



Therapeutic Class ReviewSM

Pain – oxymorphone (Opana[®]) & oxymorphone ER (Opana[®] ER)

December 2006

New Product for Review:

oxymorphone extended-release tablet (Opana[®] ER)

[Endo Pharmaceuticals]

oxymorphone tablet (Opana[®])

[Endo Pharmaceuticals]

Dossier Provided by Manufacturer: yes

Dossier Evaluation: 2

1- dossier w/missing components

2- all components present, except pharmacoeconomic model

3- all components present (comprehensive)

Executive Summary

- Oxymorphone (Opana) and oxymorphone extended release (Opana ER) are similar in action to other narcotic analgesic medications in relieving pain.
- There are safety concerns with oxymorphone and risk of patient harms that are not predictable:
 - drug levels can increase by 50% if taken with food;
 - potentially fatal increases in drug levels with alcohol consumption;
 - decreased clearance (40%) for those over 65;
 - dosage reductions required in mild renal impairment; and
 - contraindicated for patients with moderate or severe hepatic impairment.
- Like other long acting narcotic analgesics, oxymorphone ER (Opana ER) labeling includes a Black Box Warning to emphasize the potential for accidental overdose, misuse, abuse and diversion.
- Consumption of broken, chewed, dissolved or crushed tablets may lead to rapid release and absorption of a potentially fatal dose of oxymorphone.
- The bioavailability of oxymorphone increases by 57%- 65% in patients with moderate and severe renal impairment. ^[1]
- Oxymorphone ER (Opana ER) is marketed as:
 - The first oral formulation of oxymorphone.
 - A long acting opioid for treatment of multiple chronic pain conditions.
 - An extended release product offering the convenience of twice daily dosing.
 - Having minimal risk of drug interactions because it neither inhibits nor induces the cytochrome P450 system.

Evidence

- There is no useful evidence supporting the efficacy of oxymorphone (Opana) and oxymorphone extended-release (Opana ER) in the treatment of chronic pain. Large number of drop-outs was the primary reason the clinical trials were appraised as not useful. Up to 50% of participants could not complete the trials due to side effects.
- Several of the oxymorphone extended-release (Opana ER) trials did not use equal analgesic doses of the comparator.
- There is no evidence that oxymorphone (Opana) or oxymorphone extended-release (Opana ER) provides any additional clinical benefit over other immediate- or extended-release opioid analgesics in the treatment of chronic pain.
- The safety and clinical benefit of dosing oxymorphone extended-release (Opana ER) more frequently than every 12 hours is currently unknown.

Decision

- Oxymorphone (Opana) and oxymorphone extended-release (Opana ER) are non-preferred/non-formulary because:
 - These products have an unacceptable safety profile.
 - There is no useful evidence for improved efficacy over existing formulary agents at this time.
 - These products have a higher cost relative to other formulary agents, and provide no extra benefit.

Products

Drug Product	FDA Approval	FDA Approved Indication(s)	Dose/Route
fentanyl patch ^{1,2}	8/1990	Management of chronic pain in patients who require continuous opioids for pain that cannot be managed by lesser means	25-100 mcg topically per day (patches replaced q72 hr)
hydromorphone tablet ^{1,3} (generic)	12/1992	Management of moderate to severe pain	2-4 mg orally every 3 to 4 hours (chronic)
levorphanol ⁵ (generic)	1/1953	Management of pain when an opioid analgesic is appropriate	2-4 mg orally every 6 to 8 hours (chronic)
methadone tablet ^{1,6} (generic)	8/1947	1) Severe pain 2) Detoxification and treatment of narcotic addiction	2.5 to 10 mg orally every 3 to 4 hours (chronic)
morphine sulfate tablet ^{1,7} (generic)	not available	For relief of moderate to severe pain	15-30 mg orally every 3 to 4 hours (chronic)
morphine sustained release tablet ^{1,8} (generic)	5/1987	For relief of moderate to severe pain in patients who require repeated dosing of a potent opioid analgesic for a period of more than a few days	30-100 mg orally twice daily
morphine SR capsule ⁹ (Kadian [®])	7/1996	For management of moderate to severe pain when treatment with an opioid analgesic is needed for an extended period of time	20-100 mg orally once to twice a day
oxycodone tablet ¹ (generic)	not available	For relief of moderate to moderately-severe pain	5-30 mg orally every 4 to 6 hours

oxycodone sustained release tablet ¹ (generic)	not available	For relief of moderate to moderately-severe pain	5-30 mg orally every 4 to 6 hours
oxycodone controlled release tablet ^{1,10} (OxyContin [®])	12/1995	Management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time	20-80 mg orally twice daily
oxymorphone HCl (Opana [®])	6/06	Relief of moderate to severe acute pain when use of an opioid medication is appropriate	10-20mg orally every 4-6 hours as needed for pain
oxymorphone extended release (Opana [®] ER)	6/06	Relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended duration	5-40mg orally twice daily

^a Date applies to approval date for the original brand name medication where there are now generics available.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

Sustained Release Drug Name	Equianalgesic Dose
fentanyl patch ^{1,2}	75mcg/hr Q 3 days
morphine sustained release tablet ^{1,8} (generic)	120 mg BID
morphine SR capsule ⁹ (Kadian)	120 mg BID
oxycodone sustained release tablet ¹ (generic)	80 mg BID
oxycodone controlled release tablet ^{1,10} (OxyContin)	80 mg BID
oxymorphone extended-release (Opana ER)	40 mg BID

References

1. Thomson Micromedex © 1974-2006. Micromedex Healthcare Series Vol 120.
2. Duragesic[®] (fentanyl transdermal system) Product Information. Titusville, NJ: Janssen Pharmaceutica Products L.P. 2003.
3. Hydromorphone HCl Product Information. Columbus, OH: Roxane Laboratories, Inc. 1999.
4. Palladone[™] (hydromorphone extended-release capsules) Product Information. Stamford, CT: Purdue Pharma L.P. 2004.
5. Levorphanol tartrate Product Information. Columbus, OH: Roxane Laboratories, Inc. 2000.
6. Dolophine[®] (methadone HCl) Product Information. Columbus, OH: Roxane Laboratories, Inc. 2001.
7. Morphine sulfate immediate-release tablets Product Information. Columbus, OH: Roxane Laboratories, Inc. 1998.
8. Morphine sulfate extended-release tablets Product Information. Corona, CA: Watson Laboratories, Inc. 2003.
9. Kadian[®] (morphine sulfate sustained-release capsule) Product Information. Piscataway, NJ: Alpharma Branded Products Division. 2003.
10. OxyContin[®] (oxycodone extended-release tablets) Product Information. Stamford, CT: Purdue Pharma L.P. 2003.
11. Opana[®] (oxymorphone) Prescribing Information. Endo Pharmaceuticals Inc.: Chadds Ford, PA; July 2006.
12. Opana[®] ER (oxymorphone extended-release) Prescribing Information. Endo Pharmaceuticals Inc.: Chadds Ford, PA; July 2006.
13. Endo Pharmaceuticals [page on the internet] © 2006. Press release, July 24, 2006: Endo announces commercial availability of Opana[®] ER (oxymorphone HCl) extended-release and Opana[®] (oxymorphone HCl) immediate-release tablets. Available at: <http://phx.corporate-ir.net/phoenix.zhtml?c=123046&p=irol-newsArticle&ID=885302&highlight=>. Accessed on 8/10/06.
14. Endo Pharmaceuticals [page on the internet] © 2006. Press release, June 23, 2006: Endo receives FDA approval for Opana[®] ER (oxymorphone HCl) extended-release and Opana[®] (oxymorphone HCl) immediate-release tablets. Available at: <http://phx.corporate-ir.net/phoenix.zhtml?c=123046&p=irol-newsArticle&ID=875617&highlight=>. Accessed on 8/10/06.
15. Endo Pharmaceuticals [page on the internet] © 2006. Press release, May 4, 2006: Oxymorphone Studies Presented at American Pain Society Annual Meeting. Results from pivotal trials in low back pain and post-surgical pain. Available at: <http://phx.corporate-ir.net/phoenix.zhtml?c=123046&p=irol-newsArticle&ID=852093&highlight=>. Accessed on 8/10/06.
16. Hale ME, Dvergsten C, Gimbel J. Efficacy and safety of oxymorphone extended release in chronic low back pain: results of a randomized, double-blind, placebo- and active-controlled Phase III study. J Pain. 2005;6(1):21-28.

17. American Pain Society. National Clinical Guideline “Pain in osteoarthritis, rheumatoid arthritis, and juvenile chronic arthritis” Available at http://www.guideline.gov/summary/summary.aspx?doc_id=3691&mode=full&ss=15. Accessed: 11/10/06
18. OPIOID Final Report Update #4 (pdf) from the OHSU Evidence-based Practice Center
19. Kivitz A, Ma C, Ahdieh H, Galer BS. A 2-week, multicenter, randomized, double-blind, placebo-controlled, dose-ranging, phase III trial comparing the efficacy of oxymorphone extended release and placebo in adults with pain associated with osteoarthritis of the hip or knee. *Clin Ther.* 2006 Mar;28(3):352-64.
20. Gimbel JS, Walker D, Ma T, Ahdieh H. Efficacy and safety of oxymorphone immediate release for the treatment of mild to moderate pain after ambulatory orthopedic surgery: results of a randomized, double-blind, placebo-controlled trial. *Arch Phys Med Rehabil.* 2005 Dec;86(12):2284-9.
21. Matsumoto AK, Babul N, Ahdieh H. Oxymorphone extended-release tablets relieve moderate to severe pain and improve physical function in osteoarthritis: results of a randomized, double-blind, placebo- and active-controlled phase III trial. *Pain Med.* 2005 Sep-Oct;6(5):357-66.
22. Gimbel J, Ahdieh H. The efficacy and safety of oral immediate-release oxymorphone for postsurgical pain. *Anesth Analg.* 2004 Nov;99(5):1472-7; table of contents.
23. Gabrail NY, Dvergsten C, Ahdieh H. Establishing the dosage equivalency of oxymorphone extended release and oxycodone controlled release in patients with cancer pain: a randomized controlled study. *Curr Med Res Opin.* 2004 Jun;20(6):911-8.
24. Ahdieh H, Ma T, Babul N, Lee D. Efficacy of oxymorphone extended release in postsurgical pain: a randomized clinical trial in knee arthroplasty. *J Clin Pharmacol.* 2004 Jul;44(7):767-76.