PMB definition guideline for pain management
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Disclaimer:

The benefit definition guideline for pain management has been developed for the majority of standard patients. All interventions described only apply if the patient has been diagnosed with the above conditions. Regulation 15(h) and 15(l) may be applied for patients who are inadequately managed by the stated benefits.

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1. Scope and purpose

1.1. The objective of this guideline is to provide guidance on PMB level of care for the management of acute and chronic pain including chronic cancer pain, chronic non-cancer pain, bone pain and neuropathic pain.
1.2. The purpose of the document is to improve clarity with respect to funding decisions by medical schemes, taking into consideration evidence-based medicine.
1.3. Medical schemes interpret pain management benefits differently, resulting in a lack of uniformity of benefit entitlements.
1.4. It is important to note that schemes may apply formularies especially when drug classes are recommended.
1.5. There are numerous conditions associated with surgical and non-surgical causes of acute pain. When such a condition is included in the PMB Regulations, the management of pain, constitutes PMB level of care and should be funded accordingly.
1.6. Where the primary condition is categorised as a PMB, any co-morbid pain will also be categorised as a PMB and funded accordingly. If the primary condition is not categorized as a PMB, any co-morbid pain will also not be categorised as a PMB and therefore not funded. In this instance, the scheme rules will apply.
1.7. When the ICD11 is implemented, which will systematically include chronic pain diagnosis, this document will be reviewed to ensure that there is alignment.

2. Definition of pain

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (Iasp-pain.org, 2020). Chronic pain is defined as pain that lasts or recurs for more than three months (Iasp-pain.org, 2020).

3. Pain assessment

3.1. Pain should be assessed by (Beers and Berkow, 1999; SASA 2015):

- The duration
- The severity
- The site
- The characteristics of the pain - stabbing, throbbing, crushing, cramp-like etc
- Whether it is persistent or intermittent
- The relieving or aggravating factors
- The accompanying symptoms e.g. nausea and vomiting, visual disturbances
- The distribution of pain

3.2. Pain is subjective, and it is vital to record the patient's level of consciousness when assessing pain (Beers and Berkow, 1999; SASA, 2015; Wiener et al., 2008; Chetty et al., 2013; Raff et al., 2014; Chetty et al., 2017).

3.3. The assessment tool for pain needs to be appropriate to the following (Green and McGhie, 2011. SASA, 2015):

- patient's developmental age,
- cognitive status and
- emotional status

3.4. Therefore, evaluation of the patient's pain using a validated assessment tools such as a visual analogue scale (VAS) or a verbal numeric rating scale (VNRS) is important (SASA, 2015; Chetty et al., 2013; Raff et al., 2014; Chetty et al., 2017).

4. Principles of pain management

4.1. Pain management is a fundamental human right. All people with pain should have access to appropriate assessment and treatment by adequately trained health care professionals (Meyer, 2007).

4.2. A comprehensive multidisciplinary evaluation will lead to recommendations for treatment depending on the needs and expectations of the individual (Meyer, 2007).

4.3. In order to control pain effectively, a multidisciplinary team is needed to perform the following functions (Chetty, 2017; Ripamonti, 2012; SASA, 2015; Vargas-Schaffer, 2010).

- Provide specialised, prompt, efficient, safe and multimodal pain management 24 hours a day
- Develop protocols and guidelines to assist in the provision of safe and effective treatment designed
- Provide an up-to-date, evidence-based and appropriate understanding of pain
- Monitor patient outcomes and document the results in order to compare and improve services.

5. Pharmacological therapy in pain management

5.1. Pharmacological treatment forms a major component of pain therapy and analgesics are broadly classified as non-opioids, opioids and adjuvants.

5.2. The principles of analgesic use according to the WHO recommendations: **(**Rossiter, 2016; Vargas-Schaffer, 2010)

- Preferably by mouth: the route of choice to administer analgesic is the mouth unless the patient is vomiting or comatose.
- By the clock: to achieve continuous pain control, analgesic should be given regularly at a fixed dose at the appropriated time interval, reviewed and adjusted accordingly.
- By the WHO treatment ladder: treatment should be appropriated according to the type and severity of pain.

- For the individual: there is no standard dose in pain treatment. The posology (the part of medicine concerned with dosage) should be balanced to achieve the best balance between the analgesic effect and the side effects.

- Adjuvant drugs should be given where necessary to enhance analgesic effect.

5.3. The goal of pharmacotherapy should be to improve pain intensity and functioning (sleep, mood and exercise tolerance), while avoiding cognitive impairment and organ toxicity (Meyer, 2007).

5.4. Many patients don't present with pure nociceptive or neuropathic pain, but rather have a mixed pain syndrome, therefore rational polypharmacy that targets key peripheral and central mechanisms and modulating pathways often produces best outcomes (Meyer, 2007; Mishra et al., 2009).

6. Chronic cancer pain (including pain due to terminal illnesses)

6.1. Most, if not all patients with cancer will experience pain during the course of their disease or treatment process. Pain will significantly impact on the patient's quality of life, and in long-term cancer survivors, the pain can become persistent and chronic. Pain management for cancer patients should be aimed at improving patients' quality of life and reducing suffering.

6.2. Pharmacological and non-pharmacological interventions, interventional pain management procedures (e.g. coeliac plexus ablation for chronic severe pain associated with pancreatic cancer) and oncology specific treatment (e.g. chemotherapy, radiation therapy) are all components which need consideration for management of cancer pain.

6.3. Schemes should include and fund different medicine formulations to accommodate patients who are unable to swallow.

6.4. Syringe drivers are also recommended as PMB level of care.

6.5. Table 1 below shows the medicines that are recommended as PMB level of care for chronic cancer pain (including terminal illness pain).

Table 1: Medicines that are used for the management of chronic cancer pain

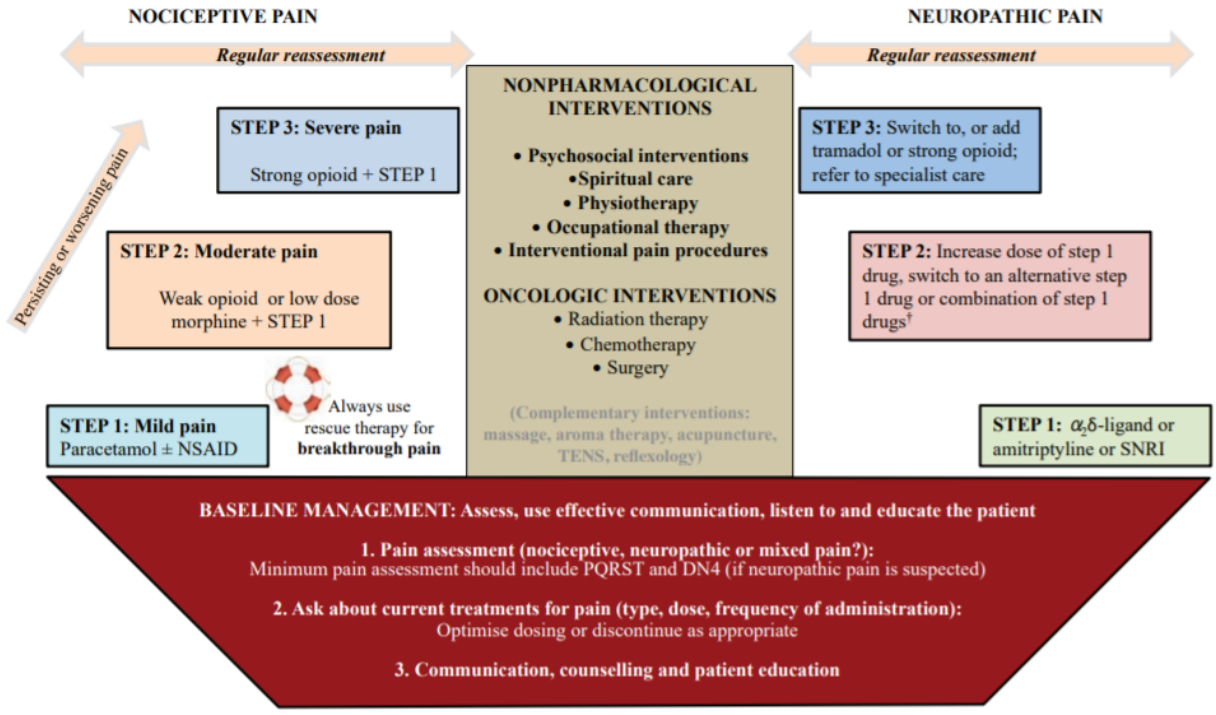
Level of care	Therapeutic class	Recommended medicines	Comment
Step 1	Non-opioids	Paracetamol and/or NSAID	
Step 2	Weak opioids for mild to moderate pain	Tramadol	
		Low dose morphine	For patients who can't tolerate tramadol
		Codeine	
Step 3	Strong opioids for moderate to severe pain.	Morphine	More than one formulation of morphine can be authorised for a given period of time, for example morphine syrup can be used for breakthrough pain for patients on a slow-release formulation. Morphine

			pumps are recommended when clinically indicated and funding is based on scheme rules.
		Fentanyl (transdermal)	Only for renal patients. Fentanyl also a good option for opioid rotation. Fentanyl patches are recommended when clinically indicated and funding is based on scheme rules.
		Oxycodone	On motivation: For a specified period of time during opioid rotation Reserved for non-responders Patient must have a trial of morphine
Adjuvant drugs	When there is a neuropathic component to the cancer pain (please refer to neuropathy below)		
Opioid rotation	Formularies to make provision for different types of opioids and not just different formulations to allow for opioid rotation when clinically indicated.		

6.6. Figure 1 below is a modification of the WHO stepladder which was created by the South African team who developed the cancer pain guidelines.

6.7. Not all non-pharmacological options included below are PMB level of care. Section 11 details non-pharmacological interventions which are recommended as PMB level of care.

Figure 1: Stepwise Healthcare Interventions for Pain (SHIP)



Source : https://painsa.org.za/wp-content/uploads/2016/02/A5-Guide-to-treatment-of-Cancer-Pain-2015.pdf

7. Chronic non-cancer pain

7.1. Description

7.1.1. The International Association for the Study of Pain has defined chronic pain as "pain that persists for longer than the time expected for healing, or pain associated with progressive, non-malignant disease". Chronic pain is seen as a disease and a social health care problem and it may cause severe suffering and reduced quality of life (Meyer, 2007).

7.1.2. Chronic pain related to ongoing tissue injury is presumably caused by persistent activation of A delta fibers and C Fibers (Garcia-Larrea and Hagiwara, 2018; Meyer, 2007; Raff et al., 2014).

7.1.3. It may be associated with an underlying chronic disease that should be diagnosed and treated accordingly. This includes nociceptive pain, arthritis related pain, neuropathic pain, fibromyalgia and several other conditions that are associated with pain. However, there are many patients with chronic pain from unknown aetiology (Meyer, 2007).

7.1.4. Chronic non-cancer pain of a PMB condition should be funded as a PMB whilst chronic non-cancer pain of a non-PMB should be funded according to scheme rules.

7.1.5. This guideline will provide further guidance for neuropathic and bone pain.

8. Bone pain

Bone pain is usually related to cancer metastases to bone (80% of which occur secondary to breast, prostate or lung cancer). Painful bone metastases frequently give rise to incident pain or pain on movement. Pain is described as dull, aching, constant and worse with movement and weight-bearing activities. It may be localised to the area of infiltration or referred pain if there is compression of nerves. Though not strictly a neuropathic injury, cancer-induced bone pain is a unique state with features of neuropathy and inflammation release (Colvin and Fallon, 2008).

8.1. **Management of bone pain**

8.1.1. Management is multimodal with radiotherapy, analgesics (opioids, NSAIDs), bisphosphonates and radioisotopes therapies (Ripamonti et al., 2012).

8.1.2. Radiotherapy is effective and is recommended for symptomatic bone metastases. Radiotherapy has specific and critical efficacy in providing pain relief caused by bone metastases. 41-90% patients experience partial relief of bone pain, following radiotherapy, with 25-50% having complete relief **(**Ripamonti et al., 2012).

8.1.3. Bisphosphonates (e.g. alendronate, zolendronic acid or ibandronic acid) are recommended as PMB level of care only if there is evidence of bone metastases for cancer patients.

8.1.4. A recent review showed that bisphosphonates reduced the number of skeletal-related events in numerous cancers. The clinical efficacy of bisphosphonates for pain relief in metastatic bone disease suggested that there was some evidence for their use as analgesics, although the effect was delayed.

9. Neuropathic pain

Definition

The International Association for the study of pain defines neuropathic pain as pain caused by a lesion or a disease of a somatosensory systems (Garcia-Larrea and Hagiwara, 2018; Chetty et al., 2017).

Neuropathic pain is associated more with lesions of temperature and pain pathways at peripheral, spinal and supraspinal levels. Peripheral nerve injury or dysfunction can result in neuropathic pain. Typical causes include nerve compression (e.g. by neuroma, tumour or herniated disc), various metabolic neuropathies cause by diabetes, renal insufficiency or undernutrition; or infectious causes e.g. Hepatitis C, HIV infection (HIV-peripheral neuropathy occurs in almost 50% of ARV-treated patients (Smyth et al, 2007)) ,syphilis, parasites (Teng and Mekhail, 2003).

9.1. **Management of neuropathic pain**

Neuropathic pain should be covered as PMB when the underlying aetiology is a PMB condition. Most cases of neuropathy respond to management of the underlying disease process or removal of the aetiological agent. In addition to the analgesics for chronic non cancer pain mentioned above, there are specific anti-neuropathic medicines that should be considered. Apart from trigeminal neuralgia, which responds well to carbamazepine, pharmacotherapy for neuropathic pain should be individualised as response can vary between individuals. A combination of medications is often necessary to control the pain. Using medication with different mechanisms of action and non-overlapping toxicities are recommended (Teng and Mekhail, 2003).

The South African guidelines, in line with other international guidelines, recommend four drug classes for neuropathic pain namely gabapentinoids, tricyclic antidepressants (TCAs), serotonin and noradrenaline reuptake inhibitors (SNRIs) and opioids (Chetty et al, 2012). Cost-effectiveness, contraindications, precautions and drug interactions should be considered when selecting the most appropriate option.

Non pharmacological interventions including physical rehabilitation and psychotherapy may form vital components of care.

9.1.1. Antidepressants

Low dose tricyclic antidepressants (e.g. amitriptyline) provide good efficacy in the management of neuropathic pain. When use is not contraindicated, TCA are recommended as first line as these are cost effective option and also require once a day dosing.

Serotonin and noradrenaline reuptake inhibitors (SNRIs) (e.g. duloxetine or venlaflaxine) block hyperalgesia induced by N-methyl-D-aspartate agonists and also have sodium channel blocking properties (Beers and Berkow, 1999; Moulin et al., 2007). Duloxetine has specifically shown more efficacy compared to venlafaxine for diabetic neuropathy. NEMLC acknowledges the efficacy of duloxetine for diabetic neuropathy, however the cost has been deemed restrictive for inclusion onto the EML list. When TCAs are contraindicated, SNRIs are recommended as PMB level of care.

9.1.2. Carbamazepine

Carbamazepine is the drug of first choice for trigeminal neuralgia (Moulin et al., 2007), and is recommended as PMB level of care.

9.1.3. Gabapentionoids

Gabapentin and pregabalin are both calcium channel α2δ ligands. Pregabalin is an analogue of gabapentin with the same mechanism of action but manifests linear pharmacokinetics and has higher affinity for the presynaptic calcium channel. In patients who show a partial response to either gabapentin/pregabalin or nortriptyline with diabetic polyneuropathy or postherpetic neuralgia, combined gabapentin/pregabalin and nortriptyline seems to be more efficacious than either drug given alone (Chandra K, et. al. 2006; Gilron I, et.al. 2009). It is recommended that α2δ Calcium channel ligands be included as PMB level of care for patients who may be refractory or resistant to other options discussed above.

Gabapentinoids are not recommended for HIV induced neuropathy. Gabapentin/pregabalin was no better than placebo in two studies of HIV-neuropathy and that carbamazepine is likely to have interactions with antiretroviral agents. Thus amitriptyline would be the primary treatment option in these patients (Hahn, et al. 2004; La Spina et al, 2001 ; Simpson et al, 2010).

9.1.4. Pyridoxine

Pyridoxine is recommended as PMB level of care for isoniazid induced polyneuropathy.

10. Side effects of opioids

Tolerance to the analgesic efficacy of opioids may develop with chronic use, dependence and abuse are further problems. The most common side effects are predictable consequences of opioid pharmacological actions and include nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation. Adverse events frequently lead to discontinuation of opioid therapy. Some of the adverse effects improve shortly after initiation of treatment or following an intended dose adjustment (Chetty et al., 2017).

10.1. Management of Opioid Related Side Effects

10.1.1. **Opioid** - associated side effects should be anticipated and appropriate counselling about common side effects and their management should be provided to patients before the first prescription.

10.1.2. **Constipation** – for patients on chronic opioids a laxative should be prescribed. Lactulose and Sennosides A and B are recommended as PMB level of care.

10.1.3. **Nausea and vomiting** – metoclopramide, promethazine and ondansetron are recommended as PMB level of care to manage nausea and vomiting for patients on chronic opioids.

11. Non-pharmacological approaches of pain management (Wiener 2008; SASA, 2013; Raff 2016).

Non-pharmacological approaches also play a key role in managing pain. Although these interventions are not discussed in detail in this document, upon referral from the treating doctor the following non-pharmacological interventions are recommended as PMB level of care.

- Non-surgical pain management interventions e.g. neurolytic ablation procedures or implantation of temporary analgesic pumps
- Access to psychological interventions including group support therapy
- Physiotherapy
- Occupational therapy

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