Protocol for the Use of Tapentadol MR (Palexia® SR) in Acute and Chronic Pain

Brief Description of Drug: Tapentadol MR (Palexia® SR) is a strong opioid (acting primarily through opioid μ-receptor agonism) and a noradrenaline reuptake inhibitor in a modified-release (MR) formulation. Under the direction of a specialist pain team (the inpatient pain team, chronic pain team or palliative care, as appropriate for the patient and setting of care), it is an option for analgesia in selected patients with acute or chronic pain, who have not responded to conventional opioid therapy.

Trust Approved Indications: In adults with severe chronic pain and moderate to severe acute pain in whom:
1) conventional opioids have failed to provide adequate pain control and/or are not tolerated; and/or
2) a neuropathic pain component cannot be excluded (subject to the Place in Therapy limitations; see below)

Place in Therapy:
1) in pain with a neuropathic component: under specialist direction from the pain services, where conventional antineuropathic pain agents AND conventional strong opioids (morphine or oxycodone) have failed to provide adequate pain relief or are not tolerated
2) in pain without a neuropathic component: under specialist direction from the pain services, where conventional strong opioids (morphine or oxycodone) have failed to provide adequate pain relief or are not tolerated.

Prescribers should refer to the Guideline for the management of neuropathic pain and Adult pain management guidelines (available on the inpatient pain service intranet page) for further information. Tapentadol should be treated like other opioid medications and co-prescription with other opioids should normally be avoided.

Prescriber Restrictions: For initiation by the pain services only (inpatient pain team, chronic pain team, or palliative care).

Primary Care Prescribing: The initial prescription will be provided by the specialist pain team, and response to this will be reviewed twice within 8-10 weeks after initiation. If treatment is to be continued, the GP will be asked to take over prescribing. A written medication plan will be provided by the pain specialist to support this, detailing the indication, dosage, formulation, titration guidance, expected duration, monitoring requirements, and arrangements for specialist pain team advice and/or follow-up.

Formulation: Prolonged-release tablets (Palexia® SR): 50 mg (white) (28-tab/ 56-tab pack); 100 mg (yellow) (56-tab pack); 150 mg (pink) (56-tab pack); 200 mg (orange) (56-tab pack) 250 mg (red) (56-tab pack).

Tapentadol is a Schedule 2 controlled drug (CD2) and therefore subject to full CD requirements relating to its prescription, safe custody and the need to keep registers.

Dosage Regimen: Prolonged-release tablets (Palexia® SR): initially 50 mg every 12 hours, adjusted according to response; max. 500 mg daily.

Unwanted Effects and Contraindications:
The adverse effect profile of tapentadol is similar to that of conventional opioids, including, for example, nausea and vomiting (particularly in initial stages), constipation, dizziness and somnolence. At higher doses, it may cause respiratory depression and reduced consciousness.

Tapentadol is contraindicated in patients who have hypersensitivity to tapentadol or any of its excipients. In common with other opioids, tapentadol is contraindicated in patients who have acute respiratory depression; depressed consciousness; head injury or raised intracranial pressure (opioid analgesics interfere with pupillary responses vital for neurological assessment); or are at risk of paralytic ileus.

Tapentadol should not be used in severe renal impairment. In significant hepatic impairment, do not exceed an initial maximum daily dose of 50 mg (with prolonged-release tablets). Tapentadol is not recommended for use during and immediately

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before labour and delivery. Limited data suggests tapentadol is excreted in breast milk, and therefore its use during breast feeding is not recommended.

**Major Interactions:**
Caution must be exercised in the co-prescription of tapentadol with other agents that affect synaptic neurotransmitter concentrations. The additive effects may cause adverse cardiovascular events (including hypertensive crisis) due to norepinephrine accumulation, or serotonin toxicity (tachycardia, hypertension, hyperthermia, altered mental state) due to serotonin accumulation.

In particular:
- Tapentadol must not be used in patients taking **monoamine oxidase inhibitors** (MAOIs) or those who have taken MAOIs within last 14 days, due to the risk of adverse cardiovascular events such hypertensive crises.
- Caution must be exercised when considering the use of tapentadol in patients taking **drugs that effect serotonin reuptake** (e.g. tramadol, selective serotonin reuptake inhibitors, serotonin–noradrenaline reuptake inhibitors), due to the risk of serotinergic toxicity

Caution must be exercised when considering the use of tapentadol in patients taking **drugs that depress consciousness** such as benzodiazepines, barbiturates and other opioids, as the sedative effects may be additive. Dosage reduction (of tapentadol and/or the other agent) must be considered. Care must also be taken when combining tapentadol with mixed μ-opioid agonist/antagonists such as pentazocine, or partial μ-opioid agonists such as buprenorphine, which may interfere with the activity of tapentadol at the opioid μ-receptor.

Caution must be exercised when considering the use of tapentadol in patients taking **drugs that are strong inducers of hepatic enzymes** (e.g. rifampicin, phenobarbitone, St John’s Wort). The effect of tapentadol may be reduced during co-administration, and may increase following withdrawal of the enzyme inducer.

**Advice to Patients:** Patients must be:
- Warned about the effect of tapentadol on their ability to drive and use machinery
- Advised that tapentadol may enhance the effects of alcohol, which should ideally be avoided
- Asked to report any side effects to their GP or pain specialist, and to report if they become pregnant

**Monitoring Including Criteria for Stopping:**
Tapentadol has the potential for abuse and addiction. All patients treated with active substances that have opioid μ-receptor activity should be monitored carefully for signs of dependence/abuse/addiction, although in practice this is not usually a problem in therapeutic use.

**References:**
Tapentadol monograph. British National Formulary (December 2016)
Tapentadol summary of product characteristics. [https://www.medicines.org.uk/emc/medicine/28375](https://www.medicines.org.uk/emc/medicine/28375); Grünenthal Ltd, last updated 15th October 2014