacist is lawful

40 www.michigan.gov/pm

International Association for the Study of Pain (IASP) Curriculum Guidelines - Pharmacy

Outline Summary of the Pharmacy Curriculum	
Introduction & overview	Pain management
Definition of pain	Clinical pharmacology
Ethical issues	Pharmaceutical concerns
Physiological & pharmacological issues	Non-pharmacological approaches to pain
Psychological & behavioral issues	Drug availability issues
Common pain etiologies	Special considerations

41 www.iasp-pain.org and www.michigan.gov/pm

Suggested Curriculum Revisions

- MI Professional Training Programs
  - Medicine
  - Nursing
  - Pharmacy
  - Dentistry
  - Psychology
  - Physical therapy
  - Occupational therapy

42 www.michigan.gov/pm

Adequate Supply of C II's in Community Pharmacies

- Adequate supply of Schedule II medications required to meet needs of patient & community
- Barriers exist affecting the willingness of Michigan's 2500 pharmacies to carry larger amounts of scheduled meds
- Proposals for upcoming discussion
  - Collaborate with Pharmacy Board & MPA
  - Suggest pharmacies carry adequate supply?
  - Referral arrangements with other pharmacies?
  - Future survey – April 2009?

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MI Automated Prescription System (MAPS)

- Replaced the Official Prescription Program
- Required by all pharmacists, veterinarians, & dispensing physicians to report all controlled substances dispensed (C II-V)
- Ability to access data statewide on any particular patient
- Generate system-wide messages
- ~ 1.3 million prescriptions monthly

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www.mi.gov/healthlicense

MI Automated Prescription System (MAPS)

	Number of Prescriptions Reported		
	2006	2007	2008
All Controlled Substances (II – V)	15,989,785	16,803,988	17,254,281
Schedule II	2,657,261	2,865,784	2,977,576
Schedule III	6,166,143	6,422,221	6,556,999
Schedule IV	6,354,017	6,628,443	6,710,068
Schedule V	812,364	887,540	1,009,638

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MI Automated Prescription System (MAPS)

	Number of Prescriptions Reported		
	2006	2007	2008
Hydrocodone + APAP	4,596,486	4,905,407	5,161,390
Meperidine (PO)	8492	7290	6663
Propoxyphene (Darvon, Darvocet)	1,092,709	1,018,567	975,269
Methadone	163,627	172,159	169,466
Pregabalin	228,757	311,813	377,499

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Clinical Aspects of Pain Management

Clinical Practice Guidelines
FDA Drug Approvals
FDA Alerts
Future Directions

Clinical Practice Guidelines

- American Pain Society (APS)
  - Acute & chronic pain in sickle cell disease (1999)
  - Pain in osteoarthritis, rheumatoid arthritis, and juvenile chronic arthritis (2002)
  - Cancer pain in adults & children (2005)
  - Fibromyalgia syndrome pain in adults & children (2005)
- National Comprehensive Cancer Network (NCCN)
  - Adult cancer pain (v.1.2008)
  - Pediatric cancer pain (v.1.2007)
  - Palliative care (v.1.2009)

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www.ampainsoc.org and www.nccn.org

Clinical Practice Guidelines

- American College of Physicians & American Pain Society
  - Diagnosis and treatment of low back pain (October 2007)
- American Pain Society & American Academy of Pain Medicine
  - Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain
  - Published February 2009

49 www.ampainsoc.org

Overview: Treatment of Pain in Sickle-Cell Disease

Comprehensive Assessment Identify Appropriate Intervention(s)			
Pharmacological Therapy	Behavioral	Psychological	Physical
APAP or NSAID's Opioids Adjuvants	Relaxation Deep breathing Behavior modification Biofeedback Exercise	Cognitive therapies Hypnotherapy Imagery Distraction Social support	Hydration Heat Massage Hydrotherapy Ultrasound Acupuncture Acupressure TENS Physical therapy
Identify Patient / Family Educational Needs			
Formulate Treatment Plan			

Guideline for the Management of Acute & Chronic Pain in Sickle Cell Disease

50

Overview: Treatment of Pain in Osteoarthritis

Pain + Patient Education			
Mild Pain	Moderate-Severe Pain + Inflammation	Non-Pharmacologic interventions	Miscellaneous (may be used at any point)
APAP (up to 4 G per day)	NSAID's (assess risks)	Cognitive-behavioral strategies Weight loss Exercise Physical therapy Occupational therapy Assistive devices Massage	Glucosamine Tramadol Adjuvants for neuropathic pain? Hyaluronic acid (intra-articular) Surgery
Pain Not Controlled / Refractory Consider: Glucocorticoid Injection (intra-articular) or Opioid Therapy			

Guideline for the Management of Pain in OA, RA, & Juvenile Chronic Arthritis

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Overview: Treatment of Pain in Rheumatoid Arthritis

Pain + Patient Education + DMARD			
Mild Pain	Moderate-Severe Pain + Inflammation	Non-Pharmacologic interventions	Miscellaneous (may be used at any point)
APAP (up to 4 G per day)	NSAID's (assess risks)	Cognitive-behavioral strategies Weight loss Exercise Physical therapy Occupational therapy Assistive devices Massage	TCA's Hyaluronic acid (intra-articular) Topical agents Glucocorticoids (PO) Surgery
Pain Not Controlled / Refractory Consider: Glucocorticoid Injection (intra-articular) or Opioid Therapy			

DMARD = disease-modifying antirheumatic drug

Guideline for the Management of Pain in OA, RA, & Juvenile Chronic Arthritis

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Overview: Treatment of Pain in Children with Juvenile Chronic Arthritis

Pain + Patient / Parent Education Treat Underlying Arthritis + NSAID		
Pain not controlled → Add APAP	Non-Pharmacologic interventions	Miscellaneous (may be used at any point)
Pain not controlled → Consider DMARD or other Add combination agent* or tramadol Pain not controlled → Consider opioid therapy	Cognitive-behavioral strategies Weight loss Exercise Physical therapy Occupational therapy Massage	Hyaluronic acid (intra-articular) Corticosteroids Surgery

DMARD = disease-modifying antirheumatic drug
*Combination agent = APAP + hydrocodone or oxycodone

Guideline for the Management of Pain in OA, RA, & Juvenile Chronic Arthritis

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Adult & Pediatric Cancer Pain

- Overview of cancer pain
- Assessment
- Algorithms
- Opioid analgesics
  - Titration
  - Equivalencies
  - Management of SE's
- APAP + NSAID's
- Specific pain problems
- Patient education

54 www.nccn.org

Overview: Treatment of Adult Cancer Pain

Pain score: 7-10 ⇒ Rapid titration

- Patient not taking opioids
  - Morphine* 2 – 5 mg IV (5-10 mg PO**)
- Patient already taking opioid therapy
  - Increase current opioid dose by 50 %
- Re-assess at 15 min (60 min PO)
- Establish effective dose – give Q4h

*Or morphine equivalent
**Immediate release (IR) product

55 www.nccn.org (v.1.2007)

Overview: Treatment of Adult Cancer Pain

Pain score: 4-6 ⇒ Slow titration

- Patient not taking opioids
  - Morphine* 5-10 mg PO**
- Patient already taking opioid therapy
  - Increase current opioid dose by 25 - 50 %
- Re-assess at 4 hours
- Establish effective dose – give Q4h

*Or morphine equivalent
**Immediate release (IR) product

56 www.nccn.org (v.1.2007)

Overview: Treatment of Adult Cancer Pain

Pain score ⇒ 1-3

- Patient not taking opioids
  - Consider NSAID or APAP
  - Consider slow titration PO opioid
- Patient already taking opioid therapy
  - Slow titration PO opioid
- Re-assess

57 www.nccn.org (v.1.2007)

Overview: Treatment of Adult Cancer Pain

- Establish effective dose
  - Administer immediate release Q4h
- Chronic pain therapy
  - Convert to sustained release (SR) product
  - Interval: Q12h
- Provide rescue doses
- Titrate to analgesia and/or side effects

58 www.nccn.org (v.1.2007)

Overview: Treatment of Fibromyalgia Syndrome

Step 1
- Confirm diagnosis
- Explain condition
- Treat comorbid illness (mood or sleep disturbances)

Step 2
- Trial with low dose TCA or cyclobenzaprine
- Cardiovascular exercise
- Consider cognitive behavior therapy

Step 3
- Specialty referral (rheumatologist, pain management, psychologist, etc.)
- Trial with SSRI's, SNRI's, or Tramadol
- Consider combined medications / anticonvulsant

59 JAMA 2004;292:2388-95.

Overview: Treatment of Fibromyalgia Syndrome

Evidence for Efficacy	Pharmacologic Therapy	Non-Pharmacologic Therapy
Strong	•Amitriptyline •Cyclobenzaprine	•Cardiovascular exercise •Cognitive behavior therapy •Patient education •Multidisciplinary therapy
Modest	•Tramadol •SSRI: Fluoxetine •SNRI's: Venlafaxine, Duloxetine •Pregabalin	•Strength training •Acupuncture •Hypnotherapy •Biofeedback
Weak	•Growth hormone	•Chiropractic & massage therapy •Electrotherapy, ultrasound
None	•NSAID's, Opioids •Corticosteroids •Benzodiazepines •Others	•Tender (trigger) point injections •Flexibility exercise

60 JAMA 2004;;292:2388-95.

Overview: Treatment of Low Back Pain

Pharmacologic Therapy	Non-Pharmacologic Therapy
•APAP •NSAID's •Skeletal muscle relaxants •Antidepressants (TCA's)* •Benzodiazepines •Tramadol •Opioids	•Spinal manipulations* •Exercise therapy* •Massage* •Acupuncture* •Yoga* •Cognitive-behavior therapy* •Progressive relaxation* •Intensive interdisciplinary rehabilitation*

*Chronic therapy (> 4 weeks)

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Ann Intern Med 2007;147:478-91.

Guidelines: Opioid Therapy for Chronic Noncancer Pain

- Published February 2009 in *The Journal of Pain*
  - American Pain Society
  - American Academy of Pain Medicine
- First of a 3 part report
- 25 recommendations

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J Pain 2009;10(2):113-30

Recent FDA Drug Approvals

2004	2006	2007	2008	2009
Depodur (Morphine sulfate liposome injection) Palladone* (Hydromorphone hydrochloride) Prialt (Ziconotide) Lyrica (Pregabalin)	Ionsys (Fentanyl ionto-phoretic) Opana (Oxymorphone) Fentora (Fentanyl buccal)	Flector (Diclofenac epolamine)	Treximet (Sumatriptan + naproxen) Ryzolt (Tramadol extended release) Cymbalta (Duloxetine) Tapentadol (trade name pending)	Savella (Milnacipran)

*Withdrawn 7/05

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www.fda.gov

Depodur®

- Morphine sulfate extended-release liposome injection
- Treatment of postoperative pain following major surgery
  - Hip arthroplasty, cesarean section
  - Prostatectomy, colon resection
- Liposomal injection
  - Single –dose administration
  - Epidural route ONLY

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Prialt® (Ziconotide)

- Derived from *Conus magus* – deadly cone snail venom
- Non-opioid analgesic - blocks N-type calcium channels
- Indications: Severe, chronic neuropathic pain or pain unresponsive to opioids & intrathecal morphine not tolerated or effective
- Intrathecal administration ONLY
  - Delivered via implanted microinfusion device

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Lyrica® (Pregabalin)

MOA	Structural derivative of inhibitory neurotransmitter gamma-aminobutyric acid (GABA)		
FDA (Pain) Indications[1]	DPN[2]	PHN[3]	Fibromyalgia
Initial Dosing[4]	150 mg/day (in 3 divided doses per day)	150 mg/day (in 2 or 3 divided doses per day)	150 mg/day (in 2 divided doses per day)
Maximum Dose[5]	300 mg/day	600 mg/day	450 mg/day
Adverse Effects	Dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, "abnormal thinking"		

[1]Also approved for partial onset seizures; [2]DPN = diabetic peripheral neuropathy
[3]PHN = postherpetic neuralgia
[4]Dose may be increased within one week. May be given with or without food
[5]Dosage adjustments required in renal insufficiency

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Ionsys™

- Fentanyl iontophoretic transdermal system
  - Needle-free
  - Patient-activated analgesic system
- Acute, post-op pain only
- In-patient use ONLY
- Delivers 40 mcg dose on demand (over 10 minutes)

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Opana® (Oxymorphone)

- Mu agonist: Moderate – severe pain
- Metabolites:
  - 6-OH-oxymorphone (active)
  - Oxymorphone-3-glucuronide (inactive)
- F = 10 %; ↑ with fatty meals
- Products
  - Immediate release (5 mg & 10 mg tabs)
  - Extended release (5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg tabs)
  - Injection (Numorphan 1 mg/ml, 1.5 mg/ml)
- Clinical advantage over morphine?

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Fentora™

- Fentanyl buccal tablet
  - 100, 200, 400, 600, 800 mcg
- Cancer related pain - breakthrough pain ONLY - in opioid tolerant patients
- CAUTION!! Cannot convert from one Fentanyl product to another on a mcg to mcg basis
  - Actiq 200 mcg = Fentora 100 mcg
  - Actiq 400 mcg = Fentora 100 mcg
  - Actiq 600 mcg = Fentora 200 mcg
  - Etc….
  - Potential for medication errors

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Flector®

- Diclofenac epolamine topical patch 1.3%
  - NSAID → inhibits prostaglandin synthesis
- Treatment of acute pain due to minor strains, sprains, & contusions
- Time to peak concentration: 10-20 hours
- One patch applied to painful area twice daily
  - Do not apply to damaged or non-intact skin
  - Avoid wearing while bathing / showering

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Tapentadol

- FDA approved November 21, 2008
- Trade name pending
- Indication: Moderate to severe pain (adults ≥ 18 y)
- Dual MOA: Mu agonist + norepinephrine reuptake inhibitor
- Clinical studies
  - Bunionectomy, joint disease
  - Low back pain, osteoarthritis of hip or knee
- Side effects: Nausea, vomiting, dizziness, somnolence, headache
- Under review by DEA for scheduling

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Savella (Milnacipran)

- FDA approved January 14, 2009
- MOA: Selective serotonin & norepinephrine reuptake inhibitor
- Indication: Fibromyalgia
- Clinical studies
  - 30% reduction in pain from baseline
  - Improvements in patient global assessments
- Side effects: Nausea, constipation, hot flushes, hyperhidrosis, vomiting, palpitations, tachycardia, dry mouth, hypertension, others

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FDA Alert: Palladone


U.S. Food and Drug Administration
CENTER FOR DRUG EVALUATION AND RESEARCH

Alert for Healthcare Professionals
Hydromorphone Hydrochloride Extende-Release Capsules (marketed as Palladone)

This product is not currently available for purchase in the U.S.

FDA ALERT [7/2005]: Alcohol-Palladone Interaction

Purdue Pharma has agreed to FDA's request that they voluntarily suspend sales and marketing of Palladone in the United States. At this time, the Agency has concluded that the overall risk/ versus benefit profile of Palladone is unfavorable due to a potentially fatal interaction with alcohol.

Pharmacokinetic data indicate that the co-ingestion of Palladone and alcohol results in dangerous increases in the peak plasma concentrations of hydromorphone. These elevated levels may be lethal, even in opioid tolerant patients.

73 www.fda.gov

FDA Alert: Fentanyl Transdermal


U.S. Food and Drug Administration
CENTER FOR DRUG EVALUATION AND RESEARCH

Fentanyl Transdermal System (marketed as Duragesic) Information

FDA ALERT [1/5/2005; Update 12/21/2007]: This update highlights important information on appropriate prescribing, dose selection, and the safe use of the fentanyl transdermal system.

In July 2005, FDA issued a Public Health Advisory and Information for Healthcare Professionals that emphasized the appropriate and safe use of the fentanyl transdermal system (fentanyl patch), marketed as Duragesic and generics). Despite these efforts FDA has continued to receive reports of death and life-threatening adverse events related to fentanyl overdose that have occurred when the fentanyl patch was used to treat pain in opioid-naïve patients and when opioid-tolerant patients have applied more patches than prescribed, changed the patch too frequently, and exposed the patch to a heat source.

The fentanyl patch is only indicated for use in patients with persistent, moderate to severe chronic pain who have been taking a regular, daily, around-the-clock narcotic pain medicine for longer than a week, and are considered to be opioid-tolerant. Patients must avoid exposing the patch to excessive heat as this promotes the release of fentanyl from the patch and increases the absorption of fentanyl through the skin which can result in fatal overdose. The directions for prescribing and using the fentanyl patch must be followed exactly to prevent death or other serious side effects from fentanyl overdose. These directions are provided in the current prescribing information and Instructions for Applying a Fentanyl Transdermal Patch.

74 www.fda.gov

FDA Alert: Fentanyl Buccal


U.S. Food and Drug Administration
CENTER FOR DRUG EVALUATION AND RESEARCH

Fentanyl Buccal Tablets (marketed as Fentora) Information

FDA ALERT [9/2007] - FDA has received reports of serious side effects including death in patients who have taken Fentora. These reports describe prescribing to non-opioid tolerant patients, misunderstanding of dosing instructions, or inappropriate substitution of Fentora for Actiq by pharmacists and prescribers. The directions for using Fentora must be followed exactly to prevent death or other severe side effects from overdosing with fentanyl. FDA has asked Cephalon, the manufacturer of Fentora, to update the Fentora label and Medication Guide for patients with additional information on the safe use of Fentora.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this when additional information or analyses become available.

75 www.fda.gov

FDA Alert: Methadone

FDA Public Health Advisory
11/2006 & 7/2007

Methadone Use for Pain Control May Result in Death and Life-Threatening Changes in Breathing and Heart Beat

76 www.fda.gov

USA Today: Methadone Error

Inside a pharmacy where a fatal error occurred
By Kevin McCoy, USA TODAY

JACKSONVILLE — It was a busy summer night in 2001 at a Walgreens (WAG) store here when pharmacy technician Tomario Lewis went to a computer and typed in the new prescription that would cost Terry Paul Smith his life.

77 USA Today 2/14/08

Methadone

Warning!!

Methadone should be initiated by or in consultation with a practitioner who has relevant knowledge and experience in using methadone

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FDA Panel Recommends Ban on Propoxyphene (Darvon)

- Public Citizen (consumer group) petitioned the FDA to withdraw Darvon due to its weak pain relief & overdose risk
- January 30, 2009
  - FDA advisory panel voted 14-12 to withdraw
- United Kingdom banned – 2005
- Clinical benefit?? [Propoxyphene = acetaminophen]
- Risks: Suicide, drug dependence, overdose

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Future Directions

Clinical Updates

- Methadone 40 mg tabs
- Ketamine
- Opioid-induced hyperalgesia
- Methyl-naltrexone
  - FDA approved 4/24/08

In the Pipeline

- Cannabinoids – CB2 agonists
- Delta receptor agonists
- Kappa receptor agonists
- Inhaled & intranasal products

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Future Directions

- Certified Pain Educator (CPE) - American Society of Pain Educators
- www.paineducators.org
- Next testing period: August 1 – September 30, 2009 (application deadline September 16)
- Eligibility
  - Healthcare professional, current license
  - 10% time devoted to pain related education
  - Completed 30 hours of pain related educational activities within last 5 years

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Summary

Balance

Adequate pain control

Drug abuse

Role of the Pharmacist

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Stay Informed on Pain Initiatives

- State of Michigan website
- www.michigan.gov/pm

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Questions

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