South African guideline for the use of chronic opioid therapy for chronic non-cancer pain

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Quick Reference Guide

1. General management

- Chronic non-cancer pain (CNCP) is defined as pain lasting for >90 days and beyond the expected time for tissue healing.
- CNCP is often associated with psychological comorbidities (anxiety and depression) and limitation of physical function.
- Management of CNCP requires a multimodal, multidisciplinary approach to address:
  - pain and comorbidities
  - psychological issues
  - functional rehabilitation
  - social issues.
- Patients should be referred to specialist practitioners for interventions when appropriate, and thereafter referred back to the general practitioner for continued care.
- Communication between the patient's healthcare team is mandatory to establish roles and expectations for continuity of care and safe use of opioids.
- Patients should identify with one doctor (usually the general practitioner) who accepts primary responsibility for their overall medical care and who should coordinate communication and consultation among clinicians.
- To help ensure correct use of medication and to reduce prescription fraud, all opioids (and preferably all other medications) for a particular patient should be dispensed through a single designated pharmacy.
- Chronic opioid therapy (COT) is defined as regular use of strong opioids for at least 3 months.

Assessment tools to evaluate patients for COT (Appendix 1 and 2)

Tool	Purpose	When to complete
BPI	To evaluate physical and psychosocial components of pain	All visits
ORT	To evaluate risk of opioid abuse	Initial visit

COT = chronic opioid therapy; BPI = Brief Pain Inventory; ORT = Opioid Risk Tool.

2. Indications for opioids

- Opioids may be appropriate in carefully selected patients with moderate to severe pain, which:
  - significantly and adversely affects quality of life, or
  - has not responded to non-pharmacological and non-opioid pharmacological therapies.
- Opioids are not appropriate as the primary medication of choice for pain disorders with strong psychosocial contributing factors.

3. Before initiating COT

- Establish a diagnosis and the cause of the pain.
- Estimate the pain intensity and functional impairment.
- Risk stratify the patient in terms of potential benefits and harms of opioid therapy to assess their suitability for COT.

3.1 Patient assessment and diagnosis

- Patient's pain disorder
- Pain intensity
- Functional impairment (impact of pain on work, school/studying, home and leisure activities)
- General medical condition
- Sleeping pattern
- Psychosocial history (living arrangements, family/social support, family obligations, work status)
- Psychiatric status
- Substance use history
- Other medications

The full version of this guideline is available online. Use the QR code to access.

3.2 Explain treatment options and address expectations

- Total pain relief is rarely achieved.
- Goals of therapy are pain reduction and functional improvement:
  - Clinically meaningful improvement is at least 30% reduction in pain (or ≥2 points on a 0 - 10 numerical rating scale) and/or 30% improvement in function.
- Caution patients against unrealistic expectations.
- Potential benefits, adverse effects, complications and risks of COT.
- Alternatives to COT.
- Consider asking the patient to sign an opioid agreement (Appendix 3).
- Initial course of COT is viewed as a short-term trial, which will be continued if response is satisfactory.
- Positive clinical response to COT may take a few days to become apparent.

Detailed notes of all assessments, discussions and treatment decisions should be maintained at all visits.

4. Choice of opioid

- Opioid analgesics for CNCP may be administered orally or transdermally.
- When choosing an appropriate opioid, consider health status, pain severity, previous exposure to opioids, attainment of therapeutic goals and predicted or observed harms, concomitant medications.
- Use immediate release (IR) oral opioids to initiate therapy and titrate to an effective dose.
- Once pain control is stable, if possible, switch to long-acting (controlled release (CR); extended release (ER), sustained release (SR)) oral opioid or transdermal opioid patch.

5. Initiation and titration of COT

- Start with a low dose: ≤10 mg/day oral morphine equivalents.
- Reassess dose after 72 h (clinical improvement and tolerability).
- Dose may be slowly increased by not more than 10 mg morphine equivalents per day over 4 - 6 weeks.
- Maximum daily dose should preferably not exceed 90 mg oral morphine equivalents.
- If repeated dose escalations are required, consider:
  - increase in the intensity of the underlying pain condition (disease progression)
  - development of an additional painful condition
  - opioid tolerance
  - opioid-induced hyperalgesia
  - drug abuse (e.g. recreational use).

Step-wise approach to opioid selection

	Mild-to-moderate pain	Severe pain
First-line	Codeine or tramadol	Morphine, high-dose oxycodone, hydromorphone, or buprenorphine
Second-line	Morphine, low-dose oxycodone, dihydrocodeine, hydromorphone or buprenorphine	Fentanyl

Oral opioids: Suggested initial dose and titration*,†

Opioid	Initial dose	Min. time interval for increase (days)	Suggested dose increase	Min. daily dose before converting IR to CR
Codeine (alone/ in combination with paracetamol/ASA)	15 - 30 mg 4-hourly as required	7	15 - 30 mg/day, max. 600 mg/day‡	100 mg
Tramadol (37.5 mg) + paracetamol (325 mg)	1 tablet 4 - 6-hourly	7	1 - 2 tablets 4 - 6-hourly as needed, max. 8 tablets/day	3 tablets
Tramadol	50 mg 4 - 6-hourly		Max. dose: 400 mg/day	NA
SR tramadol	100 mg 12-hourly	2	Max. dose: 400 mg/day	NA
IR morphine	5 - 10 mg 4-hourly as needed, max. 40 mg/ day	7	5 - 10 mg/day	20 - 30 mg
CR morphine	10 - 30 mg 12-hourly	Min. 2, recommended: 14	5 - 10 mg/day	NA
IR oxycodone	5 - 10 mg 6-hourly as needed, max. 40 mg/ day	7	5 mg/day	20 mg
CR oxycodone	10 - 20 mg 12-hourly, max. 40 mg/day	Min. 2, recommended: 14	10 mg/day	NA
ER hydromorphone	4 mg daily, max. 16 mg/ day	Min. 2, recommended: 14	2 - 4 mg/day	NA
Dihydrocodeine	30 mg 6-hourly	Min. 2, recommended: 7	Increase to 30 mg every 4 h, max. 240 mg/day	NA

IR = immediate release; CR = controlled release; ASA = acetylsalicylic acid; ER = extended release; SR = sustained release.
*Modified from the Canadian National Opioid Use Guideline Group (2010).[4]
†Due to a genetic polymorphism that influences the response to opioid analgesics, there is inter-individual variation in the doses required for adequate analgesia. Some patients will require considerably higher opioid doses than others.
‡Paracetamol dose should not exceed 3 g/day.

Equianalgesic doses for conversion from one oral opioid to another*,†

		Conversion to/from oral morphine equivalent – multiply by	
Opioid	**Equivalence to 30 mg morphine (mg)**	**To**	**From**
Morphine	30	1	1
Codeine	200	0.15	6.67
Oxycodone	20	1.5	0.67
Hydromorphone	6	5	0.2
Dihydrocodeine	180	0.16	6
Tramadol	~1:10‡		

*Adapted from the Canadian National Opioid Use Guideline Group (2010).[4]
†If converting from opioids other than morphine, calculate the equipotent morphine dose for the current analgesic and use this dose to convert to the new opioid. The new opioid should be initiated at 50% of the calculated equianalgesic dose.
‡Morphine dose equivalence not established, but approximates to 1:10 of morphine to tramadol.

Approximate equipotent doses for conversion from oral morphine to transdermal opioids

Oral morphine to transdermal fentanyl*,†								
Oral morphine equivalent (mg/24 h)	60 - 134	135 - 179	180 - 224	225 - 269	270 - 314	315 - 359	360 - 404	
Transdermal fentanyl (μg/h)‡	25	37	50	62	75	87	100	
Oral morphine to transdermal buprenorphine§,¶								
Oral morphine equivalent (mg/24 h)	10	15	30	60	90	120	180	240
Transdermal buprenorphine (μg/h)	5	10	20	35	52.5	70	105	140

*Adapted from the Canadian National Opioid Use Guideline Group (2010).[4]
†Conversion rate is 150:1,[6] e.g. 120 mg morphine over 24 h: 120 ÷ 150 = 0.8 mg fentanyl; 0.8 × 1 000 = 800 μg fentanyl over 24 h = 33.3 μg /h. Round up or down to appropriate patch.
‡Formulations include 12, 25, 50, 75 and 100 μg/h patches, but the 12 μg/h patch is generally used for dose adjustment rather than initiation of fentanyl treatment.
§Adapted from the British Pain Society (2010).[2]
¶Conversion rate is 75 - 100:1.[2,6] The conversion rate used here is based on 75:1, e.g. 30 mg morphine over 24 h: 30 ÷ 75 = 0.4 mg buprenorphine; 0.4 × 1 000 = 400 μg buprenorphine over 24 h = 16.6 μg/h. Round up or down to appropriate patch.

Common opioid-related adverse effects and their management

Adverse effect	Management
Nausea/vomiting	Anti-emetic therapies (oral or suppository); it is advisable to concurrently prescribe a prophylactic anti-emetic for a few days when initiating opioid therapy
Constipation	Increase fluid and fibre intake; stool softeners; laxatives
Pruritus	Antihistamine
Sedation, clouded mentation	Pharmacological therapies are not recommended

6. Consider switching to another opioid if:

- Analgesia is inadequate despite dose escalation
- Adverse effects are intolerable
- Stable pain control is achieved on IR opioid and it is appropriate to switch to a long-acting formulation or transdermal opioid patch.

7. Breakthrough pain

- Consider as-needed IR opioid for rescue analgesia.
- If continuous rescue doses are required, up-titrate maintenance analgesic dose by adding the extra dose per day required for breakthrough pain.

8. Long-term opioid prescribing

When a trial of opioid has been successful, treatment may be continued until:

- the underlying painful condition resolves
- the patient receives a definitive pain relieving intervention (e.g. joint replacement)
- the patient no longer derives benefit from opioid treatment
- the patient develops intolerable side-effects; or
- there is evidence of addiction, tolerance, dependence or opioid-induced hyperalgesia. It should be noted that patients who are suffering with severe pain rarely become addicted to opioids. They may require increasing doses of opioids as a result of opioid tolerance and this must be differentiated from addiction.

9. Discontinuing opioids

- Reduce dose slowly by approximately 10% per day or per week.
- Dose should be tapered more slowly in patients who are anxious about discontinuing COT and in those who are suspected of being physically dependent on opioids.
- When one-third of the original dose is reached, reduce the rate of tapering to one-half or less of the initial rate.
- If the patient experiences withdrawal symptoms or an increase in pain during tapering, discontinue dose reduction and consider increasing the current dose.

Clinical features of opioid toxicity and withdrawal

	Symptoms
Toxicity	Pinpoint pupils
	Sedation (falling asleep during conversation or activity)
	Slow respiration
	Visible cyanosis, e.g. lips, ears, nose (in severe cases)
	Myoclonic jerks
	Snoring when asleep
	Agitation
	Confusion
	Vivid dreams, nightmares or hallucinations
In more severe cases	Hypotension
	Coma
	Convulsions
Withdrawal	Sweating
	Mydriasis
	Pilo-erection
	Yawning
	Abdominal cramps/vomiting/ diarrhoea
	Bone and muscle pain
	Increase in usual pain
	Restlessness
	Anxiety
	Rhinorrhoea
	Lacrimation
	Tremor

10. Opioid-related adverse effects

Adverse effects are usually manageable and most pronounced when initiating or increasing the dose.

10.1 For intolerable adverse effects, consider

- Reducing the opioid dose.
- Switching to another opioid formulation or route of administration.
- Discontinuing the opioid and instituting alternative pain management strategies.

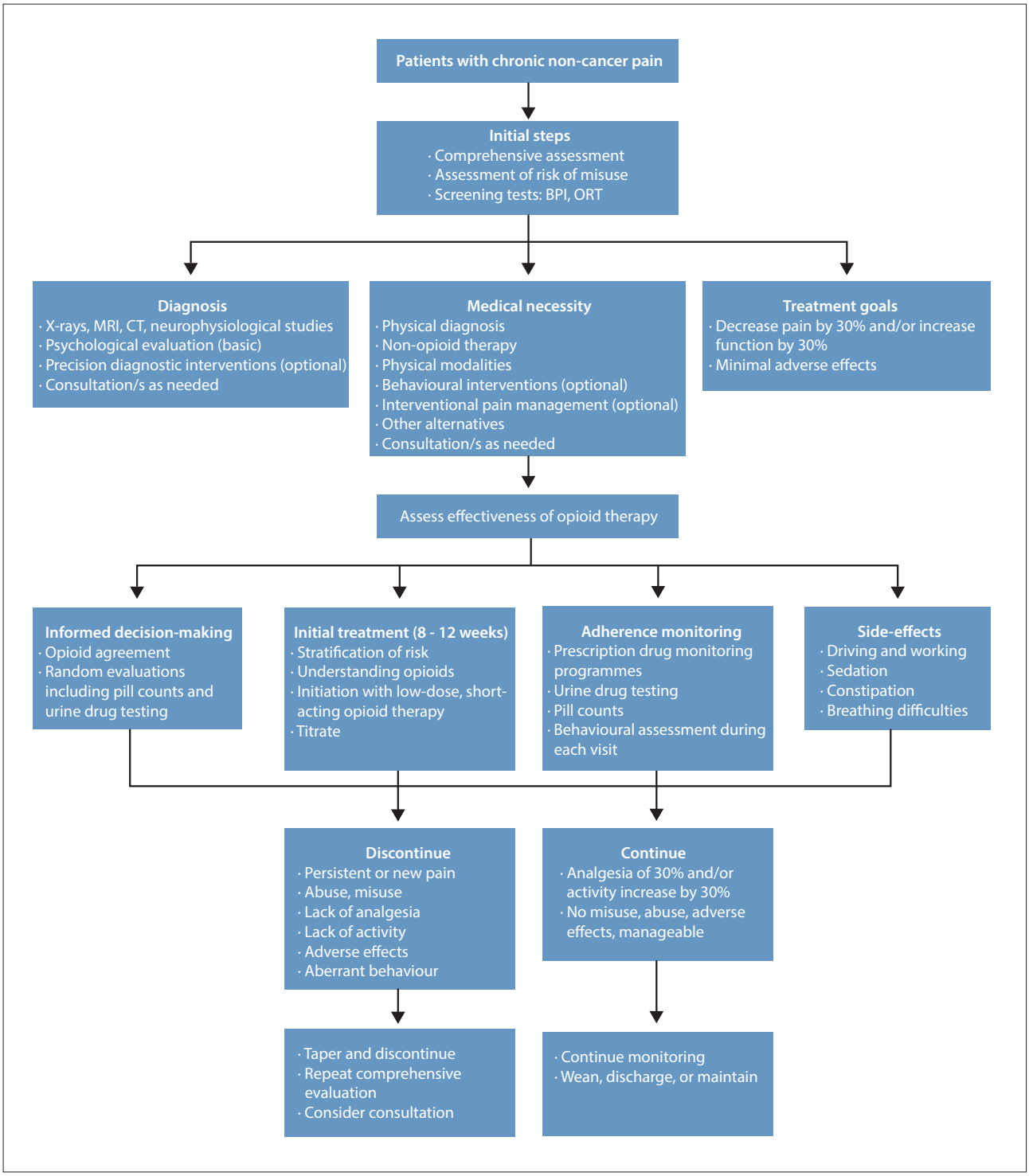
11. Driving and working while on opioids

Patients should be advised to avoid driving, working under hazardous conditions or working with hazardous machinery if:

- the condition for which they are being treated has physical consequences that might impair their driving ability, concentration or coordination
- they feel unfit to drive or work
- they have constant severe pain
- they have not been sleeping
- they have just started opioid treatment
- their dose of opioids has been recently adjusted upwards or downwards (as withdrawal may have an impact on capability)
- they have consumed alcohol or other drugs that can produce an additive sedative effect.

12. When to refer to a pain clinician or multidisciplinary pain unit

- Unable to make a definite diagnosis of the cause of pain
- Significant comorbidities or other factors that may complicate opioid use (e.g. psychiatric comorbidities, severe renal impairment, etc.)
- Inadequate response to opioid analgesia, despite titration to 90 mg/day oral morphine equivalent
- Unmanageable opioid-related side-effects
- Indications of inappropriate drug use.



Algorithm for the initiation and use of COT. Adapted with permission from Manchikanti et al.[5] *(COT = chronic opioid therapy; BPI = Brief Pain Inventory; ORT = Opioid Risk Tool; MRI = magnetic resonance imaging; CT = computed tomography.)*

Appendix 1. Brief Pain Inventory*

Name: _____

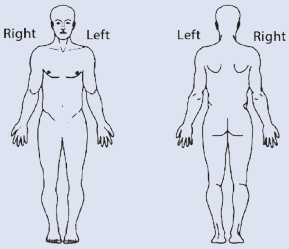
Date: _____

Time: _____

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains and toothaches). Have you had pain other than these everyday kinds of pain today?

☐ YES ☐ NO

2. On the diagram, shade the area where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the number that best describes your pain at its worst in the past 24 h.

0 1 2 3 4 5 6 7 8 9 10

No pain *Pain as bad as you can imagine*

4. Please rate your pain by circling the number that best describes your pain at its least in the past 24 h.

0 1 2 3 4 5 6 7 8 9 10

No pain *Pain as bad as you can imagine*

5. Please rate your pain by circling the number that best describes your pain on average.

0 1 2 3 4 5 6 7 8 9 10

No pain *Pain as bad as you can imagine*

6. Please rate your pain by circling the number that tells how much pain you have right now.

0 1 2 3 4 5 6 7 8 9 10

No pain *Pain as bad as you can imagine*

7. What treatments or medications are you receiving for your pain?

8. In the past 24 h, how much relief have pain treatments or medications provided? Please circle the percentage that shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

No relief *Complete relief*

9. Circle the number that describes how, during the past 24 h, pain has interfered with your:

A. General activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

B. Mood

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

D. Normal work (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

F. Sleep

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

G. Enjoyment of Life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

*Reproduced with permission from Dr Charles S Cleeland (1991).

Appendix 2. Opioid Risk Tool*

Risk factor	Male, score (max. score)	Female, score (max. score)
Family history (parents and siblings)		
Alcohol abuse	_ (3)	_ (1)
Illegal drug use	_ (3)	_ (2)
Prescription drug abuse	_ (4)	_ (4)
Personal history		
Alcohol abuse	_ (3)	_ (3)
Illegal drug use	_ (4)	_ (4)
Prescription drug abuse	_ (5)	_ (5)
Mental health		
Diagnosis of ADD, OCD, bipolar disorder or schizophrenia	_ (2)	_ (2)
Diagnosis of depression	_ (1)	_ (1)
Other		
Age 16 - 45 years	_ (1)	_ (1)
History of pre-adolescent sexual abuse	_ (0)	_ (3)
Total score		

Total score risk category:

0 - 3 = low risk: 6% chance of developing problematic behaviours

4 - 7 = moderate risk: 28% chance of developing problematic behaviours

≥8 = high risk: >90% chance of developing problematic behaviours

ADD = attention deficit disorder; OCD = obsessive-compulsive disorder.
*Reproduced with permission from Webster LR and Webster RM.[13]

Appendix 3. Sample opioid agreement

I (patient's name) _____ understand that Dr _____ is prescribing opioid medication for me to treat my chronic pain.

The opioid medication that has been prescribed is: _____ .

The risks and benefits of this medicine have been explained to me and I understand the following:

- the medicine may have certain side-effects including, but not limited to, drowsiness, dizziness, loss of coordination, constipation, nausea, vomiting and itching
- the medication may impair my ability to drive a motor vehicle, operate hazardous machinery or work under hazardous conditions
- alcohol and certain other medications may increase the risk of side-effects while I am taking opioid medication, or may reduce the effectiveness of my pain medication
- although the risk is low, addiction to opioid medication can occur; addiction is more likely to occur in people with a personal or family history of drug or alcohol abuse and/or addiction
- physical dependence to opioid medication may occur and may result in withdrawal symptoms if the medication is stopped abruptly
- opioid medication may not provide complete pain relief; if the pain or ability to be active does not improve after a reasonable trial of opioid medication, the medication may be stopped.

I agree to the following:

1. Only Dr_____ will prescribe opioids for me, and I will not seek or accept opioid medications from anyone else.
2. I will take my opioid medication exactly as instructed by Dr _____ and will not take it in larger doses or more frequently than instructed.
3. I will tell Dr _____ about all other medications I am taking and about any personal/family history of alcohol/drug abuse or illegal drug activity. I will not use any other prescribed or over-the-counter medication without discussing it with him/her first.
4. I will not give my opioid medication to anyone else and I will store it in a safe and secure place and out of the reach of children.
5. (Females only) I will tell my doctor immediately if I am planning to become pregnant or if I think that I am or might be pregnant.
6. My medical practitioner may decide to discontinue my opioid medication if my pain or ability to be active does not improve, or if I do not comply with any of the above.

Patient signature: _____ Date: _____ Witness: _____