The three main principles of the WHO analgesic ladder are: “By the clock, by the mouth, by the ladder”.

By the clock:

To maintain freedom from pain, drugs should be given “by the clock” or “around the clock” rather than only “on demand” (i.e. PRN). This means they are given on a regularly scheduled basis. The frequency will depend on whether it is a long- or short-acting preparation.

By the mouth:

The oral route is usually the preferred route for ease of use in a variety of care settings. However, it may not be possible for all patients (e.g. end-of-life, unconscious, swallowing issues). When the oral route is not feasible, the least invasive route should be considered (e.g. sub-lingual or sub-cutaneous before intra-venous.). The intra-muscular route should never be used.

By the ladder:

If pain occurs there should be prompt administration of drugs in the following order:

- non-opioids (e.g. acetaminophen)
- as necessary, mild opioids (e.g. codeine)
- then strong opioids (e.g. morphine or hydromorphone) until the patient is free of pain.

Drug selection should be appropriate to the severity of the pain. It may be most appropriate with severe pain to begin at the top of the ladder with a strong opioid; it is not always necessary to start at step one. When pain is controlled, the patient should be maintained on the dose that is effective. It is usually not necessary to step down the ladder unless the cause of pain is believed to have resolved (e.g. post-operatively, in remission from cancer).

Along any step in the ladder, additional drugs – “adjuvants”- may be used. Adjuvants include: antidepressants (e.g. amitriptyline), anticonvulsants (e.g. gabapentin), corticosteroids (e.g. dexamethasone), and anxiolytics (e.g. diazepam).

This three step approach is inexpensive and 80-90% effective when optimally utilized.

Surgical intervention on appropriate nerves may provide further pain relief if drugs are not wholly effective. More invasive routes of administration (e.g. epidural) may be necessary for a small subset of patients.