PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #181
ORAL OXYMORPHONE

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Background Oxymorphone is an old synthetic opioid, which has been available in the U.S. as an oral analgesic in both immediate- and extended-release formulations since 2006. This *Fast Fact* will review oral oxymorphone and its place in pain management.

Pharmacology

- Oxymorphone is a semi-synthetic mu-opioid receptor agonist; it has some delta-opioid receptor agonism but little activity at the kappa receptor.
- Oxymorphone is highly lipophilic. Parenterally it is about 10 times more potent than morphine, but – due to its very low oral bioavailability (~10%) – the equianalgesic ratio of oral morphine to oral oxymorphone is only ~3:1 (see below) (15).
- Oxymorphone IR has a half-life of ~8 hours, substantially longer than morphine (1.5 hours). Tmax (time to maximum serum concentration) however is rapid: ½ hour after oral administration (2).
- Oxymorphone ER has a half-life of ~10 hours and a Tmax of 2-3 hours (1).
- Oxymorphone is metabolized in the liver to 6-hydroxyoxymorphone (likely active) and oxymorphone-3-glucuronide (unknown if active). Both oxymorphone and its metabolites accumulate in renal failure; oxymorphone is removed during hemodialysis (12).
- Drug interactions have not been well-defined for oxymorphone; it does not effect CYP2C9 or CYP3A4 pathways (3).
- Taking oxymorphone IR or ER with food can increase serum levels by up to 50%; therefore it is recommended to be taken at least one hour before or two hours after a meal (4,5). **Note:** Co-ingestion of alcohol with oxymorphone ER can raise serum levels in a seemingly unpredictable and idiopathic manner (up to 270% in some patients) and should be avoided (4).

Clinical Studies Oral oxymorphone has been studied most extensively in patients with chronic non-cancer pain, in industry-funded research completed in the mid-2000s. No head-to-head comparisons with morphine have been undertaken. All studies suggest oxymorphone's side effects are similar in frequency and magnitude to other oral opioids.

- *Non-cancer pain*. Oxymorphone ER has shown similar efficacy to oxycodone ER and superiority to placebo in randomized, blinded comparisons in patients with chronic low-back pain and osteoarthritis pain (9-11,13-14). Oxymorphone IR has been shown to be safe and effective for acute post-surgical pain (7,8).
- *Cancer pain*. Only two controlled studies have been published (6,17). Both involved transitioning cancer patients from morphine or oxycodone ER to oxymorphone ER; analgesia and side effects remained stable on the oxymorphone ER. Uncontrolled follow-up data suggest oxymorphone was effective and tolerated long-term (16,18).

Dosing & Equianalgesic Conversions Oxymorphone is not approved for use in children; no data exist on pediatric dosing. Due to its long half-life, oxymorphone IR should be dosed every 6 hours. It comes as 5 and 10 mg tabs. Oxymorphone ER can be dosed q12 hours and comes in 5, 10, 20, and 40 mg tabs. Equianalgesic conversion data range from: 1.2-2:1 for oral oxycodone:oral oxymorphone and 1.8-3:1 for oral morphine:oral oxymorphone (i.e. 18-30 mg oral morphine = 10 mg oxymorphone) (6,9,10,15,17).

Cost Oxymorphone is more expensive than many other commonly used oral opioids. One hundred 5 mg immediate-release tablets costs approximately $225 USD; sixty 10 mg tablets extended-release tablets costs approximately $170 USD (September 2015, www.drugs.com).

Conclusion Despite some unique pharmacologic features, there are no clinical data to suggest oxymorphone is more effective or better tolerated than other oral opioids. Due to its increased cost, restrictions on taking it with food, and lack of evidence for superior efficacy, it is most appropriate for use in patients who have refractory intolerance to other more commonly used oral opioids.

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