SHARED CARE GUIDELINE FOR TAPENTADOL SUSTAINED RELEASE (PALEXIA SR ®) AS A SECOND LINE OPIATE OPTION WHERE MORPHINE HAS NOT BEEN TOLERATED.

INDICATION

This shared care guideline has been prepared to support the transfer of responsibility for prescribing Tapentadol sustained release (Palexia SR®) from secondary to primary care.

Tapentadol is a schedule 2 controlled drug. It is a centrally acting oral opioid analgesic combining two mechanisms of action: Mu-opioid receptor agonism and noradrenaline reuptake inhibition (MOR-NRI). It is licensed for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics.

Tapentadol sustained release capsules (Palexia SR®) have been given an AMBER categorisation within the 'traffic light' system as a second line opiate option where morphine has not been tolerated. Use of the drug is expected to be in accordance with the British Pain Society guidance on the use of opioids in persistent pain, 'Opioids Aware'.

This guideline is intended to apply to

- patients who have been initiated and prescribed tapentadol sustained release capsules (Palexia SR®) for 28 days by a consultant and in whom response to treatment has been assessed.
- patients who are under the care of a Dorset Community Pain Service consultant and who have been initiated and prescribed tapentadol by a GP after a documented direct discussion with a consultant from the Dorset Community Pain Service.

This guideline **does not** cover the use of the immediate release formulation of tapentadol.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of tapentadol can be shared between the consultant and general practitioner (GP).

GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the decision on continuing/changing treatment remains with the consultant.

If a consultant asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the Consultant, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

REFERRAL AND INITIATION

Shared Care is only appropriate if it provides the optimum solution for the patient. Patients will only be referred to the GP once the GP has agreed in each individual case.

CONSULTANT RESPONSIBILITIES	
1	To assess the suitability of the patient for treatment with tapentadol sustained release. Ensuring it is in line with the local recommendation.
2	Determine a management strategy and ensure follow-up in conjunction with the GP.
3	Where appropriate: • to initiate and stabilise the patient on treatment, providing at least 28 days' treatment; A Dorset Community Pain Service consultant will provide a clinic letter detailing the dosing regimen for treatment initiation. Patients can contact the Dorset Community Pain Service over the phone with queries for the first 28 days of treatment; if needed, additional appointments with the pain consultant will be offered and any changes in the treatment plan promptly communicated to the patient's GP. • assess response to first month's treatment; • obtain consent from the patient's GP to continue prescribing once treatment has been stabilised; A Dorset Community Pain Service consultant will seek an agreement with the GP prior to agreeing a treatment plan with the patient; • monitor the patient and their therapy at appropriate intervals; • ensure therapy is discontinued where applicable.
4	To explain the possible side effects of the medication to the patient and emphasise the importance of regular monitoring
5	Ensure that patients know what to do and who to contact if they experience adverse events or an exacerbation of their condition.
6	To provide the GP with appropriate prescribing information and any additional information requested, and to offer telephone support.
7	To agree with the GP arrangements for any ongoing monitoring of the patient's condition to ensure the safe use of tapentadol.
8	To be available for advice if the patient's condition changes and to arrange follow up in clinic at intervals to monitor the progress of the disease and review the continued use of tapentadol.
9	To ensure that procedures are in place for the rapid re-referral of the patient by the GP.
10	To ensure the patient has given informed consent to their treatment.
11	To liaise with the GP on any suggested changes in prescribed therapy / notify GP of any changes in the patient's condition as assessed on follow up.
12	To inform the GP when it is considered appropriate to discontinue treatment.
13	Report any adverse events. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Grunenthal Ltd (telephone 0870 351 8960).

GENERAL PRACTITIONER RESPONSIBILITIES	
1	Initially, to refer the patient to the specialist for pain management and advice on treatment.
2	To prescribe tapentadol sustained release at the agreed dose after the initial 28-day period and monitor the patient's ongoing response to tapentadol sustained release or to initiate prescribing of tapentadol sustained release after a documented direct discussion with a consultant from the Dorset Community Pain Service.
3	Carry out any agreed monitoring reporting the results to the specialist if appropriate.

GENERAL PRACTITIONER RESPONSIBILITIES	
4	To deal with general health issues of the patient.
5	To liaise with the consultant regarding any complications of treatment.
6	To consider any side-effects reported by the patient and to discuss with the consultant if necessary.
7	To avoid or appropriately manage the drug interactions as listed below and in the current BNF.
8	To ensure ongoing reviews of the patient's condition.
9	Ensure that therapy is discontinued where applicable.
10	Report any adverse events. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Grunenthal Ltd (telephone 0870 351 8960).

PATIENT'S ROLE (OR THAT OF CARER)	
1	Report to the specialist or GP if he/she does not have a clear understanding of the treatment.
2	Attend appropriate consultant and GP appointments.
3	Share any concerns in relation to treatment with tapentadol with their GP or consultant.
4	To report pregnancy or suspected pregnancy during treatment with tapentadol.
5	To avoid alcohol during treatment with tapentadol.
6	To seek help urgently from a healthcare professional if suspected side effects appear, or the patient is otherwise unwell.

ROLE OF COMMUNITY PHARMACIST	
1	Provide patients with written and/or verbal information about tapentadol sustained release.
2	Ensure access to medicines management support to encourage concordance, where appropriate through a Medication Use Review.

SUPPORTING INFORMATION

Assessment and monitoring

- Oral, sustained release morphine sulphate has typically been recommended as first line strong opioid (Step III of WHO analgesic pain ladder). Tapentadol sustained release is recommended in patients for who sustained release morphine sulphate is ineffective or not tolerated.
- Prior to initiation of treatment with tapentadol, the patient should be given relevant information and advice, and all contraindications should be excluded (see below).

Dosage and Administration

- Tapentadol sustained release (Palexia SR®) is available in 50mg, 100mg, 150mg, 200mg and 250mg sustained release tablets.
- In patients currently not taking opioid analgesics, start with a dose of 50mg BD (every 12 hours).
- For patients currently taking opioid analgesics, a higher initial dose may be required taking into account previous opioid type and dose.
- Titration should be in increments of 50mg twice daily every three days to achieve adequate pain control whilst minimising undesirable events.
- Total daily doses greater than 500mg have not yet been studied and are not recommended.

- Tapentadol should be taken with sufficient liquid. tapentadol can be taken with or without food.
- There is no dose adjustment recommended in patients with mild or moderate renal impairment.
- There is no dose adjustment recommended in patients with mild hepatic impairment.

Contraindications

Tapentadol is **contraindicated** in:

- Patients with hypersensitivity to tapentadol or to any of the excipients (including lactose)
- Situations where active substances with mu-opioid receptor agonist activity are contraindicated, i.e. patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercapnia.
- In any patient who has or is suspected of having paralytic ileus.
- In patients with acute intoxication with alcohol, hypnotics, centrally acting analgesics, or psychotropic active substances.

Tapentadol is **not recommended** in:

- Patients with severe hepatic impairment due to lack of trial data.
- Patients with severe renal impairment due to lack trial data.
- Children or adolescents below 18 years of age
- Patients with a seizure disorder, due to a lack of trial data

Special Warnings

- Tapentadol has a potential for abuse and addiction. This should be considered when prescribing and all patients receiving ongoing treatment with tapentadol should be carefully monitored for potential signs of abuse, misuse, or diversion.
- Tapentadol sustained release should be used with caution in patients with moderate hepatic impairment. Treatment in these patients should be initiated at the lowest available dose strength, i.e. 50 mg tapentadol sustained release tablet, and not be administered more frequently than once every 24 hours. At initiation of therapy a daily dose greater than 50 mg tapentadol sustained release tablet is not recommended.
- At high doses or in mu-opioid receptor agonist sensitive patients, tapentadol may produce dose-related respiratory depression. Therefore, should be administered with caution to patients with impaired respiratory functions and should be employed only under careful medical supervision at the lowest effective dose in such patients. If respiratory depression occurs, it should be treated as any mu-opioid receptor agonist-induced respiratory depression.
- A dose adaptation in elderly patients is not required. However, as elderly patients are more likely to have decreased renal and hepatic function, care should be taken in dose selection.
- Tapentadol should not be used in patients who may be particularly susceptible to the intracranial effects of carbon dioxide retention (such as those with evidence of increased intracranial pressure, impaired consciousness, or coma). Analgesics with mu-opioid receptor agonist activity may obscure the clinical course of patients with head injury.
- Tapentadol should be used with caution in patients with head injury and brain tumours.
- Active substances with mu-opioid receptor agonist activity may cause spasm of the sphincter of Oddi therefore tapentadol should be used with caution in patients with biliary tract disease, including acute pancreatitis.
- Withdrawal symptoms could occur after abrupt discontinuation of treatment with tapentadol, or when switching to another opioid drug. When a patient no longer requires therapy with tapentadol, it is advisable to taper the dose gradually to prevent symptoms of withdrawal.

Drug Interactions

- Medicinal products like benzodiazepines, barbiturates and opioids may enhance the risk of respiratory depression if taken in combination with tapentadol sustained release. Central nervous system (CNS) depressants (e.g. benzodiazepines, antipsychotics, H1- antihistamines, opioids, alcohol) can enhance the sedative effect of tapentadol and impair vigilance. Therefore, when a combined therapy of tapentadol sustained release with a respiratory or CNS depressant is contemplated, the reduction of dose of one or both agents should be considered.
- There have been reports of serotonin syndrome in a temporal connection with the therapeutic use of tapentadol in combination with serotoninergic medicinal products such as selective serotonin re-uptake inhibitors (SSRIs).
- Treatment with tapentadol should be avoided in patients who are receiving monoamine oxidase (MAO) inhibitors or who have taken them within the last 14 days due to potential additive effects on synaptic noradrenaline concentrations which may result in adverse cardiovascular events, such as hypertensive crisis.
- For patients on tapentadol treatment, caution should be exercised if concomitant drug administration of strong enzyme inducing drugs (e.g. rifampicin, phenobarbital, St John's Wort (hypericum perforatum)) starts or stops, since this may lead to decreased efficacy or risk for adverse effects, respectively.
- Concomitant administration of tapentadol with strong inhibitors of the UGT1A6, UGT1A9 and UGT2B7 isoforms (e.g. ketoconazole, fluconazole, meclofenamic acid) may lead to increased systemic exposure of tapentadol.

Pregnancy, lactation, labour and delivery

- There is very limited amount of data from the use in pregnant women. Studies in animals have not shown teratogenic effects. However, delayed development and embryotoxicity were observed at doses resulting in exaggerated pharmacology. Tapentadol sustained release should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.
- Tapentadol is not recommended for use in women during and immediately before labour and delivery. Due to the mu-opioid receptor agonist activity of tapentadol, new-born infants whose mothers have been taking tapentadol should be monitored for respiratory depression.
- There is no information on the excretion of tapentadol in human milk. From a study in rat pups, it was concluded that tapentadol is excreted via milk. Therefore, a risk to the suckling child cannot be excluded, and tapentadol should not be used during breast feeding.

Side Effects

Side effects associated with all opioid drugs – frequency common (more than 1/100, but less than 1/10) or very common (more than 1/10):

Biliary spasm; bradycardia; confusion; constipation; dependence; difficulty with micturition; dizziness; drowsiness; dry mouth; dysphoria; euphoria; flushing; hallucinations; headache; hypotension (larger doses); miosis; mood changes; muscle rigidity (larger doses); nausea (particularly in initial stages); oedema; palpitation; postural hypotension; pruritus; rash; respiratory depression (larger doses); sexual dysfunction; sleep disturbances; sweating; tachycardia; ureteric spasm; urinary retention; urticaria; vertigo; visual disturbances; vomiting (particularly in initial stages)

Side effects also associated with tapendatol (frequency not known):

Abdominal discomfort; anxiety; ataxia; decreased appetite; diarrhoea; dysarthria; dyspepsia; hypoaesthesia; malaise; muscle spasms; paraesthesia; seizures; tremor; weight loss

Effects on ability to drive and use machines

Tapentadol sustained release may have major influence on the ability to drive and use machines due to the fact that it may adversely affect central nervous system functions. This has to be expected especially at the beginning of treatment, at any change of dosage as well as in connection with alcohol or tranquilisers. Patients should be cautioned as to whether driving or use of machines is permitted.

This guideline was prepared using information available at the time of preparation, but users should always refer to the manufacturer's current edition of the Summary of Product Characteristics (SPC) for more details. SPC's are usually available to view via the electronic medicines compendium at: www.emc.medicines.org.uk

COST

Prices at of August 2017[2]

Strength	**28 tablet pack**	**56 tablet pack**
50mg M/R capsules	£12.46	£24.91
100mg M/R capsules	£49.82	
150mg M/R capsules	£74.73	
200mg M/R capsules	£99.64	
250mg M/R capsules	£124.55	

Annual treatment cost: £323.83 to £1619.15 (dose range of 50mg BD to 250mg BD).

REFERENCES

1. Summary of product characteristics for Palexia SR® (Tapentadol). Accessed August 2017
2. BNF online (August 2017)

Developed by	Dr Maher Michel	October 2011
Reviewed by	Celina Tadel and CCG medicines management team	May - August 2017
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OPIATE DOSE CONVERSION CHART, ORAL AND OPIATE PATCHES

Use the conversion chart to work out the equivalent doses of different opiate drugs. The formula to work out the dose is under each drug name. This is to be used as a guide rather than a set of definite equivalences. Some doses have been rounded up or down to fit with the preparations available.

Oral morphine SR should always be the first line treatment for the management of severe chronic pain in adults requiring treatment with an opioid analgesic (Step III of WHO ladder). Tapentadol should only be considered as a second-line option for those unable to tolerate morphine SR or where morphine SR has failed to provide adequate pain control.

Oral opiate (mg)						Opiate by patch
Morphine 12hr dose (BD) MST/Zomorph	**Morphine 24 hour total dose**	**Tapentadol 12hr dose (BD)** Palexia SR	**Tapentadol 24-hour total dose**	**Oxycodone 12hr dose (BD)** Oxycontin SR	**Oxycodone 24-hour total dose**	**Fentanyl Transdermal Patch change every 72 hrs**
		Palexia SR: Oxycodone CR- 5:1 Palexia SR: oral morphine 2.5:1	Calculated by multiplying 24hr oral morphine dose by 2.5		Calculated by dividing 24hr oral morphine dose by 2	If stopping or starting patches refer to Fentanyl SPC for guidance.
	5					
	10					
	15					
10	20			5	10	
15	30	50	100	7.5	15	12
30	60	50	100	15	30	12
45	90	100	200	25	50	25
60	120	150	300	30	60	37
90	180	200	400	45	90	50
120	240	250	500	60	120	62

When switching between opioids, the nature of the previous medicinal product, administration and the mean daily dose should be taken into consideration. The patient should be counselled on the likelihood of it being a more difficult period whilst they change between drugs. They may experience an increase in pain before it becomes controlled again and they may require dose adjustments more or less frequently than expected. After initiation of therapy the dose should be titrated individually to a level that provides adequate analgesia and minimises undesirable effects

Renal impairment:

Morphine metabolites may accumulate & usually a dose reduction is required. Tapentadol requires no dose adjustment for patients with mild or moderate renal impairment