



Therapeutic Class ReviewSM

Hydromorphone ER capsule (Palladone™)

May 2005

New Product for Review:

hydromorphone ER capsule (Palladone™) - Purdue Pharma L.P.

Dossier Provided by Manufacturer: No

Available Therapeutic Alternatives:

Preferred/Formulary:	Non-preferred/non-formulary:
fentanyl patch (Duragesic®) [Janssen Pharmaceutica Products L.P.]	Avinza® (morphine sulfate ER-24h capsule) [Ligand Pharmaceuticals]
hydromorphone tablet (generic) [various]	
levorphanol tablet (generic) [various]	
methadone tablet (generic) [various]	
morphine sulfate tablet (generic) [various]	
oxycodone tablet (generic) [various]	
morphine SR tablet (generic) [various]	
oxycodone SR tablet (OxyContin®) [Purdue Pharma L.P.]	
Kadian® (morphine sulfate SR capsule) [Alpharma]	

Executive Summary

- Hydromorphone extended-release [24h] capsules (Palladone) offer the convenience of once daily dosing.
- There is no evidence that hydromorphone extended-release [24h] capsules (Palladone) provide any additional clinical benefit over hydromorphone or other immediate-release oral opioid analgesics in the treatment of chronic pain.
- There is no evidence that hydromorphone extended-release [24h] capsules (Palladone) provide any additional clinical benefit over other preferred/formulary extended-release opioid analgesics in the treatment of chronic pain.
- The Food and Drug Administration (FDA) has expressed concern over the safety of Palladone.
- Palladone labeling includes a Black Box Warning to emphasize the potential for accidental overdose, misuse, abuse and diversion.

Conclusion

Hydromorphone extended-release [24h] (Palladone) is non-formulary/non-preferred because there is no additional clinical benefit for its additional cost.

Products

Drug Product	Date of FDA Approval	FDA Approved Indication(s)	Dose/Route	AWP Cost*	Potential Off-Label Uses
fentanyl patch (Duragesic®) ^{1,2}	8/1990	Management of chronic pain in patients who require continuous opioid for pain that cannot be managed by lesser means	25-100 mcg topically per day (patches replaced q72 hr)	\$160 to \$595	Meniere's disease
hydromorphone tablet ^{1,3} (generic)	12/1992	Management of moderate to severe pain	2-4 mg orally every 3 to 4 hours (chronic)	\$90-\$150	cough
hydromorphone ER capsule (Palladone™) ⁴	9/2004	Management of persistent, moderate to severe pain in patients requiring continuous around the clock analgesia with a high potency opioid for an extended period of time, generally weeks to months or longer.	12-32 mg orally once per day	\$231 to \$502	
levorphanol ⁵ (generic)	1/1953	Management of pain when an opioid analgesic is appropriate	2-4 mg orally every 6 to 8 hours (chronic)	\$129 to \$258	
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)	\$31 to \$45	restless leg syndrome
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)	\$55 to \$92	secretory diarrhea
morphine SR 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	\$102 to \$295	secretory diarrhea
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	\$159 to \$507	secretory diarrhea
oxycodone tablet ¹ (generic)	not available	For relief of moderate to moderately-severe pain	5-30 mg orally every 4 to 6 hours	\$60 to \$228	secretory diarrhea, restless leg syndrome
oxycodone ER tablet ^{1,10} (OxyContin®) [80 mg tablet is available as a generic product]	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	\$188 to \$531	secretory diarrhea

*AWP (average wholesale price) based on First Data Bank as of February 2005 for 30 days of therapy.

References

1. Thomson Micromedex © 1974-2004. 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. Data on File, Purdue Pharma L.P.
12. Vashi V, Harris S, El-Tahtawy A, et al. Clinical pharmacology and pharmacokinetics of once-daily hydromorphone hydrochloride extended-release capsules. *J Clin Pharmacol.* 2005;45:547-54.
13. U.S. Food and Drug Administration (FDA). Controlled Substances Staff (CSS) abuse liability analysis of Palladone (hydromorphone hydrochloride extended release capsules) 12mg, 16mg, 24mg, and 32mg. Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) Meeting, September 9-10, 2003. Materials available at: http://www.fda.gov/ohrms/dockets/ac/03/briefing/3978B1_05_A-FDA-Tab%204.pdf. Accessed on 2/17/05.
14. A National Clinical Guideline. Control of pain in patients with cancer. Edinburgh, Scotland: Scottish Intercollegiate Guidelines Network (SIGN) 2000. Available at: <http://www.sign.ac.uk/pdf/sign44.pdf>. Accessed on 12/23/04.
15. Quigley C. Hydromorphone for acute and chronic pain. *The Cochrane Database of Systematic Reviews* 2002, Issue 1, Art. No.:CD003447. DOI: 10.1002/14651858.CD00347. Available at: <http://www.update-software.com/publications/cochrane/>. Accessed on 12/21/04.
16. Drover DR, Angst MS, Valle M, et al. Input characteristics and bioavailability after administration of immediate and a new extended-release formulation of hydromorphone in healthy volunteers. *Anesthesiology.* 2002;97(4):827-36.
17. Petersen KL, Maloney A, Hoke F, et al. A randomized study of the effect of oral lamotrigine and hydromorphone on pain and hyperalgesia following heat/capsaicin sensitization. *J Pain.* 2003;4(7):400-6.
18. Hagen N, Thirlwell MP, Dhaliwal HS, et al. Steady-state pharmacokinetics of hydromorphone and hydromorphone-3-glucuronide in cancer patients after immediate and controlled-release hydromorphone. *J Clin Pharmacol.* 1995;35(1): 37-44.
19. Hays H, Hagen N, Thirlwell, et al. Comparative clinical efficacy and safety of immediate release and controlled release hydromorphone for chronic severe cancer pain. *Cancer.* 1994;15(6):1808-16.
20. Oregon Health Resources Commission. Long-acting OPIOID analgesics for non-cancer pain, Update #2. Health Resources Commission 2004;1:1-13. Available at <http://www.ohpr.state.or.us/>. Accessed on 12/22/04.