CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-272

REMS

NDA 22-272
OxyContin® (oxycodone hydrochloride controlled-release) Tablets

Opioid Agonist

Purdue Pharma L.P.
One Stamford Forum
Stamford, CT 06901-3431

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

Goal 1: To inform patients and healthcare professionals about the potential for abuse, misuse, overdose, and addiction of OxyContin®

Goal 2: To inform patients and healthcare professionals about the safe use of OxyContin®

II. REMS ELEMENTS

A) Medication Guide

In accordance with 21 CFR 208.24, a Medication Guide will be dispensed with each OxyContin® prescription. Purdue Pharma L.P. will ensure that the Medication Guide is available for distribution to patients receiving a prescription for OxyContin® by providing sufficient numbers to distributors and authorized dispensers.

1. One copy of Full Prescribing Information, which includes the Medication Guide, will be packaged with each bottle of OxyContin®.
2. Two separate additional Medication Guides will also be packaged with each bottle of OxyContin®.
3. Per 21CFR 208.24(d) the label of each container or package of OxyContin® will include a prominent and conspicuous statement:

   a) instructing authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed (eg, “Attention Dispenser: Accompanying Medication Guide must be provided to each patient upon dispensing”), and

   b) stating how the Medication Guide is provided.

4. Medication Guides will also be available via Purdue Pharma L.P. Field Sales representatives, through an Internet presence, and from Purdue's Medical Services Department (1-888-726-7535).

Please see appended Medication Guide.

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe OxyContin® will receive training.

   a. Purdue will ensure that training will be provided to healthcare providers who prescribe OxyContin®. To become trained, each prescriber will be provided with the OxyContin® Educational materials.

      The Training includes the following:

      i) Proper patient selection;

      ii) Appropriate OxyContin® dosing and administration;

      iii) General principles of safe opioid use, including information about opioid abuse and how to identify patients who are at risk for addiction;

      iv) Potential abuse, misuse, overdose and addiction from exposure to opioids, including OxyContin®;

      v) Risks of OxyContin®, including:

         1. The risk of overdose caused by exposure to an essentially immediate-release form of oxycodone by consuming broken, chewed, crushed or dissolved OxyContin® tablets;

         2. The risk of addiction from exposure to OxyContin®; and

         3. The risk of overdose in patients who have not developed tolerance to the sedating or respiratory-depressant effects of opioids from exposure to a single dose of OxyContin greater than 40 mg;

      vi) Information to counsel patients and caregivers on the need to store opioid analgesics safely out of reach of children and household acquaintances and the need to properly dispose of unused drugs when no longer needed by the patient; and

      vii) Importance of providing each patient a Medication Guide with each prescription and instructing the patient to read the Medication Guide.

   b. Purdue will ensure that at least 3 weeks prior to first availability of OxyContin® to healthcare professionals, a Dear Healthcare Professional letter will be mailed to prescribers most

experienced in treating chronic pain with opioid agonists, including pain specialists, physiatrists, and primary care physicians. This letter is designed to convey and reinforce the risks of abuse, misuse, overdose and addiction of OxyContin® as well as the need to complete the OxyContin® REMS Educational Program. This letter will be available on the Purdue website (www.oxycontinrems.com) for 1 year from the date of mailing.

c. The mailings will include the following OxyContin® REMS Educational Program materials:

   i) OxyContin® Medication Guide

   ii) Prescribing OxyContin® Tablets CII: A Guide for Healthcare Providers

   iii) OxyContin® Education Confirmation Form

d. Additional printed educational material will be available through field-force distribution and by calling the toll-free number at Purdue (1-888-726-7535).

e. The educational material will also be available for download at www.oxycontinrems.com.

f. Purdue will maintain a list of all prescribers who have completed the OxyContin® REMS Educational Program.

Prescribers will be re-trained every two years or following substantial changes to the OxyContin® REMS. Substantial changes may include changes in the OxyContin® Full Prescribing Information, OxyContin® Medication Guide, or OxyContin® REMS that require substantial modification of the educational materials.

The following materials are part of the REMS and are appended:

- Dear Healthcare Professional Letter
- Medication Guide
- The Healthcare Provider Guide, "Prescribing OxyContin® Tablets CII: A Training Guide for Healthcare Providers"
- OxyContin® Education Confirmation Form

C. Implementation System

Because OxyContin® can be approved without the Elements to Assure Safe Use described under FDCA 505-1(f)(3) (B), (C), and (D) of the Act, an implementation system is not required.

D. Timetable for Submission of Assessments

Purdue Pharma L.P. will submit REMS Assessments to FDA every 6 months for the first year from the date of approval of the REMS and annually thereafter. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. Purdue L.P. will submit each assessment so that it will be received by the FDA on or before the due date.

MEDICATION GUIDE

OXYCONTIN® (ox-e-KON-tin) (CII)
(oxycodone hydrochloride controlled-release)
Tablets

Read this Medication Guide before you start taking OxyContin and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about OxyContin?

- **OxyContin can cause serious side effects, including addiction or death.**
- **Do not cut, break, chew, crush, or dissolve OxyContin before swallowing. If OxyContin is taken in this way, the medicine in the tablets will be released too fast. This is dangerous. It may cause you to stop breathing, and may lead to death.**
- OxyContin is not for use to treat pain that you only have once in a while ("as needed").
- **Do not take OxyContin 60 mg or 80 mg tablets unless you are "opioid tolerant."** Opioid tolerant means that you regularly use OxyContin or another opioid medicine for your constant (around-the-clock) pain and your body is used to it.
- **Do not take more than 40 mg of OxyContin in one dose or more than 80 mg of OxyContin in one day unless you are "opioid tolerant."** This may cause you to stop breathing and may lead to death.

- **OxyContin is a federally controlled substance** (CII) because it is a strong opioid pain medicine that can be abused by people who abuse prescription medicines or street drugs.
- **Prevent theft, misuse and abuse.** Keep OxyContin in a safe place, to keep it from being stolen. OxyContin can be a target for people who misuse or abuse prescription medicines or street drugs.
- **Never give OxyContin to anyone else, even if they have the same symptoms you have. It may harm them and even cause death.**
- Before taking OxyContin, tell your doctor if you or a family member have been addicted to or abused other medicines, street drugs, or alcohol, or if you have a history of mental illness.

- **Do not drink alcohol while using OxyContin. Using alcohol with OxyContin may increase your risk of dangerous side effects, including death.**

- **Certain medicines can interact with OxyContin and cause you to have high levels of oxycodone in your blood. This may cause you to stop breathing and lead to death. Before taking OxyContin, tell your healthcare provider if you take an antibiotic, an antifungal medicine, or an anti-HIV medicine.**

What is OxyContin?

- OxyContin is a prescription medicine used when an opioid medicine is needed to manage moderate to severe pain that continues around-the-clock and is expected to last for a long period of time.
- It is not known if OxyContin is safe and effective in children younger than 18 years.
- OxyContin is not for use:
    - to manage pain "as needed"
    - before surgery to manage any pain from your surgery
    - to manage pain after surgery if the pain is mild and is not expected to last for a long period of time
- If you already take OxyContin, it may be used to manage your pain after surgery if:
    - it has been at least 12 to 24 hours after your surgery, and
    - your pain from surgery is expected to be moderate to severe, and last for a long period of time.

Who should not take OxyContin?

Do not take OxyContin if you:

- are allergic to any of its ingredients. See the end of this Medication Guide for a list of the ingredients in OxyContin.
- have had a severe allergic reaction to a medicine that contains oxycodone. Ask your healthcare provider if you are not sure.
- are having an asthma attack or have severe asthma, trouble breathing, or lung problems
- have a bowel blockage called paralytic ileus

What should I tell my healthcare provider before taking OxyContin?

OxyContin may not be right for you. Before taking OxyContin, tell your doctor if you:

- have trouble breathing or lung problems
- have had a head injury
- have liver or kidney problems
- have adrenal gland problems, such as Addison's disease

- have severe scoliosis that affects your breathing
- have thyroid problems
- have enlargement of your prostate or a urethral stricture
- have or had convulsions or seizures
- have a past or present drinking problem or alcoholism
- have hallucinations or other severe mental problems
- have past or present substance abuse or drug addiction
- have any other medical conditions
- are pregnant or plan to become pregnant. If you take OxyContin regularly before your baby is born, your newborn baby may have signs of withdrawal because their body has become used to the medicine. Signs of withdrawal in a newborn baby can include:
    - irritability
    - crying more than usual
    - shaking (tremors)
    - jitteriness
    - breathing faster than normal
    - diarrhea or more stools than normal
    - sneezing
    - yawning
    - vomiting
    - fever

    If you take OxyContin right before your baby is born, your baby could have breathing problems at birth.
- are breast-feeding. You should not take OxyContin if you are nursing. Some oxycodone from OxyContin passes into breast milk. A nursing baby could become very drowsy or have difficulty breathing or feeding well.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Sometimes the doses of medicines that you take with OxyContin may need to be changed if used together.

- **See "What is the most important information I should know about OxyContin?"**
- Be especially careful about taking other medicines that make you sleepy such as:
    - pain medicines

- sleeping pills
- anxiety medicines
- antihistamines
- anti-depressants
- tranquilizers
- anti-nausea medicine

Do not take other medicines without talking to your healthcare provider. Your healthcare provider will tell you if it is safe to take other medicines while you take OxyContin.

Know the medicines you take. Keep a list of your medicines to show your healthcare provider and pharmacist.

How should I take OxyContin?

- See "What is the most important information I should know about OxyContin?"
- **Take OxyContin exactly as prescribed. Do not change your dose unless your healthcare provider tells you to**.
- **Swallow OxyContin tablets whole. Do not cut, break, chew, crush, or dissolve before swallowing.**
- Take OxyContin every 12 hours
- You can take OxyContin with or without food.
- If you miss a dose, take it as soon as possible. Take your next dose 12 hours later. Do not take more than your prescribed dose of OxyContin. Call your healthcare provider if you are not sure about your dose of OxyContin or when to take it.
- **If you take more OxyContin than prescribed**, or overdose, call your local emergency number (such as 911) or your local Poison Control Center right away, or get emergency help.
- **Talk with your healthcare provider regularly about your pain** to see if you still need to take OxyContin.

What should I avoid while taking OxyContin?

- **Do not drink alcohol while using OxyContin.** See **"What is the most important information I should know about OxyContin?" Do not drive, operate heavy machinery, or do other dangerous activities, especially when you start taking OxyContin and when your dose is changed, until you know how you react to this medicine. OxyContin can make you sleepy, and also cause you to feel dizzy. Ask your healthcare provider to tell you when it is okay to do these activities.**

What are the possible side effects of OxyContin?

OxyContin can cause serious side effects, including:

- **See "What is the most important information I should know about OxyContin?"**
- **OxyContin can cause serious breathing problems that can become life-threatening, especially if OxyContin is used the wrong way. Call your healthcare provider or get medical help right away if:**
  - your breathing slows down
  - you have shallow breathing (little chest movement with breathing)
  - you feel faint, dizzy, confused, or
  - you have any other unusual symptoms

  These can be signs or symptoms that you have taken too much OxyContin (overdose) or the dose is too high for you. **These symptoms may lead to serious problems or death if not treated right away.**
- **Central nervous system effects, including sleepiness, dizziness, passing out, becoming unconscious, or coma.**
- **OxyContin may cause a worsening of seizures in people who already have seizures.**
- **OxyContin can cause your blood pressure to drop.** This can make you feel dizzy and faint if you get up too fast from sitting or lying down. Low blood pressure is also more likely to happen if you take other medicines that can also lower your blood pressure. Severe low blood pressure can happen if you lost blood or take certain other medicines.
- **OxyContin can cause physical dependence.** Do not stop taking OxyContin or any other opioid without talking to your healthcare provider about how to slowly stop your medicine. You could become sick with uncomfortable withdrawal symptoms because your body has become used to these medicines. Physical dependence is not the same as drug addiction. Tell your healthcare provider if you have any of these signs or symptoms of withdrawal while slowly stopping OxyContin:
  - feel restless
  - tearing eyes
  - runny nose
  - yawning
  - sweating
  - chills or hair on your arms "standing up"
  - muscle aches, backache
  - dilated pupils of your eyes
  - feel irritable or anxious
  - nausea, loss of appetite, vomiting, diarrhea

- increase in your blood pressure, breathing faster, or your heart beats faster

- **There is a chance of abuse or addiction with OxyContin.** The chance is higher if you are or have been addicted to or abused other medicines, street drugs, or alcohol, or if you have a history of mental problems.

The most common side effects of OxyContin include:

- constipation
- nausea
- drowsiness
- dizziness
- itching
- vomiting
- headache
- dry mouth
- weakness
- sweating

Some of these side effects may decrease with continued use. Talk with your healthcare provider if you continue to have these side effects. These are not all the possible side effects of OxyContin. For a complete list, ask your healthcare provider or pharmacist.

Constipation (not often enough or hard bowel movements) is a very common side effect of pain medicines (opioids) including OxyContin, and is unlikely to go away without treatment. Talk to your healthcare provider about dietary changes, and the use of laxatives (medicines to treat constipation) and stool softeners to prevent or treat constipation while taking OxyContin.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088.

How should I store OxyContin?

- **Keep OxyContin out of the reach of children.** Accidental overdose by a child is dangerous and can lead to death.
- Store OxyContin at 59° F to 86°F (15° C to 30° C)
- Keep OxyContin in the container it comes in.
- Keep the container tightly closed and away from light.
- After you stop taking OxyContin, flush the unused tablets down the toilet.

General information about OxyContin
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use OxyContin for a condition for which it was not prescribed. Never give your OxyContin to other people even if they have the same symptoms you have.

Selling or giving away OxyContin may harm others, even causing death, and is against the law.

This Medication Guide summarizes the most important information about OxyContin. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about OxyContin that is written for health professionals. For more information about OxyContin, go to www.purduepharma.com or call 1-888-726-7535.

What are the ingredients of OxyContin?

Active ingredient: oxycodone hydrochloride
Inactive ingredients in all strengths: butylated hydroxytoluene (BHT), hypromellose, polyethylene glycol 400, polyethylene oxide, magnesium stearate, titanium dioxide

- The 10 mg tablets also contain: hydroxypropyl cellulose.
- The 15 mg tablets also contain: black iron oxide, yellow iron oxide, and red iron oxide.
- The 20 mg tablets also contain: polysorbate 80 and red iron oxide.
- The 30 mg tablets also contain: polysorbate 80, red iron oxide, yellow iron oxide, and black iron oxide.
- The 40 mg tablets also contain: polysorbate 80 and yellow iron oxide.
- The 60 mg tablets also contain: polysorbate 80, red iron oxide and black iron oxide
- The 80 mg tablets also contain: hydroxypropyl cellulose, yellow iron oxide and FD&C Blue #2/Indigo Carmine Aluminum Lake

Always check to make sure that the medicine you are taking is the correct one. The dosage strength and appearance of each OxyContin tablet are as follows:

- 10 mg: white-colored with “OP” on one side and “10” on the other
- 15 mg: gray-colored with “OP” on one side and “15” on the other
- 20 mg: pink-colored with “OP” on one side and “20” on the other
- 30 mg: brown-colored with “OP” on one side and “30” on the other
- 40 mg: yellow-colored with “OP” on one side and “40” on the other
- 60 mg: red-colored with “OP” on one side and “60” on the other

- 80 mg: green-colored with “OP” on one side and “80” on the other

Purdue Pharma L.P.
Stamford, CT 06901-3431

This Medication Guide has been approved by the U.S. Food and Drug Administration.

March 22, 2010
301734-0A

REMS APPENDIX 2 – OXYCONTIN® DEAR HEALTHCARE PROFESSIONAL LETTER

[Date]

[prescriber name]

[street address]

[city, state zip code]

Dear Prescriber:

Purdue Pharma, L.P. is introducing a Risk Evaluation and Mitigation Strategy (REMS) for OxyContin® (oxycodone HCl controlled-release) Tablets to educate prescribers about the potential abuse, misuse, overdose and addiction from exposure to OxyContin® (oxycodone HCl controlled-release) Tablets.

The goals of the OxyContin® REMS program are:

Goal 1: To inform patients and healthcare professionals about the potential for abuse, misuse, overdose, and addiction of OxyContin®

Goal 2: To inform patients and healthcare professionals about the safe use of OxyContin®.

OxyContin® Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. OxyContin® Tablets are not intended for use on an as needed (prn) basis.

OxyContin® is not intended for the management of pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild, or not expected to persist for an extended period of time. OxyContin® is indicated for postoperative use following the immediate post-operative period only if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.) OxyContin® is not indicated for pre-emptive analgesia (preoperative administration for the management of postoperative pain). OxyContin® is not indicated for rectal administration.

OxyContin® contains oxycodone which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine. Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin® in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, overdose, and addiction.

OxyContin® Tablets are contraindicated in:

- patients who have significant respiratory depression
- patients who have or are suspected of having paralytic ileus
- patients who have severe bronchial asthma
- patients who have known hypersensitivity to any of its components or the active ingredient, oxycodone

Serious adverse reactions which may be associated with OxyContin® tablet therapy in clinical use are those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, or shock. The most common adverse events (>5%) reported by patients at least once during therapy include constipation, nausea, somnolence, dizziness, pruritus, vomiting, headache, dry mouth, asthenia, and sweating.

Prescribing and Dispensing

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, proper dispensing, and correct storage, handling and disposal are appropriate measures that help to limit the diversion and abuse of opioid drugs. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests is strongly advised.

Prescribing OxyContin® 60 mg or 80 mg Tablets, or a single dose greater than 40 mg, should be reserved only for those patients who have developed tolerance to the sedating and respiratory-depressant effects of opioids. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression when administered to patients who are not tolerant to the sedating and respiratory depressant effects of opioids. Patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for *one week or longer*.

The concomitant use of OxyContin® with all cytochrome P450 3A4 inhibitors such as macrolide antibiotics (eg, erythromycin), azole-antifungal agents (eg, ketoconazole), and protease inhibitors (eg, ritonavir) may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse effects and may cause potentially fatal respiratory depression. Patients receiving OxyContin® and a CYP3A4 inhibitor should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted.

When the patient no longer requires therapy with OxyContin® Tablets, doses should be tapered gradually to prevent signs and symptoms of withdrawal in the physically dependent patient.

Safe Use, Storage and Disposal

As described in the boxed warning, OxyContin® Tablets are to be swallowed whole and are not to be cut, broken, chewed, crushed, or dissolved. Taking cut, broken, chewed, crushed, or dissolved OxyContin® Tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone.

Compromising the controlled-release delivery system of OxyContin® will result in the uncontrolled delivery of oxycodone and poses a significant risk that could result in overdose and death.

Misuse and Abuse

Abuse may occur by taking intact tablets without legitimate purpose, by crushing and chewing or snorting the crushed formulation, or by injecting a solution made from the crushed formulation. The risk of fatal overdose is

further increased when oxycodone is abused concurrently with alcohol or other CNS depressants, including other opioids.

Patient Counseling

Patients should be counseled about the importance of storing opioid analgesics, including OxyContin®, safely and out of the reach of children, other household members, visitors and pets.

Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

You are strongly advised to discuss the risks associated with OxyContin® with your patients and/or their caregivers and encourage them to read the Mediation Guide. This Medication Guide contains important information on the safe and effective use of OxyContin®. In addition to the OxyContin® Full Prescribing Information, we have enclosed a copy of the OxyContin® Medication Guide, which should be provided to patients every time OxyContin® is dispensed.

We are providing you with a packet which contains important information regarding the prescribing of OxyContin®, which we encourage you to review. In addition, the packet contains educational materials that discuss the risk of abuse, misuse, overdose and addiction from exposure to opioids, how to identify patients who are at risk for addiction, and information to counsel patients on proper safe storage of medications. Please complete the OxyContin® Education Confirmation Form and return once you have read the materials. A pre-addressed return envelope is included for your convenience.

The following items are included in this packet:

- **OxyContin® Full Prescribing Information**
- **OxyContin® Medication Guide**
- **Prescribing OxyContin® Tablets CII: A Training Guide for Healthcare Providers**
- **OxyContin® Education Confirmation Form**

Please see the attached Full Prescribing Information, including the boxed warning, and the sections specifically addressing overdose with and addiction to OxyContin®.

For more information or to request additional copies of any of these materials, please contact your Purdue Sales Representative or visit us online at www.oxycontinrems.com. In addition, healthcare professionals and patients who have questions about prescribing, dispensing, or taking OxyContin® Tablets should contact the Purdue Medical Services department at (888)726-7535, prompt #1.

Please report any adverse event information associated with the use of OxyContin® Tablets to Purdue Pharma L.P., at (888)726-7535 (prompt #2), or to the FDA MedWatch system by phone at (800)FDA-1088, by fax at (800)FDA-0178, or via the Internet at www.FDA.gov/medwatch.

Sincerely,

Craig J. Landau, MD
Chief Medical Officer

Purdue

OXYCONTIN

REMS HCP Training Guide

March 24, 2010

Cover

(HEADLINE) **PRESCRIBING OXYCONTIN® TABLETS CII**

(Subhead) A Training Guide for Healthcare Providers

(Copy) Please see Important Safety Information on Page 2 and accompanying full Prescribing Information, including the boxed warning and Medication Guide.

Page 2

(HEADLINE) **IMPORTANT SAFETY INFORMATION**

(Box Warning)

WARNING: IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE[1]

OxyContin contains oxycodone which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

OxyContin can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

OxyContin is a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

OxyContin is not intended for use on an as-needed basis.

Patients considered *opioid tolerant* are those who are taking at least: 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid *for one week or longer*.

OxyContin 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in opioid-tolerant patients, as they may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory-depressant or sedating effects of opioids.

Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse and addiction.

OxyContin must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved. Taking cut, broken, chewed, crushed or dissolved OxyContin tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone.

The concomitant use of OxyContin with all cytochrome P450 3A4 inhibitors such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir) may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse effects and may cause potentially fatal respiratory depression. Patients receiving OxyContin and a CYP3A4 inhibitor should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted.

Page 3

(HEADLINE) **INTRODUCTION**

(Copy) OxyContin is indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. It is associated with significant, potentially life-threatening risks, relative to its benefits.

A Risk Evaluation and Mitigation Strategy (REMS) for OxyContin has been created to educate prescribers about the potential risks associated with OxyContin which are reflected in the goals of the REMS:

Goal 1: To inform patients and healthcare professionals about the potential for abuse, misuse, overdose and addiction of OxyContin

Goal 2: To inform patients and healthcare professionals about the safe use of OxyContin

The purpose of this training guide is to provide prescribers with important safety information about OxyContin so they can prescribe, dispense and counsel patients appropriately about the potential risk of OxyContin misuse, abuse and addiction.

Selection of patients for treatment with OxyContin should be governed by the same principles that apply to the use of similar opioid analgesics. You should individualize treatment in every case using a progressive plan of pain management such as that outlined by the World Health Organization, the Federation of State Medical Boards Model Policy, and the American Pain Society. Healthcare providers should follow appropriate pain management principles of careful assessment and ongoing monitoring.

In addition, patients and their caregivers must be told to carefully read the OxyContin Medication Guide (included in the accompanying Full Prescribing Information). The Medication Guide contains important information to ensure the safe and appropriate use of OxyContin, and to help prevent misuse, abuse, addiction and overdose.

Finally, it is critical that you counsel patients and their caregivers about the need to store OxyContin out of the reach of children, household visitors and pets in a safe and secure place. This will help reduce the risk of an accidental overdose, which may result in death.

Please see Important Safety Information on Page 2 and accompanying full Prescribing Information, including the boxed warning and Medication Guide.

Page 4

(HEADLINE) **TABLE OF CONTENTS**

(Copy)

Page 5

(HEADLINE) **RISKS OF OVERDOSE WITH OxyContin**

(Copy) It is important for all healthcare providers who prescribe opioid analgesics to understand the safety profiles of individual products. Indications and usage for different opioid analgesics vary and the Full Prescribing Information for any specific product should always be consulted before prescribing.

(Copy) Instruct patients against the use by individuals other than the patient for whom you have prescribed OxyContin, as such inappropriate use may have severe medical consequences, including death.

Following is important information about overdose risks with OxyContin.

(Subhead) Risk of Overdose from Intact Tablets

Any person who had not developed tolerance to the respiratory depressant or sedating effects of OxyContin is at risk for overdose from exposure to inappropriate doses of OxyContin, especially with concomitant exposure to drugs that depress respiratory drive or consciousness, whether there is a legitimate need for an analgesic or not.

(Subhead) Risk of Overdose from Alteration of Tablets

(Copy) **OxyContin tablets must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved.** Compromising the controlled-release delivery system will result in the uncontrolled delivery of OxyContin, which could result in overdose and death.[1]

Death due to overdose has occurred in people who chewed or snorted crushed OxyContin tablets and in people who injected a solution made from crushed tablets. The risk of a fatal overdose is even greater when OxyContin is abused together with alcohol or other CNS depressants, including other opioids.[1]

(Subhead) Risk of Overdose from Higher Doses

(Copy) Patients can overdose by taking just one dose of OxyContin.[1]

OxyContin 60 mg and 80 mg Tablets, single doses greater than 40 mg, or total daily doses of 80 mg, are for use in opioid-tolerant patients only. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression in patients who are not tolerant to the respiratory depressant effects of opioids.[1]

(Bold Copy) **Please see full Prescribing Information for complete details on the dosing and administration of OxyContin.**

Page 6

(HEADLINE) **RISK OF RESPIRATORY DEPRESSION**

(Copy) Respiratory depression is the most significant serious adverse event risk with OxyContin and can result in death.[1]

This risk is increased in elderly or debilitated patients and following large initial doses in any patient who is not tolerant to the respiratory-depressant or sedating effects of opioid analgesics. Risk is also increased when OxyContin is given together with other agents that depress respiratory drive or consciousness, such as sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol.[1]

Even the usual therapeutic doses of OxyContin may decrease respiratory drive to the point of apnea in patients with significant chronic obstructive pulmonary disease or cor pulmonale, substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression.[1] Alternative non-opioid analgesics may need to be considered for these patients.[1]

Page 7

(HEADLINE) **ADDITIONAL SIDE EFFECTS**

(Subhead) Serious Side Effects

(Copy) OxyContin may increase the risk of serious adverse reactions observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, or shock. [1]

(Subhead) Common Side Effects

(Copy) The most frequent side effects of OxyContin include constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, sweating, and asthenia.[1]

Drowsiness, dizziness, or lightheadedness may impair mental and/or physical ability required for the performance of potentially hazardous tasks (eg driving, operating machinery). Patients should be cautioned accordingly.[1]

Please see accompanying Full Prescribing Information, including the boxed warning and Medication Guide.

Page 8

(HEADLINE) **RISKS OF ABUSE, MISUSE, AND ADDICTION**

(Subhead) OxyContin Has an Abuse Liability Similar to Morphine

(Copy) OxyContin has been abused by people who chew, snort or inject tablets that have been crushed and/or dissolved. OxyContin abuse has also included taking intact tablets without legitimate purpose. In addition, OxyContin abuse can occur in the absence of addiction and is characterized by taking more OxyContin than prescribed or taking it for non-medical purposes, often in combination with other psychoactive substances.[1]

With parenteral abuse, the tablet excipients can result in death, local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases, such as hepatitis and HIV.

(Subhead) Addiction to OxyContin Is Possible

(Copy) There is a potential for drug addiction to develop following exposure to OxyContin, even during appropriate medical use.[1]

People who have abused prescription medications in the past may have a higher chance of abusing or developing addiction again when prescribed OxyContin.[1]

Behaviors that suggest drug abuse exist on a continuum, and pain-relief seeking behavior can be mistaken for drug-seeking behavior. All patients treated with OxyContin require careful monitoring for signs of addiction and drug abuse.[1]

Page 9

(HEADLINE) **ADDICTIVE DISORDER VS. PHYSICAL DEPENDENCE**

(Copy) It is important to differentiate between a person with an addiction disorder and a patient with pain who is adherent to therapy and has developed a physical dependence on opioid analgesic medications.[1]

(Subhead) Patients With Addiction Disorders:[7]

- Suffer from a chronic, neurobiologic disease with genetic, psychosocial, and environmental components
- Seek a drug in order to quickly affect the "reward center" of their brains
- Crave drugs and use them compulsively
- Continue abuse despite negative, even life-threatening, physical, mental, and/or social consequences
- These persons often develop physical dependence to the substances they are abusing and are, therefore, at risk for signs and symptoms of a withdrawal syndrome upon exposure to an antagonist (in the case of physical dependence on an opioid or benzodiazepine), significant reduction in dose or abrupt cessation of administration of the drug

(Subhead) Patients With Physical Dependence Who Do Not Have an Addiction Disorder:[7]

- Experience a normal response to the ongoing use of certain medicines, including opioids
- Want sufficient medicine to reach opioid receptors to induce analgesia
- Take medicines to relieve pain—not to satisfy a craving for a psychic effect or to stave off withdrawal syndrome
- Can generally discontinue their medicine with mild to no withdrawal syndrome once their symptoms are gone by gradually tapering the dosage according to their doctor's orders

(Copy) Please see Important Safety Information on Page 2 and accompanying Full Prescribing Information, including the boxed warning and Medication Guide.

Pages 10-11

(HEADLINE) **SCREENING FOR PATIENTS AT RISK FOR OPIOID ABUSE OR ADDICTION**

(Copy) Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed an opioid, and all patients receiving opioids should be routinely monitored for signs of misuse, abuse and addiction.

(Subhead) Patient/Family History[1]

(Copy) Persons at increased risk for opioid abuse include those with a personal or family history of substance use disorder (including drug or alcohol abuse or addiction) or mental illness (eg, major depression).

Participation or recommended participation in drug abuse treatment programs should be determined. Patients who have undergone opioid detoxification in the past are at higher risk for re-emergence of substance use disorders.

(Subhead) Screening Tests and Physical Appearance

(Copy) Many drug abuse screening tests have been developed for use in clinical practice, including the CAGE and CAGE-AID Questionnaire, the Addiction Behaviors Checklist, the Opioid Risk Tool, The Brief MAST, and the Two-Item Conjoint Screening (TICS) for Alcohol & Other Drug Problems.[2,3]

Physical screening may reveal signs of possible drug abuse. Initial screening clues may include unkempt appearance, ill-fitting clothes suggestive of weight loss/gain, sniffles, watery eyes, cough, nausea; lethargy, drowsiness, and nodding. Careful examination of skin may reveal marks caused by repeated injections.[4]

While these signs might suggest abuse, they should not be the only criteria for determining whether opioid abuse has occurred.

Please visit www.oxycontinremscom for additional information and resources.

(Subhead) Laboratory Tests

(Copy) Laboratory signs that may suggest substance abuse include elevated MCV and abnormal liver enzymes.[2,3]

Urine drug testing may yield unexpected results. The use of this technology requires understanding of specificity and sensitivity of the particular analytic method employed. Some point-of-care urine tests for “opioids” or “opiates” do not, for example, detect semisynthetic or synthetic opioid analgesics.[2,5]

All laboratory markers are nonspecific for alcohol or drug use and should be viewed as screens, not as diagnostic criteria.

(Subhead) Other Signs[1]

(Copy) Signs of compulsive drug use include covertly obtaining prescription medications from more than one physician, referred to as “Doctor Shopping,” concurrent abuse of related illicit drugs, altering or forging prescriptions, and repeated unsanctioned dose escalations despite warnings.

Other signs of compulsive drug use may be more subtle, including frequent visits to emergency rooms, and hoarding of drugs obtained from routine prescriptions.

Page 11

(HEADLINE) **SCREENING FOR PATIENTS AT RISK FOR OPIOID ABUSE OR ADDICTION (CONT'D)**

(Subhead) When You Suspect Addiction or Drug Abuse

(Copy) Following are some suggestions about what to do if you suspect a patient is addicted to or abusing OxyContin:[6]

- Remember, a person abusing drugs or affected by addictive disorder is in need of treatment for that disorder and any concomitant medical or mental conditions they have, although self-administered opioid analgesics may not be indicated
- Refer the patient to an addiction specialist or substance use treatment center, if warranted
- If you are not the primary care physician, always consult a patient's regular physician before initiating treatment with an opioid analgesic
- Contact authorities if you are threatened in any way

Pages 12-13

(HEADLINE) **PROPER PATIENT SELECTION**

(Bold Copy) **Careful patient selection is key to initiating the appropriate use of OxyContin. The decision to use OxyContin must balance the potential benefits with the risks of OxyContin treatment. The following points should be reviewed when considering OxyContin treatment for your patients.**

(Subhead) Who May Be Appropriate for Treatment With OxyContin

(Copy) OxyContin is a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.[1]

As used here, "moderate" and "moderate to severe" pain do not include commonplace and ordinary aches and pains, pulled muscles, cramps, sprain, or similar discomfort.

OxyContin is not intended for use on an as-needed (prn) basis.[1]

OxyContin is not indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery) because safety during this time frame has not been established.[1]

OxyContin is not indicated for pain during the postoperative period if the pain is mild, or not expected to persist for an extended period of time.[1]

OxyContin is indicated for postoperative use, after the immediate postoperative period, only:[1]

- If the patient has already been receiving the drug prior to surgery, or
- If the postoperative pain is expected to be moderate to severe and persist for an extended period of time

Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines).[1]

OxyContin is not indicated for preemptive analgesia (administration preoperatively for the management of postoperative pain).[1]

OxyContin is not indicated for rectal administration.[1]

Please see Important Safety Information on Page 2 and accompanying full Prescribing Information, including boxed warning and Medication Guide.

Page 13

(HEADLINE) **PROPER PATIENT SELECTION (CONT'D)**

(Subhead) Some Patients Should Never Receive OxyContin

(Copy) For some patients, the risks associated with OxyContin therapy outweigh any potential benefits, and therefore, its use is contraindicated in such patient populations.

OxyContin is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated, including:[1]

- Patients who have significant respiratory depression
- Patients who have or are suspected of having paralytic ileus
- Patients who have acute or severe bronchial asthma

The safety and effectiveness of OxyContin has not been established in pediatric patients below the age of 18 years.[1]

(Subhead) Assess for Risks of Opioid Abuse or Addiction before Starting Treatment With OxyContin

(Copy) Patients should be assessed for risks of opioid abuse or addiction before they start treatment with OxyContin. In addition to a complete medical history, a detailed history of alcohol and other substance use in the patient and family is important to establish before initiating treatment with OxyContin.[1,2]

(Copy) Persons at increased risk for opioid abuse include those with a personal or family history of substance use disorders (including drug or alcohol abuse or addiction) or mental illness (eg, major depression).[1,2]

Documentation and maintenance of careful prescribing and treatment records is essential for supporting the evaluation, the reason for OxyContin prescribing, the overall pain management plan, and any consultations received.[1,2] Documentation should include:

- Name, strength and quantity of the opioid prescribed
- Dose and frequency of administration
- Timeliness of requests for another prescription
- Initial and ongoing assessment of patients' pain
- Proper prescribing practices
- Periodic reevaluation of all therapy prescribed or recommended, including progress toward established treatment goals.

Pages 14-16

(HEADLINE) **APPROPRIATE DOSING AND ADMINISTRATION**

(Copy) OxyContin is available in 7 dosage strengths (10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg and 80 mg tablets) and is to be administered every 12 hours.

60 mg and 80 mg tablets, single doses of greater than 40 mg, or daily doses greater than 80 mg are for use in opioid-tolerant patients only.

Initial doses should be low, especially in patients receiving concurrent treatment with muscle relaxants, sedatives, or other central nervous system (CNS) medications.

To avoid the risk of a potentially fatal dose, tablets must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved.

(Subhead) Starting Therapy

(Copy) Physicians should initiate OxyContin treatment only in patients who are at the appropriate point along the progression from non-opioid analgesics, such as non-steroidal anti-inflammatory drugs and acetaminophen, to opioids, such as OxyContin, in a plan of pain management such as outlined by the World Health Organization, the Federation of State Medical Boards Model Guidelines, or the American Pain Society.[1]

It is critical to initiate and adjust the dosing regimen for each patient individually, taking into account:

- Risk factors for abuse or addiction
- Age, general condition and medical status of the patient
- Current and anticipated pain intensity (eg, stable, increasing, decreasing)
- Patient's opioid exposure and degree of opioid tolerance (if any)
- Special instructions for patients who are not opioid tolerant
- Major organ function that may affect absorption, distribution, metabolism or excretion of OxyContin®
- Pharmacokinetic and pharmacodynamic interactions with concomitant medications
- Incomplete cross-tolerance among opioid analgesics
- Genetic variability in pharmacokinetics or pharmacodynamics
- Balance between pain control and adverse reactions of OxyContin®

Page 14

(HEADLINE) **APPROPRIATE DOSING AND ADMINISTRATION (CONT'D)**

For patients who are new to opioid therapy

Experience indicates a reasonable starting dose of OxyContin for patients who are taking non-opioid analgesics and require continuous around-the-clock therapy for an extended period of time is 10 mg every 12 hours.

For patients who are NOT opioid-tolerant

Use low initial doses, especially in patients who are receiving concurrent treatment with muscle relaxants, sedatives, or other CNS medications.

Do not begin treatment with 60 mg or 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg, as these doses may cause fatal respiratory depression.

For patients previously taking opioids

See full prescribing information for full details on converting from existing opioid therapy to OxyContin and for operational criteria for opioid tolerance**.**

Page 15

(Subhead) Monitoring Effects of Concomitant Exposure to CYP3A4 Inhibitors and Inducers

(Copy) Since the CYP3A4 isoenzyme plays a major role in the metabolism of OxyContin, drugs that alter CYP3A4 activity may cause changes in clearance of oxycodone which could lead to changes in oxycodone plasma concentrations.

The expected clinical results with CYP3A4 inhibitors would be an increase in oxycodone plasma concentrations and possibly increased or prolonged opioid effects. The expected clinical results with CYP3A4 inducers would be a decrease in oxycodone plasma concentrations, lack of efficacy or, possibly, development of an abstinence syndrome in a patient who had developed physical dependence to oxycodone.

If co-administration is necessary, caution is advised when initiating OxyContin treatment in patients currently taking, or discontinuing, CYP3A4 inhibitors or inducers. It is important to evaluate these patients at frequent intervals and consider dose adjustments until stable drug effects are achieved.

(Subhead) Individualizing Dosage

Copy) After therapy is initiated, individually titrate OxyContin to a dose that provides an appropriate balance between pain relief and opioid-related side effects.

- Patients who experience breakthrough pain may need dosage adjustment or rescue medication
- OxyContin dose adjustments may be made every 1-2 days
- The 12-hour dosing interval should not be changed; it is most appropriate to increase the q12h dose, if analgesic goals are not being met and it is anticipated that side effects can be managed.
- The total daily dose can usually be increased by 25% to 50% of the current dose
- If significant adverse reactions occur, treat them aggressively until they are under control, then resume upward titration, if appropriate

During periods of changing analgesic requirements, including initial titration, maintain frequent communication with other members of the healthcare team, your patient, and the caregiver/family.

Page 16

(HEADLINE) **APPROPRIATE DOSING AND ADMINISTRATION (CONT'D)**

(Subhead) Continuing Therapy

(Copy) During chronic opioid therapy, especially for non-cancer pain syndromes, the continued need for around-the-clock opioid therapy should be reassessed periodically (eg, every 6 to 12 months) as appropriate.[1]

OxyContin therapy should be reviewed and adjusted, taking into consideration the patient's own reports of pain and side effects and the health care provider's clinical judgment. OxyContin should be individually titrated to a dose that provides an appropriate balance between analgesia and side effects. All patients treated with OxyContin should be routinely monitored for signs of misuse, abuse, and addiction.[1]

(Subhead) Stopping Therapy

(Copy) When the patient no longer requires therapy with OxyContin, taper the dose gradually to prevent signs and symptoms of withdrawal in the physically-dependent patient.

(Copy) Please see Important Safety Information on Page 2 and accompanying full Prescribing Information, including boxed warning and Medication Guide.

Page 17

(HEADLINE) **WHAT YOU NEED TO TELL PATIENTS ABOUT OxyContin**

(Copy) Once you have identified an appropriate patient for OxyContin treatment, it is important to discuss the following information with the patient and/or their caregiver to ensure safe and appropriate use and disposal, and help to prevent misuse, abuse, and risk of overdose.

- **Patients and caregivers must be told to carefully read the OxyContin Medication Guide that is provided with each OxyContin prescription. It is extremely important to remind them that the important safety information in the Medication Guide could have changed since their last OxyContin prescription was filled**.
- Patients and caregivers should be told that **s**ince OxyContin first became available, there have been reports of misuse, overdose, abuse, and addiction in some people, so the patient needs to decide if he or she wants to use, or continue to use OxyContin.[1]
- ***Also tell patients and caregivers:***

1. Always follow the prescribing directions about OxyContin *exactly* and never change the dose, the dosing frequency, or suddenly stop taking OxyContin without consulting the doctor first.[1]
2. Take OxyContin only by mouth and swallow the tablets whole. Do not break, crush, dissolve, or chew them before swallowing as this can be very dangerous, causing an overdose, and possibly death.[1]
3. OxyContin is an opioid. You should only take doses more than 40 mg at one time if you have already been taking opioids and your prescribing doctor has said it is okay.[1]
4. OxyContin may impair mental and/or physical ability required to perform potentially hazardous tasks (eg, driving, operating heavy machinery).
5. You should not combine OxyContin with alcohol or other central nervous system depressants (eg, sedatives, hypnotics) because dangerous additive effects may occur, resulting in serious injury or death.
6. Women of childbearing potential who become, or are planning to become, pregnant should consult their doctor regarding the effects of analgesics and other drug use during pregnancy on themselves and their unborn child.
7. Keep OxyContin away from children, household visitors and pets in a safe and secure place, such as locked box or cabinet. Accidental overdose by a child is dangerous and may result in death.
8. OxyContin and other opioid analgesics should not be stored in the bathroom medicine cabinet because bathroom medicine cabinets rarely lock, in the glove compartment of a car or in kitchen cabinets, inside purses, coat pockets, nightstands, or other locations easily accessed by others.[1]
9. OxyContin contains a drug that some people may want to abuse. OxyContin should only be used by the patient who was prescribed

OxyContin. A patient should protect his or her OxyContin from being stolen.[1]

10. Giving or selling OxyContin to other people is very dangerous and against the law.[1]
11. When OxyContin is no longer needed, patients should flush unused tablets down the toilet.[1]OxyContin tablets and other opioid analgesics should not be discarded in the wastebasket where children or others can find them.
12. If a patient suspects that someone has stolen their OxyContin, he or she should report to the local police department.[1]
13. Never take or give medicine in the dark. Patients should always turn the light on and wear their glasses if they need them for reading before taking or administering medication.
14. Use child-resistant packaging on medicines whenever possible.

- Caregivers should be told to check the label every time they give medicine to a loved one.

This guide for healthcare providers was written to support the REMS for OxyContin. For more information, please see the accompanying full Prescribing Information and visit www.oxycontinrems.com.

Page 18

(HEADLINE) **REFERENCES**

(References)

1. OxyContin [Full Prescribing Information]. Purdue Pharma LP; Stamford, CT.
2. Chou R, Fanciullo GJ, Fine PG, et al; for the American Pain Society– American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130.
3. Ewing, JA. Detecting alcoholism: the CAGE questionnaire. *JAMA.1984;* 252 (14): 1905-1907.
4. The National Clearinghouse for Alcohol and Drug Information. Drug categories for substances of abuse. Available at: http://ncadi.samhsa.gov/govpubs/rpo926//. Accessed November 13, 2009.
5. Gourlay DL, Caplan YH, Heit HA. Urine drug testing in clinical practice: dispelling the myths and designing strategies. Available at: http://www.familydocs.org/files/udtmonograph.pdf. Accessed November 13, 2009.
6. Weaver MF, Jarvis MAE, Schnoll SH. Role of the primary care physician in problems of substance abuse. *Arch Intern Med*. 1999;159:913-924.
7. American Pain Society. Definitions related to the use of opioids for the treatment of pain. Available at: http://www.ampainsoc.org/advocacy/opioids2.htm. Accessed Sept 16, 2009.

(Copy) Please see Important Safety Information on Page 2 and accompanying Full Prescribing Information, including the boxed warning and Medication Guide.

REMS APPENDIX 4 – OXYCONTIN® EDUCATION CONFIRMATION FORM

(Logo) **OxyContin® (OXYCODONE HYDROCHLORIDE CONTROLLED-RELEASE) TABLETS CII**

(HEADLINE) **EDUCATION CONFIRMATION FORM**

Completion of this form does not affect your ability to prescribe OxyContin®.

The purpose of this form is to confirm that you have read the REMS Education Materials for OxyContin® and understand the major risks associated with OxyContin and how to appropriately select and educate patients to whom OxyContin is prescribed.

I attest that I have read and understand the REMS Education Materials for OxyContin®.

Signature Date

(Copy)

Prescriber Name *(Please Print)* Professional Designation

Specialty

Affiliation *(if any)*

Address

City State Zip Code

Telephone # Fax #

E-mail Address

(Copy) Please answer the following questions to verify your understanding of the information contained in the REMS Education materials. **Completion of the questions does not affect your ability to prescribe OxyContin®.**

PLEASE RETURN IN THE PRE-ADDRESSED ENVELOPE PROVIDED.

(Question)

1. Which of the following is the most significant serious adverse event risk with OxyContin®?
   - ☐ Heart attack
   - ☐ Constipation
   - ☐ Dizziness
   - ☐ Respiratory depression
   - ☐ Drowsiness

2. Patients should be assessed for their risks for opioid abuse or addiction prior to being prescribed OxyContin®. Which of the following persons are at increased risk of opioid abuse? *(Please check all that apply.)*
   - ☐ Individuals who have low back pain
   - ☐ Individuals with a personal history of substance abuse
   - ☐ Individuals with a family history of substance abuse
   - ☐ Individuals with mental illness (e.g., major depression)
   - ☐ Individuals with a family history of hypercholesterolemia

3. OxyContin® is indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time
   - ☐ True
   - ☐ False

4. Proper use of OxyContin® involves the following:
   (*Please check all that apply)*
   - ☐ Unused OxyContin® should be stored indefinitely in unlocked cabinets
   - ☐ OxyContin® must be swallowed whole
   - ☐ OxyContin® must not be chewed or ingested after crushing, breaking, or dissolving
   - ☐ 60 mg and 80 mg tablets of OxyContin® are for use only in opioid-tolerant patients
   - ☐ None of the above

5. OxyContin® needs to be stored in a secure place away from children, pets, and household visitors
   - ☐ True
   - ☐ False

6. Which of the following statements are true regarding the proper dosing of OxyContin® in opioid naïve patients?
   (*Please check all that apply)*
   - ☐ Use low initial doses, especially in patients who are receiving concurrent treatment with muscle relaxants, sedatives, or other CNS medications
   - ☐ A 60 mg starting dose is appropriate in an opioid naïve patient
   - ☐ When converting patients from a non-opioid analgesic, 10 mg q12h is a reasonable starting dose
   - ☐ OxyContin® dose adjustments may be made every 1-2 days

7. As a result of reviewing the information in the training guide, do you feel that you have sufficient information to counsel patients about the proper use, storage, and disposal of OxyContin®?
   - ☐ Yes
   - ☐ No *If no, please visit www.oxycontinrems.com for more information or contact Purdue's Medical Services Department at 1-888-726-7535 with any questions or concerns.*

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BOB A RAPPAPORT
04/05/2010