TABLE 1

Overview of opioids and their use in palliative care

Opioid	Commonly-used formulations	Hepatic Metabolism		Half-life (T1/2)			Approximate dose equivalence
		Major metabolic pathway	Active metabolite(s)	T1/2 under normal conditions	Severe renal impairment	Severe hepatic impairment	
Morphine	● I/R tablets ● I/R oral solution ● M/R 12 hourly preparations ● Solution for injection	Morphine is conjugated with glucuronic acid to produce morphine-3-glucuronide and morphine-6-glucuronide **(phase 2 reaction)**	Morphine-6-glucuronide	1.5-4.5 hours	**AVOID** ● Morphine-6-glucuronide (active metabolite) can accumulate with its T1/2 increasing to upwards of 50 hours ● Avoid, but if no alternatives, seek specialist advice	**USE CAUTIOUSLY** ● T1/2 increased by up to 100% ● Note that reduced first-pass metabolism leads to a higher oral bioavailability. ● Use cautiously, titrate slowly, I/R products can be given regularly e.g. every 6-8 hours.	**Oral morphine to subcutaneous morphine:** — Divide dose by 2 (e.g. 10mg of oral morphine equals 5mg of subcutaneous morphine)
Oxycodone	● I/R capsules ● I/R oral solution ● M/R 12 hourly preparations ● Solution for injection	Oxycodone undergoes N-dealkylation via CYP3A4 to produce noroxycodone and O-demethylation via CYP2D6 to oxymorphone **(phase 1 reaction)**	Noroxycodone is weakly active and oxymorphone is active, but is produced in minor quantities.	2-4 hours	**USE CAUTIOUSLY** ● Oxycodone and its metabolites can accumulate in renal impairment. ● T1/2 extends to 3-5 hours. ● Use cautiously, I/R products can be given regularly at a reduced dose. Start with 1-2mg three to four times daily plus when required	**AVOID** ● T1/2 increased by up to 400% ● Avoid, but if no alternatives, seek specialist advice	**Oral morphine to oral oxycodone:** — Oxycodone regarded as being 1.5 - 2 x more potent than morphine (local practice may vary, so check local guidelines, as they may recommend a 2:1 rather than a 1.5:1 morphine:oxycodone conversion ratio) — Divide dose by 1.5 (e.g. 15mg of oral morphine equals 10mg of oral oxycodone) **Oral oxycodone to subcutaneous oxycodone:** — Divide dose by 2 (e.g. 10mg of oral oxycodone equals 5mg of subcutaneous oxycodone)
Alfentanil	● Solution for injection ● No other formulations available	Alfentanil undergoes oxidative N- and O-dealkylation via CYP3A4 **(phase 1 reaction)**	No	1.5 hours	**SAFE TO USE** ● T1/2 unchanged in severe renal impairment ● Generally regarded as safe to use. Usual starting dose is 0.5-1mg over 24 hours via syringe pump with 100 micrograms when required	**USE CAUTIOUSLY** ● T1/2 increased, repeat administration may lead to unwanted accumulation ● Low doses may be sufficient	**Oral morphine to subcutaneous alfentanil:** — Divide dose by 30 (e.g. 30mg of oral morphine equals 1mg of subcutaneous alfentanil)
Fentanyl	● T/D patches	Fentanyl undergoes N-dealkylation and hydroxylation via CYP3A4 **(phase 1 reaction)**	No	13-22 hours when used trans-dermally	**SAFE TO USE** ● T1/2 increase possible ● Generally regarded as safe to use, but lower doses may be sufficient	**SAFE TO USE** ● T1/2 unchanged ● Generally regarded as safe to use	**Oral morphine to transdermal fentanyl:** — Fentanyl is 100 times more potent (e.g. 60mg of daily oral morphine divided by 100 equals 0.6mg of fentanyl daily) — Convert this to micrograms (e.g. 0.6mg x 1000 = 600 micrograms of fentanyl/24h) — Finally, convert this to an hourly rate, (e.g. 600 micrograms / 24 hours = 25 micrograms per hour of transdermal fentanyl)
Buprenorphine	● T/D patches	Buprenorphine undergoes N-dealkylation via CYP3A4/3A5 and also undergoes conjugation. **(phase 1 and 2 reactions)**	Norbuprenorphine is pharmacologically active at opioid receptors, but has limited penetration across the blood brain barrier, hence central action is limited	13 – 36 hours when used trans-dermally	**SAFE TO USE** ● T1/2 increase possible ● Generally regarded as safe to use, but lower doses may be sufficient	**USE CAUTIOUSLY** ● Possible increase in T1/2 ● 66% of drug excreted unchanged in faeces via biliary tract (accumulation may occur in cholestatic disease) ● Due to limited experience consider alternative opioid first. If no alternatives seek specialist advice.	**Oral morphine to transdermal buprenorphine:** — Buprenorphine is 100 times more potent (e.g. 50mg of oral morphine divided by 100 is equivalent to 0.5mg of buprenorphine daily) — Convert to micrograms (e.g. 0.5mg x 1000 = 500 micrograms of buprenorphine / 24h) — Finally, convert to this to an hourly rate (e.g. 500 micrograms / 24 hours = approx. 20 micrograms per hour of transdermal buprenorphine)

I/R: immediate release; M/R: modified release; T/D: transdermal"