Oxycodone

Updated (minor change) January 2025

Class

Strong opioid analgesic.

Indications

Moderate–severe cancer and post-operative pain, severe non-cancer pain, †an alternative in cases of intolerance to other strong opioids,[1,2] restless legs syndrome (Targinact®; see Box A).

Contra-indications:

Moderate-severe hepatic impairment. Otherwise none absolute if titrated carefully against a patient's pain (also see **Strong opioids**).

Pharmacology

Oxycodone is a strong opioid with similar properties to **morphine**.[3–5] Its main effects are the result of activity at the μ-opioid receptor, although this may involve different G-protein subunits and thereby different downstream effects to **morphine** (also see **Strong opioids**).[6–9] Studies in rodents suggest oxycodone may also possess activity at δ- and κ-opioid receptors.[10,11]

Like **morphine**, oxycodone shows efficacy in pure neuropathic pain states (diabetic and postherpetic neuropathy), with an NNT of 5.7 (95% CI 4.0–9.9) for moderate benefit. However, as with **morphine**, the evidence is considered very low quality.[12]

Oxycodone appears to be less immunosuppressive than **morphine**. In patients with cancer pain, although one small retrospective study found the incidence of infections to be less in those receiving oxycodone compared to **morphine**, another found no difference between **fentanyl**, **morphine** and oxycodone, with the risk of infection increasing with dose (see **Strong opioids**).

Most of the analgesic effect arises from oxycodone itself. [13] The main metabolite, noroxycodone (via CYP3A4), is active at the μ-opioid receptor but to a much lesser degree. Another metabolite, **oxymorphone** (via CYP2D6), is produced in relatively small amounts but has ≥10 times the affinity and activity of oxycodone. [13] However, studies in postoperative and cancer pain found no differences between CYP2D6 ultra-rapid, extensive or poor metabolizers in the dose requirements or analgesic efficacy of oxycodone, suggesting **oxymorphone** contributes little overall. [14,15] Nonetheless, case reports suggest that opioid-naïve CYP2D6 ultra-rapid metabolizers may be at greater risk of undesirable CNS effects when starting oxycodone, because of an enhanced production of **oxymorphone** (also see **Variability in response to drugs**). [16] (Note. **Oxymorphone** is commercially available in some countries (not UK) and is 3 times and 10 times more potent than PO and parenteral **morphine** respectively.) [17]

By mouth, oxycodone has a mean bio-availability of 75%, whereas **morphine**'s is about half this. This partly explains why PO oxycodone is more potent than PO **morphine** (i.e. *fewer* mg of oxycodone are needed than **morphine** to have a comparable analgesic effect). [18–23]

For general considerations when converting opioids ± switching routes, see **Opioid dose conversion ratios**. According to the UK manufacturer, oxycodone PO is twice as potent as **morphine** PO. This almost certainly exaggerates the actual potency of oxycodone, and, whilst reasonable in terms of caution and safety when switching *to* oxycodone, risks toxicity if switching *from* oxycodone back to **morphine**. A conversion ratio of PO **morphine** to PO oxycodone of 1.5:1 better reflects the conversion ratios found in trials, [24] i.e. the dose of oxycodone PO should be two-thirds of the **morphine** PO dose (e.g. oxycodone 10mg PO is equivalent to **morphine** 15mg PO).

Parenterally, when the bio-availability of **morphine** and oxycodone are comparable, the situation is different. Despite a short-term (2h) postoperative PCA study which suggested that **morphine** is less potent parenterally than oxycodone (i.e. *more* mg of **morphine** will be needed, as with PO administration), [25] earlier single-dose studies and two more recent longer PCA studies (1–2 days) suggest that by injection **morphine** is more potent than oxycodone, in the region of 4:3. Thus, *fewer* mg of **morphine** will be needed (**morphine** 10mg being approximately equivalent to oxycodone 13mg). [17, 18, 26] However, given the modest difference in potency together with the constraints of ampoule size, it is reasonable in clinical practice to use a conversion ratio of 1:1, i.e. when converting from **morphine** injection to oxycodone injections (or vice versa), regard SC/IV **morphine** 10mg as equivalent to SC/IV oxycodone 10mg. This ratio is also consistent with the SPC.

When switching from PO oxycodone to SC/IV oxycodone, although the UK manufacturer recommends a conversion ratio of 2:1, because mean PO bio-availability is 75%, this may be too conservative for some patients. Thus, some centres use a conversion ratio of 1.5:1, i.e. the oxycodone SC/IV 24h dose should be two-thirds of the oxycodone PO 24h dose.

For switching from PO **morphine** to SC/IV oxycodone, the above *studies* suggest a conversion ratio of about 2:1 (derived using an intermediate step of either PO oxycodone (i.e. 1.5 x 1.5 = 2.25) or SC **morphine** (i.e. 2 x 1 = 2)). [Note. Use of the *manufacturer's* recommended ratios leads to confusion because a ratio of 4:1 is obtained if deriving the conversion ratio via the intermediate step of PO oxycodone (i.e. 2 x 2 = 4) but not when via SC **morphine** (i.e. 2 x 1 = 2)].

About 20% of oxycodone is excreted unchanged in the urine. In mild–moderate hepatic impairment, oxycodone and noroxycodone concentrations increase by 50% and 20% respectively (but the **oxymorphone** concentration decreases), and the elimination halflife increases by about 2h. In renal impairment, the clearance of oxycodone, noroxycodone and conjugated **oxymorphone** are reduced. Oxycodone plasma concentration increases by 50% and the halflife lengthens by 1h. [19, 27] Nonetheless, oxycodone is used as an alternative to **morphine** in mild–moderate renal impairment and is used cautiously in some centres in severe renal impairment for initial pain management (see Dose and use, and **Renal impairment**).

The clearance of oxycodone reduces with increasing age, probably because of the age-related decline in renal and hepatic function. Consequently, compared with younger adults, plasma concentration, overall exposure and halflife increase in the elderly. [28] In the presence of systemic inflammation sufficient to increase C-RP and IL-6 levels, there is inhibition of CYP3A, resulting in higher plasma levels of oxycodone. [29]

Bio-availability 75% PO, ranging from 60–87%. [30,31]

Onset of action 20–30min PO.

Time to peak plasma concentration 1–1.5h; 3h m/r.

Plasma halflife 2–4h (4.5h m/r); 3–5h (5.5h m/r) in ESRF

Duration of action 4–6h; 12h m/r.

Cautions

Renal and mild hepatic impairment (see Dose and use, and **Renal impairment** and **Hepatic impairment**).

Drug interactions

Concurrent treatment with ≥2 CNS depressants (e.g. benzodiazepines, gabapentinoids, opioids) increases the risk of respiratory depression, particularly in susceptible groups, e.g. the elderly and those with renal or hepatic impairment. [32,33]

Inhibitors of CYP3A4 (e.g. **clarithromycin**, **erythromycin**, **fluconazole**, **itraconazole**, **voriconazole**, see **Variability in response to drugs, Table 8**) can inhibit oxycodone metabolism and may enhance its effects. [34–38] However, inhibition of CYP2D6 (e.g. with **quinidine**) appears to have no detectable clinical impact. [39]

Inducers of CYP3A4 (e.g. **rifampicin**, **St John's wort**, see **Variability in response to drugs, Table 8**) decrease plasma concentrations of oxycodone. [34,40,41] Case reports suggest that the enzyme inducer **enzalutamide** reduces the analgesic efficacy of oxycodone. [42]

Undesirable effects

See **Strong opioids, Box B**. Various studies have suggested possible differences in the undesirable effect profiles of oxycodone and **morphine**.[43] However, systematic reviews comparing efficacy and tolerability of oxycodone versus **morphine** and other opioids found no strong evidence of any overall difference in their undesirable effect profiles.[4,5]

Dose and use

Patients using opioids must be monitored for undesirable effects, particularly nausea and vomiting, and constipation. Depending on individual circumstances, an anti-emetic should be prescribed for regular or p.r.n. use (see **QCG: Nausea and vomiting**) and, routinely, a laxative prescribed (see **QCG: Opioid-induced constipation**).

When converting between routes of administration or switching opioids, it is essential to read the **General approach in Appendix 2.**

Opioids can impair driving ability, and patients should be counselled accordingly (see **Drugs and fitness to drive**).

Although oxycodone is similar to **morphine** (and **hydromorphone**) in terms of efficacy and undesirable effects,[2] because it is more expensive it should generally be reserved for patients who cannot tolerate **morphine**. In Scotland, oxycodone injections are restricted to cancer patients who cannot tolerate **diamorphine** or **morphine** injections.

A combination product of oxycodone with **naloxone** is available (e.g. Targinact®; Box A).

Remains of m/r tablets (e.g. Oxycontin®, Longtec®, Targinact®) may appear in the patient's faeces ('ghost tablets'), but these are inert residues and do not affect the efficacy of the products.

Oral

> Immediate-release oxycodone products are available as capsules, oral solutions and now tablets (see Supply). When both immediate-release and m/r tablets are used, appropriate caution must be used to avoid unnecessary confusion.

Immediate-release oxycodone is generally given q4h but, in some patients, q6h is satisfactory. Oxycodone 12-hourly m/r tablets are biphasic in their release of oxycodone; i.e. there is an initial fast release which leads to the early onset of analgesia, and a slow release which provides a prolonged duration of action. Modified-release tablets should be swallowed whole; crushing or chewing them will lead to a rapid release of an overdose of oxycodone.

For strong opioid-naïve patients:

- start with oxycodone 5mg q4–6h for immediate-release products (see Supply)
- start with oxycodone 10mg b.d. for 12-hourly m/r tablets
- halve the above doses in elderly/frail patients or those with mild–moderate renal impairment or mild hepatic impairment (also see below)
- if necessary, titrate the dose upwards, guided by p.r.n. use; conventionally, p.r.n. PO doses are 1/10–1/6 of the total 24h PO dose.

For patients switching from PO **morphine** to PO oxycodone (see Pharmacology for an explanation of the ratio used):

- PO **morphine** to PO oxycodone (using a conversion ratio of 1.5:1): decrease the dose by one third, e.g. **morphine** 15mg PO → oxycodone 10mg PO.

Always consider if a reduction of the predicted dose is necessary (see **General approach, Appendix 2)**.

Box A Oxycodone combined with naloxone (Targinact®)

Targinact ® is marketed as a range of tablets containing m/r formulations of oxycodone and naloxone in a fixed dose ratio of 2:1, i.e. oxycodone/naloxone 5mg/2.5mg, 10mg/5mg, 20mg/10mg and 40mg/20mg. The addition of naloxone is to antagonize the constipating effect of oxycodone. The desire to develop a formulation that deters misuse (e.g. by crushing and injecting IV) is also relevant.

Targinact ® is authorized for severe pain. Evidence to support claims of improved pain control, better GI tolerability, and improved quality of life are based mostly on uncontrolled observational studies. [44,45]

RCTs have mostly involved relatively young non-cancer (mid–late 50s) and cancer patients (early 60s) with either moderate or severe pain, and with no significant hepatic or renal impairment. Reported use in older non-cancer (early 80s) and cancer patients (mean age 70) is mostly limited to open-label studies. [46–49]

In most of the non-cancer studies, those unwilling or unable to tolerate a 'restricted laxative regimen' were excluded, i.e. the most severely constipated. Although Targinact ® improved bowel function and reduced the number of patients requiring laxatives, the absolute differences were small (e.g., on average, one extra bowel action/week and a reduction of 0.6mg/24h in bisacodyl dose). However, laxatives were taken only p.r.n. [50–53]

In RCTs including cancer patients, Targinact ® improved bowel function and there was a trend towards a reduction in laxative use. However, absolute differences were of similar magnitudes as above, and laxatives were taken only p.r.n. [52,54]

Targinact ® is significantly more expensive than the equivalent dose of m/r oxycodone alone or an equivalent dose of morphine + regular laxatives. Because the benefit of Targinact ® in patients taking laxatives *regularly* is uncertain, the Scottish Medicines Consortium, the *Drug and Therapeutics Bulletin* and *PCF* do *not* recommend its use. [55]

Although Targinact ® is also authorized as a second-line treatment for restless legs syndrome refractory to dopaminergic therapy, the available evidence is limited. [56,57]

If clinicians choose to prescribe Targinact ®, its use should be restricted to occasions when the upward titration of regularly administered laxatives is ineffective (see **Laxatives**). [58] Because constipation is generally multifactorial in origin, Targinact ® is likely to augment rather than replace laxatives. [50,51]

The m/r formulation of naloxone avoids a 'bolus dose', and >97% is removed by first-pass metabolism in the liver. Thus, the main effect of naloxone is on the GI tract, with insufficient amounts reaching the systemic circulation to adversely affect analgesia. [59,60] However, plasma concentrations of naloxone can increase significantly in:

- *hepatic impairment:* use of Targinact ® requires caution in mild impairment and is contra-indicated in moderate–severe impairment
- *portosystemic shunt:* collateral circulation bypasses the liver, caused by, e.g. chronic liver disease, portal vein thrombosis [61,62]
- *renal impairment:* use Targinact ® with caution.

The increase in naloxone can antagonize the analgesic effect of oxycodone, resulting in either frank opioid withdrawal or the need to increase to an artificially higher dose. [63] Thus, in a patient with progressive hepatic impairment, a switch from Targinact ® to the same dose of oxycodone m/r, resulted in opioid-induced respiratory depression within 12h. [63]

Dose recommendations:

- in opioid-naïve patients, generally start with oxycodone/naloxone 10mg/5mg b.d.

- in elderly/frail patients, start with 5mg/2.5mg b.d.
- in those already taking strong opioids, switch to the equivalent dose of oxycodone
- maximum dose 80mg/40mg b.d.

When higher analgesic doses are required, the manufacturer recommends supplemental oxycodone m/r tablets, taken at the same time as the m/r combination tablets. However, this reduces the impact of the naloxone, and oxycodone:naloxone ratios >4:1 have no significant effect on bowel function. [51,64] A recent study used doses ≤90mg/45mg b.d. [65]

Common undesirable effects include nausea, vomiting, abdominal pain and diarrhoea. The manufacturer warns that patients on long-term opioids may develop opioid-withdrawal symptoms when switched to Targinact®.

Note. Cheaper branded generic products are available, e.g. Myloxifin®, see Supply.

Subcutaneous administration

Oxycodone injection may be given SC as a bolus or by CSCI (and also IV by bolus and by CIVI). For CSCI, dilute with WFI, sodium chloride 0.9% or glucose 5%.

For strong opioid-naïve patients:

- start with oxycodone 7.5mg/24h CSCI
- if necessary, titrate the dose upwards, guided by p.r.n. use; conventionally, p.r.n. SC doses are 1/10–1/6 of the total 24h CSCI dose.

For those already receiving a strong opioid (see Pharmacology for an explanation of the ratios used):

- PO oxycodone to CSCI oxycodone (using a conversion ratio of 1.5:1): decrease the dose by one third, e.g. oxycodone 30mg/24h PO → oxycodone 20mg/24h CSCI
- PO **morphine** to CSCI oxycodone (using a conversion ratio of 2:1): halve the dose, e.g. **morphine** 60mg/24h PO → oxycodone 30mg/24h CSCI
- CSCI **morphine** to CSCI oxycodone (using a conversion ratio of 1:1): give the same dose, e.g. **morphine** 30mg/24h CSCI → oxycodone 30mg/24h CSCI.

Always consider if a reduction of the predicted dose is necessary (see **General approach, Appendix 2**).

Two strengths of injection are available, 10mg/mL and high-strength 50mg/mL. The latter may be useful in situations where high doses cause volume difficulties for CSCI. However, there is an increased risk of serious mistakes being made when more than one strength is readily available.[66,67] There are also differences in compatibility with other drugs (see below) and, on a mg for mg basis, the high-strength injection costs about twice as much.

CSCI with oxycodone 10mg/mL

There are 2-drug compatibility data for mixtures in WFI with **clonazepam**, **dexamethasone**, **glycopyrronium**, **haloperidol**, **hyoscine *butylbromide***, **hyoscine *hydrobromide***, **levomepromazine**, **metoclopramide**, **midazolam** and **octreotide**.

Concentration-dependent incompatibility may occur when oxycodone (hydrochloride) is mixed with **cyclizine** (lactate); for more details see **Compatibility Chart 1**.

CSCI with oxycodone 50mg/mL

Differences in compatibility with other drugs for the 10mg/mL and 50mg/mL formulations of oxycodone have been reported.[68,69] This may be due to the different ratios of excipients in each formulation (see **Compatibility Table 1**). It is important *not* to extrapolate compatibility information from one formulation to the other.

More details

For 2-drug and 3-drug compatibility data for oxycodone 10mg/mL in WFI, and for currently available data for oxycodone 50mg/mL, see **Compatibility Chart 1**, **Chart 6** and **Table 1**.

Information on compatibility in sodium chloride 0.9% is also available, see **Compatibility Chart 8**, **Chart 13** and **Table 1**.

Renal or hepatic impairment

Because of the risk of impaired metabolism or elimination:

- lower than usual starting doses are advised in mild–moderate renal impairment or mild hepatic impairment, i.e. start with a maximum of 10mg/24h PO as for frail/elderly patients
- in severe renal impairment or ESRF, start with 1-2mg PO q6-8h and p.r.n.; once pain is controlled, consider switching to an equivalent dose of TD fentanyl (see **Renal impairment**)
- oxycodone is contra-indicated in moderate-severe hepatic impairment. If unavoidable, lower the usual starting dose *and* increase the dosing interval of immediate-release products to q8h (see **Hepatic impairment**).

For a general approach when renal or hepatic function deteriorates rapidly, see **Strong opioids**.

Supply

All preparations are Schedule 2 **CD**.

Immediate-release oral products

Oxycodone oral solution is available in two strengths, 1mg/mL and a high potency concentrate of 10mg/mL; incidents have occurred from confusion between the two formulations. [70,71] Prescribing should be in *mg* not mL to minimize the risk of 10 times the intended dose being given.

Oxycodone (generic)

Capsules 5mg, 10mg, 20mg, 5mg dose = £0.12.

Oral solution 5mg/5mL, 5mg dose = £0.19.

Concentrated oral solution 10mg/mL, 5mg dose = £0.19.

Injection 10mg/mL, 1mL and 2mL amp = £1.36 and £2.75 respectively.

High-strength injection 50mg/mL, 1mL amp = £12.

Oxyact ® (G.L. Pharma)

Tablets 5mg, 10mg, 20mg, 5mg dose = £0.09.

Modified-release 12-hourly oral products

> As for all m/r opioids, **brand prescribing** is recommended to reduce the risk of confusion and error in dispensing and administration. [71]

Oxycodone (generic)

Tablets m/r 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg, 28 days @ 5mg or 120mg b.d. = £5.50 and £115 respectively. *Note. The 15mg, 30mg, 60mg and 120mg tablets are not available for all brands; only Longtec ® and OxyContin ® have the full range of strengths available.*
Brands include Ixyldone ®, Longtec ®, Oxeltra ®, OxyContin ®, Oxylan ®, Oxypro ®, Reltebon ®.

Oxycodone/naloxone combined

Targinact ® (Napp)

Tablets m/r containing oxycodone/naloxone in a fixed ratio of 2:1, 5mg/2.5mg, 10mg/5mg, 20mg/10mg, 40mg/20mg, 28 days @10mg/5mg b.d. = £42.

Myloxifin ® (Zentiva)

Tablets m/r containing oxycodone/naloxone in a fixed ratio of 2:1, 5mg/2.5mg, 10mg/5mg, 20mg/10mg, 40mg/20mg, 28 days @10mg/5mg b.d. = £30.

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