PRESCRIBING OPIOIDS

- Apart from resources stated below, further information can be found in the *index* of Palliative Care Guidelines Plus website: **http://book.pallcare.info/**

General

- Morphine and other strong opioids are **Schedule 2 Control Drugs**
  - Misuse of Drugs Regulations 2001 and its amendments define the classes of person authorised to supply and possess controlled drugs in their professional capacities and defines legal regulations where drugs are divided into five schedules each specifying the requirements governing such activities as import, export, production, supply, possession, prescribing, and record keeping which apply to them
    - For more details see BNF online homepage **www.bnf.org/bnf/index.htm** (*but you need to be able to sign in to bnf on-line complete.com*) searching for "*control drugs" >* look for *"Controlled Drugs and drug dependence: British National Formulary Guidance on prescribing"*
- Morphine is the 'Gold Standard' strong opioid to be considered first line for:
  - relieving severe (*even moderately severe*) pain
  - cough
  - breathlessness
  - painful skin lesions (*topical*)
  - mucositis (*topical*)
- When patients are opioid naive (*ie they are currently not taking weak nor strong opioid*) a starting dose of morphine IR 2.5mg PO 4H regularly with morphine IR 2.5mg PO PRN 1H is used
- Diamorphine is sometimes preferred to morphine in a syringe driver because it is much more soluble
- Using another strong opioid (*eg. oxycodone, buprenorphine, fentanyl, alfentanil*) usually requires you to have a PARTICULAR REASON eg:
  - intolerable morphine side effects
  - renal impairment
  - compliance issues needing non-oral route (*eg. topical patch*)
  - unable to take oral medication (*topical patches and sub.cut syringe driver infusions*)
- Contra-indications and cautions: with correct titration, contraindications are not absolute in palliative care; one opioid may be selected over another (*eg renal impairment*) but there are some contra indications and cautions from manufacturers (*see Table 1*) – as you will see they are not always absolute in palliative patients

TABLE 1: MANUFACTURERS CONTRA-INDICATIONS TO MORPHINE

- delayed gastric emptying
- paralytic ileus
- acute abdomen
- acute diarrhoea associated with antibiotic induce pseudomembranous colitis
- acute hepatic disease
- respiratory depression
- obstructive airways disease (*morphine can release histamine*)
- head injury
- phaechromocytoma (*due to risk of pressor response to histamine release*)
- concurrent MAOI use – or use within 2 weeks of stopping them (*initial very low doses, small titrations & regular review can make this safe*)

Precautions

- agitation
- restlessness
- hallucinations
- pin point pupils (*myosis*)
- paraesthesia
- respiratory depression
- exacerbation of pain (*opioid induced hyperalgesia*)

- Side effects of Morphine are shown in Table 2, other opioids have similar side effects although some may be more common than others and some opioids have other risks (*see individual drug monographs*)

TABLE 2: MORPHINE ADVERSE EFFECTS

- nausea
- vomiting
- anorexia
- constipation
- dry mouth
- myoclonus
- dyspepsia
- biliary pain
- euphoria
- drowsiness
- confusion
- sweating
- itching
- headache
- vertigo
- insomnia
- visual disturbance
- urinary retention
- sexual dysfunction
  - *reduced libido*
  - *amenorrhoea*
  - *erectile dysfunction*
- general weakness
- pancreatitis worsened

Especially in high dose:

- agitation
- restlessness
- hallucinations
- pin point pupils (*myosis*)
- paraesthesia
- respiratory depression
- exacerbation of pain (eg. *opioid induced hyperalgesia*)

- Opioid potency (*see Opioid Conversion Tables below*): **EITHER**
  - **expressed as a ratio:** eg. morphine PO:morphine SC = 2:1; morphine PO: diamorphine SC = 3:1 **OR**
  - **expressed as an equianalgesic (equipotent) dose:** eg. morphine PO 2mg= morphine SC 1mg; morphine 3mg= diamorphine SC 1mg

  for some opioids (*eg. tramadol, oxycodone*) you may see *more than one* potency – SO, EITHER, CONSULT YOUR LOCALLY AGREED OPIOID CONVERSION TABLE OR ASK FOR A SENIOR OPINION
- Changing to another strong opioid is called *OPIOID ROTATION* (*see Opioid Conversion Tables below*)

Find out more in:
- Oxford Handbook of Palliative Care 2nd edition: M Watson et al - Oxford publications
- Palliative Care Formulary 5th edition(PCF4): R Twycross et al - **palliative**drugs.com publications
- Drugs in Palliative Care 2nd edition: A Dickman – Oxford publications

COMMON CONVERSIONS INCLUDE:

- **change of route** for **SAME** opioid: ORAL TO SUBCUTANEOUS = potency ratio 2:1
  eg. morphine 30mg PO = morphine 15mg SC
  eg. oxycodone MR 15mg 12H PO = oxycodone 15mg CSCI
  NB: *you may see a potency ratio of 1.5:1 for oxycodone PO:SC BUT manufacturer says use 2:1* ***which is what is locally used***
- **weak opioids PO to morphine PO**: potency ratio 10:1
  eg. codeine 240mg PO = morphine 24mg PO
  eg dihydrocodeine 120mg = morphine 12mg PO
  eg. tramadol 400mg PO = morphine 40mg PO
  NB: *you may see higher potency ratios for tramadol but for safety*
  ALL weak opioids are CURRENTLY treated the same
- morphine **PO to diamorphine SC** = potency ratio 3:1
  eg. morphine 30mg PO = diamorphine 10mg SC
  eg. morphine MR 30mg 12H PO = diamorphine 20mg CSCI
- **morphine PO to oxycodone PO** = potency ratio 3:2
  eg. morphine 30mg PO = oxycodone 20mg PO
  eg. morphine MR 30mg 12H PO = oxycodone MR 20mg 12H
  NB: *currently in this area the 2:3 ratio is being used. HOWEVER*
  the previous conversion was change *to 2:1 which may still be used in some areas*

- Patients and their carers should be warned about what to look out for with side effects and ideally given this in writing*; ***morphine modifies people's reactions/reaction times so patients on opioids should be warned NOT to operate machinery INCLUDING DRIVING IF AFFECTED*** [#] [@]

  ✱ The British Pain Society publish information for patients on opioids and pain management. Current link is*:*
  http://www.britishpainsociety.org/pub_patient.htm

  # The Driver and vehicle Licensing Authority (DVLA) publish current medical guidelines for driving on their website. Current link is*:*
  https://www.gov.uk/government/organisations/driver-and-vehicle-licensing-agency/series/current-medical-guidelines-dvla-guidance-for-professionals

  @ From March 2015, a new Drug Driving law came into being – with opioids being one of the drugs affected - *see separate guidance for healthcare professionals and patients on Trinity website resources C3b-iii, iv, v and* **www.gov.uk/drug-driving-law**

- If morphine is not tolerated due to side effects, other opioids may be better tolerated:
  - oxycodone
  - buprenorphine
  - fentanyl
  - alfenanil
- In renal impairment the metabolites of Morphine and Diamorphine accumulate so the following are often considered:
  - oxycodone (*but 10% renally eliminated and so can accumulate – especially with severe renal impairment*)
  - buprenorphine, fentanyl and alfentanil are not renally eliminated and so are *safer* to use in renal impairment
- When prescribing opioids, the ORAL route is preferred unless there are problems, when other routes such as topical patches & subcutaneous infusions via syringe driver can be used; sometimes the route dictates which opioid is used (*eg. Fentanyl & Buprenorphine patches, Alfentanil via syringe driver*); buccal transmucosal & nasal routes are available (*eg fentanyl*) currently for breakthrough medication when more conventional preparations are not working and Buprenorphine has a sub.lingual tablet for breakthrough pain

Opioid Conversion (Substitution) Tables

- There may be times when you need to convert one opioid route to another (*eg oral to sub.cut*) OR rotate one opioid to another (*eg. morphine to oxycodone because of side effects OR morphine to another opioid that is safer in renal impairment such as oxycodone or alfentanyl*)
- Opioid conversion tables exist to makes this easier but there are some points to consider

1. Most opioid conversion tables give *equipotent doses of drugs*
   - *Eg. Morphine 60mg PO/24hrs = Oxycodone 30mg PO/24hrs*

     BUT some tables just give *the potency ratios* leaving YOU to do the calculation
   - *Eg. Potency ratio of Morphine PO: Oxycodone PO = 1:2* (*may change to 1:1.5* *)
     ie Morphine PO 2mg = Oxycodone PO 1mg (*WITH CHANGE morphine 3mg PO = oxycodone 2mg PO*)

     TIP the *equipotent dose* of two opioids for <u>any given route</u> (*ie oral/subcut etc*)
     is the *REVERSE of the potency ratio expressed in mgs – see example above*

     ✱ for exams this can be confusing BUT IT REFLECTS REAL MEDICINE, SO…
     unless the conversion is given to you in the question OR you are expected to go from the BNF OR it is not clear from BNF (which is unlikely to happen very often)

     I SUGGEST….
     > state this is an area of *'controversy'* – even quote different potency ratios if you can remember them!
     > state what conversion you saw used on your attachment (*don't make I up! – learn what we give you*)
     > base your calculations on the conversion above

Opioid Conversion Tables cont.

2. When converting from oral to parenteral (*ie subcut*) route for THE SAME OPIOID *eg. Morphine,* conversion tables will show that the equipotent parenteral dose is half the oral dose; BUT if there are SUSPECTED problems with absorption of the oral dose, the parenteral route may be MORE EFFECTIVE and so the dose from the table may need to be REDUCED *eg. by 1/4 or 1/3 or 1/2*
3. When ROTATING from one opioid to another (*eg morphine to oxycodone*) the equipotent dose in the conversion table ASSUMES many things, including that the *pharmacodynamic* (*including bioavailability*) of the two drugs (*which is affected by many things like liver and renal function and con-current drug use* etc) and *pharmacokinetic* aspects for both drugs are similar. One *pharmacokinetic* factor is a person's *tolerance* to both drugs (*also known as the cross tolerance*). The tables assumes it is the same, but a person's tolerance for an opioid they have been taking for a while will probably be less than their tolerance for the new opioid to be used. FOR THIS REASON, OPIOID CONVERSION TABLES **ARE ONLY A GUIDE** and once you have looked up your equipotent dose for the new opioid ***you should consider reducing it by up to 50%*** (*eg. by 1/4 or 1/3 or ½*) *especially for frail +/or elderly +/or renally impaired patients*

Opioid Patches

- Buprenorphine patches: indications are moderately severe non-malignant pain unresponsive to non-opioid medication (*BuTrans*) and moderate to severe cancer pain, similarly unresponsive to non-opioid medication (*Transtec*); Fentanyl is similar as well as severe chronic pain provided the pain is opioid responsive
- Patches are used when patients have intolerable side effects to morphine (or oxycodone), are unable to swallow oral medicines, have poor compliance with oral medicines and with renal failure.
- They are not suitable for patients who need a rapid titration of analgesia in severe uncontrolled pain
- Opioid patches act as opioid reservoirs, slowly transferring opioid into the subcutaneous fat. Thus when a patch is removed opioid remains in the body (*for at least 12 hours for fentanyl and 24hours for buprenorphine*)
- Like modified release oral opioids patches are usually prescribed by *brand.* It is not possible to ensure safe interchangeablitly between different brands of fentanyl patch and BuTrans and Transtec have different times for changing.
- They have similar cautions as morphine; plus exposure to heat sources (*eg hot water bottles, baths, saunas,* etc) should be avoided because opioid absorption is increased.
- The need for laxatives is similar, however, buprenorphine and fentanyl may not cause constipation to the same extent as morphine and so laxative dosage may need to be reduced with opioid patches
- Patches should be applied to clean, dry, non-irritated skin (*ideally non-hairy, but if not possible, hair should be clipped as short as possible not shaved*) in the upper body or arm and patch sites rotated regularly to reduce chance of skin reactions. The same site should be avoided for at least 6 days (*Transtec*), at least 3 weeks (*BuTrans*) and no specific time is mentioned for fentanyl except 'do not use same site twice'
- If a patient shows opioid toxicity, the patch(es) should be removed as soon as possible and the patient monitored. (*for at least 24hours for buprenorphine and at least 12 hours for fentanyl for reasons stated above*)
- Buprenoprhine patches can be used in opioid naive patients:
    - **BuTrans:** For moderate pain unresponsive to non-opioids
        - the starting dose is 5microgm/hr = morphine PO 10mg/24hr (*if aleady on an opioid, the patch strength depends upon their current opioid dosage ie need to look it up in conversion table*)
        - analgesic effect cannot be assessed for at least 72hrs whilst plasma levels of buprenorphine slowly stabilise
        - patients need to have another immediate release opioid for PRN use whilst adjusting the patch dose
        - doses are adjusted every 3 days by either applying a patch of the next strength OR using two patches of the same strength applied at the same time (*no more than two patches should be used at a time*)
        - once correct dose achieved, BuTrans patches are changed every 7 days
    - **Transtec:** For moderate to severe pain unresponsive to non-opioids
        - Manufacturer states the starting dose for the opioid naive is 35microgm/hr **BUT this equates to morphine PO 60mg/24hr AND SO MAY NOT BE SAFE** (*if already on an opioid, the patch strength depends upon their current opioid dosage ie need to look it up in conversion table*)
        - analgesic effect cannot be assessed for at least 24hrs whilst plasma levels of buprenorphine slowly stabilise
        - patients need to have another immediate release opioid for PRN use whilst adjusting the patch dose
        - doses are adjusted every 4 days by either applying a patch of the next strength OR using two patches of the same strength applied at the same time (*no more than two patches should be used at a time*)
        - once correct dose achieved, Transtec patches are changed every 96 hours

Opioid Patches continued

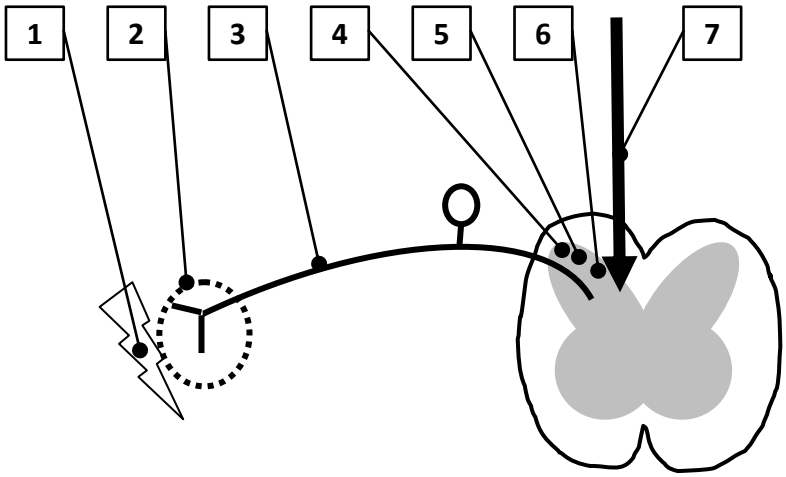
Fentanyl should **not be used in opioid naive patients** and should have been taking morphine 60mgPO /24hr or equivalent (*this equates to 25microgm/hr patch – this is the licensned starting patch. The 12 microgm/hr patch is licensed for dose titration, however, is is being used off license as a starting patch in whgich case the patient needs to have be taking morphine 30mg PO/24hr or equivalent*)

- the starting dose is 25microgm/hr (*or 12microgm/hr*) - *see above* OR if patient on higher doses of morphine than stated above, a higher strength patch can be selected from the opioid conversion table
- analgesic effect cannot be assessed for at least 24hrs whilst plasma levels of fentanyl slowly stabilise over 36-48hours
- patients need to have another immediate release opioid for PRN use whilst adjusting the patch dose
- doses are adjusted every 72 hours by adding either a 12microgm.hr or a 25microgm/hr patch (*no more than two patches should be used at a time*)
- once correct dose achieved, fentanyl patches are changed every 72 hours – however, some specialist palliative care doctors may recommend every 48hrs if pain is returning before 72hours – this is a senior doctor decision

- Patch initiation in relation to other opioid use:
  - If on 4hrly IR morphine/oxycodone: continue this for first 12hrs after applying patch then stop
  - if on 12hr MR morphine/oxycodone: give the last oral dose at same time as applying patch
  - If on 24hr MR morphine: apply patch 12hrs after last oral dose
  - If on CSCI: continue driver for 12 hrs after patch applied then stop
- When using a syringe driver eg. At end of life, provded there are not problems with patch adherence, the patch is usually left on. Any extra opioid (*eg your increase up to 50%*) goes into the syringe driver.

  HOW TO CALCULATE EXTRAS
  - The doing on a patch is only a guide to the maximum dose that a person is receiving (*they may be receiving less*). So when you are converting the patch to a different opioid for *safety* it can be a good idea to *dose reduce the converted dose.* A very cautious reduction would be 50%, more often 1/4 or 1/3 may be used
    - eg. fentanyl 25microgm/hr = 30mg oxycodone PO/24hrs = 15mg oxycodone CSCI/24hrs
      Thus dose reducing by 1/3 gives: 20mg oxycodone PO/24hrs = 10mg oxycodone CSCI/24hr
  - Once you have converted the patch to the opioid you have selected for the syringe driver **write this down in the special instruction box for the patch prescription to show what you calculations are based on**
    - For the example above, this would be *"fentanyl 25microgm/hr taken as oxycodone 10mg CSCI"*
  - For your calculations, you then proceed as you would with any other regular (background) opioid (*effectively treating the patch as if it was a second CSCI with that amount of opioid*). So your increases should not be more than 50% and the increase goes into a syringe driver as a CSCI
    - For the example above, if we use the maximum dose increase we are allowed to use then oxycodone 10mg x 50% = 5mg would be the dose in the syringe driver
  - Finally you have to calculate the new breakthrough using the same calculation used for any other regular opioid, but you need to make sure you include all the opioid the person is receiving
    - For the example above:
      breakthrough dose of SC oxycodone = (total regular oxycodone in 24hrs)/6
      = (patch equivalent as SC oxycodone + oxycodone in the syringe driver)/6
      = (10 + 5)/6 = **oxycodone 2.5mg SC 1H PRN**
- When patches are stopped to start another form of background opioid (*eg PO IR or MR opioid OR CSCI*), because the opioid remains in body after patch removed, **delay the start of this new opioid for 12 hours after patch removed (*for fentanyl*) or 24hours after patch removed (*for buprenorphine*)** and use PRN opioid to manage pain

Sites of action of peripheral & spinal non-opioids



1. **Reducing the painful stimulus**
   - Malignant bone pain: *bisphosphonates*
   - Skeletal muscle spasm: *baclofen, benzodiazepines*
   - Smooth muscle spasm: antimuscarinics, nitrates, nifedipine
2. **Reducing peripheral sensitization**
   - NSAIDs/COX-2s
   - Corticosteroids
3. **Sodium Channel blockade**
   - Carbamazepine
   - Lidocaine
4. **Calcium Channel Blockade**
   - Gabapentin
   - Pregabalin
5. **Reduced central prostaglandin transmission**
   - Paracetamol
   - NSAIDs/COX-2s
   - Corticosteroids
6. **Reduced central sensitization (glutamate-NMDA)**
   - Ketamine
   - Methadone
7. **Enhancing Inhibition of descending tracts**
   - Antidepressants
   - Tramadol

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Using NSAIDs/COX-2 – two groups of anti-inflammatory agents

- They act by inhibiting CycloOXygenase isoenyzmes 1 +/or 2 (COX-1 +/or COX-2)
  - NSAIDs: non-selective Non-Steroidal Anti-Inflammatory Drugs – inhibit both COX-1 & COX-2 eg. IBUPROFEN, NAPROXEN, DICLOFENAC
  - COX-2 – Selective COX-2 inhibitors eg. CELECOXIB, ETORICOXIB

NOTE ALSO:NABUMATONE
A *'new'* class of NSAID with *'potentially'* fewer GI & platelet side effects
A pro-drug liver metabolised into active metabolite 6-methoxy-2-naphthyl-acetic acid (6MNA) 6MNA, structurally similar to *Naproxen, BUT* preferentially inhibits COX-2

- NSAIDs/COX-2s are associated with following side effects:
  - Renal impairment (RI)
  - Cardiovascular disease (CVD) – *ischaemic heart disease(IHD), cerebrovascular disease (CVD) & peripheral vascular disease (PVD)*
  - Gastro-Intestinal (GI) toxicity –*upper GI pain, mucosal inflammation/ulceration, GI bleeds*

  Gastro-Intestinal protection (GIP) can be provided b co-administering either a Proton Pump Inhibitor (PPI) eg Omeprazole, Lansoprazole (cardio-protective effect of Clopidogrel is reduced if co-administered with certain PPIs) OR Misoprostol

  NB: BP & renal function needed before & 7 days after starting OR increasing a dose with patients at risk

  NB: all NSAIDs/COX-2s should be used with caution in the elderly

- An approach to using NSAIDs/COX-2s

Step	No GI or CVD risk	CVD risk +/- GI risk	GI risk no CVD risk
1	Alternative analgesia	Alternative analgesia	Alternative analgesia
2	Non-selective NSAID +GIP (*eg. ibuprofen, nambutone, diclofenac*)	Naproxen + GIP	COX-2 + GIP
3	COX-2 + GIP	(Celecoxib)*	Nambutone + GIP
4	-	-	Non-selective NSAID +GIP (*eg. ibuprofen,nambutone diclofenac*)

✱ Multidiscilplinary European panel have suggested that celecoxib may be used in ***rheumatic disease*** in spite of the contraindications to CVD – **NOT COMMON PRACTICE IN PALLIATIVE CARE AT PRESENT**

Using Dexamethasone

- Uses and dosing in palliative care include:

Dosing: (dexamethasone 750mcgm = hydrocortisone 20mg = prednisolone 5mg equianti-inflammatory doses)	
Appetite Stimulation:	2-6mg OD PO morning[1, 2, 3, 4]
Syringe Driver Site Reactions:	0.5-1mg CSCI OD – *care still needed to check compatibility with other drugs being used*
Breathlessness, Pain (including bone):	4-8mg PO/SC/(IV) morning[1, 2,3 4] OR 4-8mg CSCI/24H[1, 2,3 4]
Nausea & Vomiting:	4-16mg PO/SC/(IV) morning[1, 2, 3, 4] OR 4-16mg CSCI/24H[1, 2, 3, 4] – review after 2-4 days
Bowel Obstruction: Spinal Cord Compression: Superior Vena Cava Obstruction:	8-16mg PO/SC/(IV) morning[1, 2, 3, 4] OR 8-16mg CSCI/24H[1, 2, 3, 4] – review after 2-4 days
Cerebral Oedema:	Mild symptoms: 4-8mg PO/SC/(IV) morning[1, 2,3 4] Mod-severe: 8-16mg PO/SC/(IV) morning OR[1, 2,3 4] review after 2-4 days & consider stopping over 5-7days 8mg PO/SC (IV) BD – last dose before 2pm ALSO: 8-16mg CSCI/24H via syringe driver[1, 2,3 4]

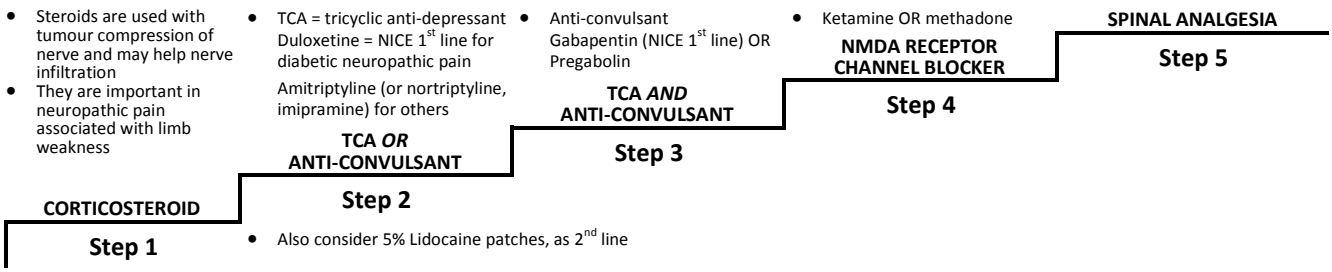
1. The physiological dose of dexamethasone is approx. 1mg, doses greater than this for >3weeks require gradual withdrawal of dexamethasone to avoid acute adrenal insufficiency. Doses of up to 6mg for 3weeks or less can be withdrawn abruptly in majority of patients (*certainly with 2 weeks or less*) Gradual withdrawal is particularly recommended if repeated systemic corticosteroids have been used for >3 weeks +/or dexamethasone >6mg doses used +/or repeated evening doses taken (unusual). No guidelines exist for withdrawal but dose can be halved daily to physiological dose (*1mg OD*) then reduced by 500microgm per week over 2 weeks. In a dying patient, steroids may be abruptly withdrawn BUT additional analgesia may be needed in patient's with brain tumours because cerebral oedema may return leading to pain +/or restlessness
2. Dose reduction is guided by clinical (symptom) response
3. Consider gastro-intestinal protection with a PPI, misoprostol or H2 antagonist
4. Risk of Osteoporosis and bone fracture is increased in patients >65yrs with steroid courses >3months OR 3 or more steroid courses in previous 12 months so prophylactic treatment with calcium + vit.D or bisphosphonate are recommended in these patients

- Side effects include:
  - Fluid retention with cardiac failure, oedema, low potassium, hypertension
  - Endocrine changes with hyperglycaemia, hirsuitism, hyperlipidaemia & weight gain
  - Gastrointestinal with peptic ulceration(perforation), bleeding, acute pancreatitis
  - Musculoskeletal with proximal myopathy, osteoporosis, tendon rupture, avascular necrosis
  - Neurological with agitation, insomnia, confusion, low mood, euphoria, pschycosis, reduced fit threshold in epilepsy
  - Sweating, impaired healing, susceptibility to infections and glaucoma

- Therefore dexamethasone should be used with caution in:
  - people on NSAIDs/COX-2s
  - peptic ulceration
  - diabetes
  - sepsis
  - heart failure
  - recent myocardial infarction
  - uncontrolled hypertension
  - epilepsy
  - psychotic disorders
  - osteoporosis

Neuropathic pain

- If nerve pain is not responding to opioid and NSAID/COX-2, choice of adjuvant drug includes:



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Using Gabapentin

- Indications:
  - Monotherapy & adjunctive treatment for partial seizure with/out 2ndry generalization
  - Peripheral neuropathic pain
  - Malignant bone pain
  - Insomnia
  - Pruritis
  - hiccups
  - restless legs syndrome
  - sweats
- Dose titration for pain:

DAY	Licensed Dose	Suggested Dose
1	300mg PO ON	100mg PO ON
2	300mg PO BD	100mg PO BD
3	300mg PO TDS	100mg PO TDS
	Increase by 300mg PO OD according to response up to maximum of 1200mg PO TDS	Increase by 100mg PO TDS every 2 days as needed up to maximum of 1200mg PO TDS
	MAXIMUM DOSE ADJUSTMENT FOR RENAL IMPAIRMENT	
	Creatinine Clearance (ml/L)	**Maximum Dose**
	≥80	1200mg PO TDS
	50-79	600mg PO TDS
	30-49	300mg PO TDS
	15-29	300mg PO OD
	<15	300mg PO ALT DAY

Using Pregabalin

- Indications:
  - Adjunctive treatment for partial seizures
  - Central & Peripheral neuropathic pain
  - Malignant bone pain
  - Insomnia
  - Uremic Pruritis
  - hiccups
  - restless legs syndrome
  - sweats
- Dose titration for pain:

DAY	Licensed Dose	Suggested Dose
1	75mg PO BD	25mg PO ON
3-7	150mg PO BD	25mg PO BD
10-14	300mg PO BD	75mg PO BD
	Increase according to response up to maximum of 600mg PO /24H	Increase by 25mg PO OD/BD every 2 days as needed up to maximum of 600mg PO /24H
	MAXIMUM DOSE ADJUSTMENT FOR RENAL IMPAIRMENT	
	Creatinine Clearance (ml/L)	**Maximum Dose**
	≥60	300mg PO BD
	≥30-<60	150mg PO BD
	≥15-<30	75mg PO BD or 150mg PO OD
	<15	75mg PO OD

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NOTES ON PRESCRIBING (see examples of prescribing)

When prescribing opioids you need to think about the following:

- REGULAR & PRN
- DRUG NAME (including generic OR brand?)
- DOSE
- ROUTE (of administration)
- FREQUENCY TO BE GIVEN/ DRUG TIMES
- START DATE
- SPECIAL INSTRUCTIONS (*IF ANY*)
- SIGNATURE & OTHER

REGULAR & PRN (*As Required*)

- As stated opioids are usually written up with BOTH a REGULAR DOSE given as:
  - 6 hourly for weak opioids (*CODEINE, DIHYDROCODEINE, TRAMADOL*)
  - Modified Release (MR) 12 hourly oral – or 24 hourly but hospice does not use this preparation of morphine
  - Immediate release (IR) 4 hourly (*also known as Standard Release*)
  - Continuous sub. Cut infusion (*CSCI*) via *syringe driver*
  - Topical (*patches*)
  - Also Intravenous (IV) – not considred here as this route is not usual in palliative care, but is used in other specialties *eg anaesthetics*

  and a corresponding PRN DOSE (*ie 1/6th TOTAL REGULAR DOSE)* usually given as:
  - Oral (PO/O) (up to 1 hourly)
  - Sub Cutaneously (SC) up to 1 hourly
  - Buccal or nasal for transmucosal preparations of fentanyl (*not condiered here*)

    NB: IM route NOT USED routinely in palliative care

DRUG NAME (*Generic or Brand?*)

- In large organisations opioids may be prescribed GENERICALLY and in the community setting the long acting preparations (*modified release oral medication and topical patches*) are usually BRAND prescribed
- The reason is that each drug company produces its own drug delivery system for patches or modified release preparations which differs from other companies; Thus even though the drug dose may be the same (*eg. Zomorph 100mg capsules and MST Continus 100mg tablets both contain 100mg oral morphine to be released over 12 hours*) an individual may 'handle' the drug differently when one brand is swapped for another (*eg different bioavailablity etc*) with the possibility of toxicity occurring; Thus it is recommended that individuals stick to the same brand (*and thus same delivery system*) for long acting preparations
- If you prescribe a brand then ONLY that brand can be given to the patient.
- If a drug is prescribed generically then ANY brand can be used
- Organisations such as hospices and hospitals tend to use a particular brand (*often for reasons of cost*) but want generic prescribing in case there a problem with drug availability; although swapping to a different brand does mean possible risk of toxicity, since patients are (*or should be*) frequently observed in such organisations, toxicity should be picked up earlier; this is not the case in the community where a patient may be alone or not regularly observed by others
- TWO exceptions to this that may have to be prescribed by BRAND in hospitals and hospices may be:
  - *Buprnorphine* patches as their are TWO different preparations (*BuTrans which is changed every 7 days & Transtec which is changed every 96 hours*) so *Buprenoprhine* patches
  - Transmucosal Fentanyl *eg Abstral, Actiq, Effentora, Instanyl & PecFent – each preparation HAS ITS OWN DOSING REGIME PECULIAR TO THE BRAND*

DRUG DOSE

- See other above for dosing

  Remember starting dose of oral morphine for opioid naive patients = morphine IR 2.5mg 4H PO

ROUTE

- ***Table 3 shows the latin abbreviations that are often used in prescribing***
- See Regular & PRN above for how doses are often given
- When prescribing you can use abbreviations; the following are usually acceptable BUT you should ALWAYS think to check with your organisation for what abbreviations are acceptable
  - O/PO = oral
  - SC = subcutaneous
  - CSCI = continuous subcurtaneous infusion (ie via syringe driver)
  - IM = intramuscular (*only for few drugs eg codeine, dihydocodeine SC or deep IM – not often used)*
  - TOP = topical (ie opioid patches)

  Also transmucosal fentanyl preparations (rapid acting preparations for break through pain) may be:
  - SUBLING = sublungual
  - BUCC = buccal (held against buccal mucosa)
  - NAS = intranasal spray

Find out more in:

- Oxford Handbook of Palliative Care 2nd edition: M Watson et al - Oxford publications
- Palliative Care Formulary 5th edition(PCF4): R Twycross et al - **palliative**drugs.com publications
- Drugs in Palliative Care 2nd edition: A Dickman – Oxford publications

Table 3
Latin abbreviations

Directions should be in English without abbreviation. However, Latin abbreviations have been used when prescribing.
The following is a list of appropriate abbreviations. It should be noted that the English version is not always an exact translation.

a. c.	=	*ante cibum*	(before food)
b. d.	=	*bis die*	(twice daily)
o. d.	=	*omni die*	(every day)
o. m.	=	*omni mane*	(every morning)
o. n.	=	*omni nocte*	(every night)
p. c.	=	*post cibum*	(after food)
p. r. n.	=	*pro re nata*	(when required)
q. d. s.	=	*quater die sumendum*	(to be taken four times daily)
q. q. h.	=	*quarta quaque hora*	(every four hours)
stat	=	*immediately*	
t. d. s.	=	*ter die sumendum*	(to be taken three times daily)
t.i.d.	=	*ter in die*	(three times daily)

FREQUENCY & DRUG TIMES

- The frequency that opioids are given depends upon the preparation (*see Regular & PRN above*)
  - NB: Regular ORAL opioids that are Modified Release (MR) ARE ALWAYS GIVEN 12 HOURLY (*12H*) and NEVER 'BD' OR 'TWICE DAILY' or as a patient may take the second dose sooner then 12 hours SO SPECIFY A TIME eg *10am & 10pm and not* 'BREAKFAST & BED TIME'
  - NB: Regular ORAL opioids that are Immediate Release (IR) are prescribed 4 HOURLY so SPECIFY TIMES *eg 6am, 10am, 2pm, 6pm, 10pm*
  - NB: PRN opioids can be prescribed (PO or SC) UPTO 1 HOURLY if needed
  - NB: syringe drivers are CSCIs written as shown in examples below if using standard drug prescription sheet (*hospices such as Trinity have separate syringe driver sheets*)
  - NB: opiod patches VARY in their times for changing; Fentanyl is EVERY 72 HOURS; Buprnorphine BuTrans is weekly; Buprenorphine Transtec is every 96 hours – *see examples given below*
  - NB: transmucosal Fentanyl has BRAND SPECIFIC PRESCRIBING

START DATE

- This should be clearly stated and if it is not at the start of the drug administration box, it is good practice to cross off those boxes that do not apply (see examples below)

SPECIAL INSTRUCTIONS

- This usually does not apply but may do for transmucosal fentanyl which has brand specific prescribing instructions *eg. Abstral doses are written in pairs & 2nd dose can be given 15-30mins after 1st , Abstral is also prescribed in two phases, the first is a Tritration Phase to get the correct dose which is then given in the next, Maintenance Phase. We are not expecting you to know about transmucosal fentanyl apart from that is exists and when to use it. It is highly expensive and different organisations will have their own favoured preparation which you should be taught on how to prescribe and use*

SIGNATURE & OTHER MATTERS

- You often have to print your name beside your signature and organisations will have other specific prescribing requirement *eg. Your bleep number*
- PRN prescribing sheets can have a MAXIMUM DOSE box; for opioids we often do not complete this in palliative care because we prescribe PRN opioids 1 hourly (1H), assuming that if the patient is asleep they do not need extra pain relief and if they are awake but giving a nurse cause for concern the patient should be reviewed
- When you *stop* a drug, complete the *Date Stopped* box (*usually adding your initials*), put a line through the prescribing box AND put a bar in the *drug administration table*

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