714FM.3 MANAGEMENT OF NEUROPATHIC PAIN IN ADULTS

This guideline covers the treatment of neuropathic pain in adults in primary and secondary care. Paediatric patients with neuropathic pain should be referred to secondary care for Specialist advice.

Contents

Glossary of terms

AEC	Anticholinergic effect on cognition
CNS	Central nervous system
CBT	Cognitive behavioural therapy
CIs	Contraindications
CKS	Clinical knowledge summaries
CrCl	Creatinine clearance
CRPS	Complex regional pain syndrome
DVLA	Driver and Vehicle Licensing Agency
ECG	Electrocardiogram
MSK	Musculoskeletal Service
NNT	Number needed to treat
PILs	Patient information leaflets
SPC	Summary of product characteristics
TCA	Tricyclic antidepressants

GP Referral Pathway for Neuropathic Pain

If RED flags present, REFER on 2 week referral pathway as appropriate
Any sudden, rapid deterioration of pain control or condition associated with pain, **reassess red flags for possible onward referral**
Provide ESSENTIAL INFORMATION Table 1 (below) for ALL referrals.

SPINAL Neuropathic Pain
Initial presentation of low **back pain WITH sciatica or cervical radiculopathic pain** after 6 to 8 weeks of analgesia with NO improvement

↓

REFER to MSK
Investigations triage, +/- psychosocial support.
MSK may refer into Neuropathic Pain Pathway or discharge patient back to GP

↓

NON-SPINAL Neuropathic Pain
(e.g. post herpetic neuralgia, post-surgical pain)
REFER to Pain Team.
For specific conditions below, REFER to the Specialist Team for initial diagnosis:
Trigeminal neuralgia - refer to Maxillofacial/Neurology;
Diabetic neuropathy - refer to Diabetes;
CRPS – refer to Orthopaedics.

↓

Neuropathic Pain Treatment Pathway

At every step

- Check Table 2 for prescribing information.
- Give patient realistic expectations. The treatment process may not remove pain completely.
- Provide self-help advice e.g. Pain Society PILs and pain assessment tools (Useful Resources – Appendix 1).
- Consider non-pharmacological treatment e.g. CBT (via referral to Healthy Minds).
- If intolerance occurs, step down dose to the level prior to which side effects occurred.
- Review medicine after 8 weeks at max tolerated dose. If pain has stabilised, attempt dose reduction/ withdrawal*. If no improvement, move to the next step. Check RED FLAGS for URGENT referral.
- Prescribe capsaicin 0.075% cream if patient unwilling to take orals, intolerance or CIs and localised area

Primary Care

Step 1: Trial of a TCA at max tolerated dose for 8 weeks. 1st choice: Amitriptyline
Check anticholinergic burden of all drugs before starting a TCA. See Table 2 and www.medichec.com.
If sedation is problematic, switch to imipramine. If cardiovascular intolerance (e.g. palpitations), switch to nortriptyline. If intolerable anticholinergic effects before a reasonable dose is achieved, go to step 2.

↓

REVIEW* If no improvement, withdraw **TCA** and move to next step.

↓

Step 2: Trial of Gabapentin at max tolerated dose for 8 weeks

↓

REVIEW* and REFER if no improvement
For optimisation and consideration of alternative treatments e.g. duloxetine, pregabalin.
Whilst awaiting appointment, continue to step 3.

↓

Step 3: Trial of gabapentin and TCA (if appropriate) at max tolerated doses for 8 weeks.
Amitriptyline low dose for nocturnal sedation benefit may be prescribed if appropriate

Secondary Care

↓

Step 4: Secondary care initiates trial of duloxetine or pregabalin at max tolerated dose for 8 weeks

↓

Secondary Care REVIEW* after 8 weeks' treatment at max tolerated doses
Secondary care review at 3 and 6 months. If no improvement, WITHDRAWAL recommended.
If improvement, continuation recommended.

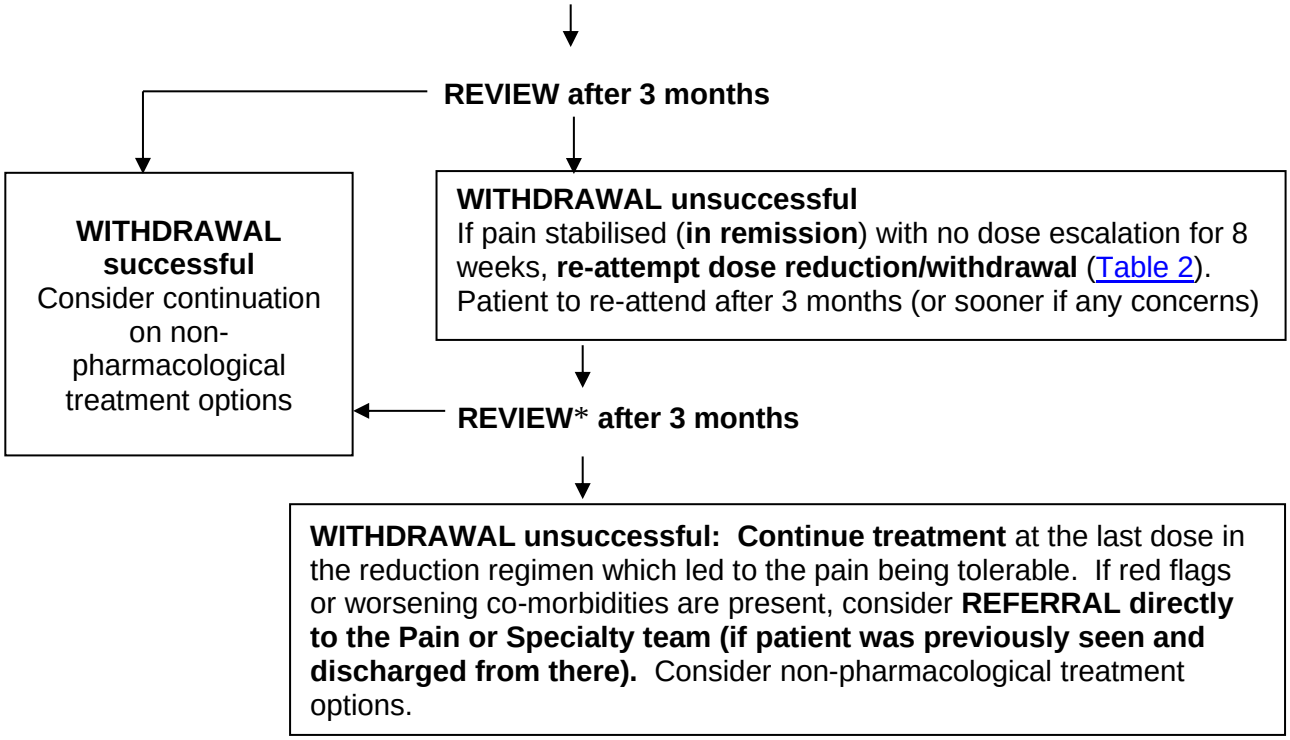
↓

Step 5: Secondary care recommend other treatments e.g. antiepileptics

Neuropathic Pain Treatment Pathway (continued)

*Dose reduction and withdrawal in primary or secondary care

REVIEW after 8 weeks' treatment at max tolerated doses
If pain stabilised (**in remission**) with no dose escalation for 8 weeks, attempt dose reduction and withdrawal (Table 2).



NOTE

- Regular efforts should be made to reduce doses and gradually withdraw treatments, particularly as many drugs are associated with safety and/or dependence issues following long-term use.
- If total withdrawal is unsuccessful, patients should be engaged in discussion about long term goals and non-pharmacological management.

Neuropathic pain definition and treatment goals

Neuropathic pain is either pain of nerve origin or pain that has not resolved within the normal healing time for a condition (pain which has continued for three months or longer).

The goal of neuropathic pain treatment is to support initial symptomatic relief such that patients are sufficiently able to engage in non-pharmacological treatment, e.g. light exercise, physiotherapy, relaxation techniques and rehabilitation. Pain free status is not usually achievable and 20 - 50% reduction in pain is a commonly used end-point in clinical trials.

Table 1: REFERAL AND DISCHARGE INFORMATION

Essential information to be communicated to secondary care prior to referral

1. Summary of clinically relevant context.
2. History of pain including presence of red flags if relevant.
3. Full drug history (all drugs, strengths, doses and durations of treatment for all indications).
4. Drug and non-drug treatment(s) trialed for the treatment of pain.
5. Dose and duration when drug treatment(s) have been deemed
   - Successful.
   - Unsuccessful/discontinued and reason(s) for discontinuation.

Information to be communicated from secondary to primary care at discharge

1. Short and long term treatment plan.
2. Plan for dose reduction of other medicines e.g. opioids.
3. Recommendation of when referral back to secondary care may be required.

Trigeminal neuralgia referral

Refer patients to Maxillofacial or Neurology teams. Whilst waiting for an appointment, start carbamazepine (see Table 2 for prescribing information). See also NICE CKS https://cks.nice.org.uk/trigeminal-neuralgia.

Red flags for trigeminal neuralgia

- Sensory changes: Deafness or other ear problems.
- History of skin or oral lesions that could spread perineurally.
- Pain only in the ophthalmic division of the trigeminal nerve (eye socket, forehead, and nose), or bilaterally.
- Optic neuritis.
- Family history of multiple sclerosis.
- Age of onset before 40 years.

Table 2: PRESCRIBING INFORMATION

General

- For full details, refer to the Summary of Product Characteristics (SPC) www.medicines.org.uk/emc and the BNF.
- Doses in this guideline are lower than in the SPCs and BNF. They are based on the views of local Specialists in the context of the needs of most neuropathic pain patients in primary care. Doses can be exceeded if clinically appropriate.
- **Medicines should be up-titrated to a dose which manages the pain and minimises side effects. When this is achieved, no further dose increases should take place.**

Pain medicines and driving

- The DVLA produces comprehensive guidance for medical professionals on assessing fitness to drive. https://www.gov.uk/guidance/assessing-fitness-to-drive-a-guide-for-medical-professionals.
- The British Pain Society guideline Driving and Pain https://www.rcoa.ac.uk/sites/default/files/FPM-Driving-and-Pain-members-information.pdf states: Doctors should inform their patients that most pain medication may impair driving, and that patients should not drive if this is the case. Patients are most at risk of impairment when commencing a new pain medicine, when increasing or reducing the dose, when another drug is added that may affect driving ability, when medication is taken in conjunction with alcohol.

Anticholinergic effect on cognition (AEC)

- Check the AEC score of all of the patient's medicines before starting neuropathic pain medicines. See www.medichec.com.

Drug	AEC score
Amitriptyline	3
Carbamazepine	1
Citalopram	1
Duloxetine	0
Escitalopram	0
Gabapentin	0
Imipramine	3
Nortriptyline	3
Pregabalin	0
Sertraline	1
Venlafaxine	0

Source www.medichec.com accessed 23 March 2020

- A score of 3 (individual drug score or total score for all drugs) indicates the need to review, and consider withdrawal or switching in order to reduce AEC risks.
- Note: drug dosage is not taken into account when using the above scale

Tricyclic Antidepressants (TCAs): Amitriptyline, imipramine, nortriptyline: GREEN

Contraindications

Severe liver disease, immediate recovery period after a myocardial infarction (MI), arrhythmias, heart block, during the manic phase of bipolar disorder, concomitant use of monoamine oxidase inhibitors (MAOIs) or other antidepressants at high doses due to increased risk of CNS toxicity.

Cautions

Cardiovascular disease; chronic constipation; diabetes; epilepsy; history of bipolar disorder; history of psychosis; hyperthyroidism; increased intra-ocular pressure; patients with a significant risk of suicide; phaeochromocytoma; prostatic hypertrophy; susceptibility to angle-closure glaucoma; urinary retention,

Drug interactions

TCAs and anticholinergic effect on cognition – see above.

TCAs with gabapentin, pregabalin and commonly used antidepressants

Amitriptyline or nortriptyline (at doses recommended in this guideline) may safely be added to the following:

- Gabapentin (increased risk of hyponatraemia).
- Pregabalin
- Citalopram 20 mg PO daily (increased risk of hyponatraemia)
- Duloxetine 60 mg PO daily (increased risk of hyponatraemia)
- Sertraline 50 mg PO daily (increased risk of hyponatraemia).

For combinations of TCAs with the above antidepressants at higher doses, or with other antidepressants, contact the secondary care Specialist or the Medicines Resource Centre Bucks.medicinesresourcecentre@nhs.net or 01494 425355.

Equivalent antidepressant doses of TCAs and commonly used antidepressants[10]

Amitriptyline	**60 mg**
Citalopram	**18 mg**
Escitalopram	**9 mg**
Imipramine	**70 mg**
Nortriptyline	**50 mg**
Sertraline	**50 mg**
Venlafaxine	**75 mg**

TCAs with opioids can have CNS depressant effects

Time to response: 6 to 8 weeks

Dose

TCA UP-TITRATION

- Increase daily dose by 10 mg each week
- Pain consultants advise a maximum daily dose of 30 to 40 mg if patient derives benefit with limited side effects.

TCA DOWN-TITRATION / WITHDRAWAL

- Reduce daily dose by 10 mg each week over a four week period.

Dose for nocturnal sedation effect: 10 to 25 mg PO at night.

Side effects

Dry mouth, sedation, reduced concentration, blurred vision, constipation, difficulty in micturition, cardiovascular effects (e.g. ECG changes, arrhythmias, postural hypotension, tachycardia, syncope – more common with higher doses).

Counselling: If side effects experienced, reduce dose by 10 mg for 2 weeks before attempting an increase. Take 1 to 2 hours before bed; if morning sedation/hangover effect is problematic, the dose may be taken in the early evening e.g. 6pm.

Gabapentin and Pregabalin: **Schedule 3 (CD No Register Exempt Safe Custody)**

Caution regarding abuse and dependence

MHRA Drug Safety Update April 2019 https://www.gov.uk/drug-safety-update/pregabalin-lyrica-gabapentin-neurontin-and-risk-of-abuse-and-dependence-new-scheduling-requirements-from-1-april[9]

Public Health England guidance PHE-NHS England Pregabalin and Gabapentin Advice Dec 2014[5]

Gabapentin **GREEN**

Cautions

- Increased risk of CNS and severe respiratory depression[5]. Consider reduced doses in elderly, patients with compromised respiratory function, respiratory or neurological disease, or renal impairment, and patients taking other CNS depressants (MHRA Oct 2017).[6]
- If a patient develops acute pancreatitis, gabapentin discontinuation should be considered
- History of substance abuse, psychotic illness.
- Diabetes mellitus.

Drug interactions

- Gabapentin with opioids or TCAs: CNS depression.
- Gabapentin with TCAs or duloxetine: increased risk of hyponatraemia

Time to response: 2 weeks. Time to full response; several weeks.

Dose

Two speeds of up-titration are possible.

- **SLOW UP-TITRATION** for milder pain, elderly, frailty, renal impairment (see renal dosing below) and patients less tolerant of side effects.
- **FAST UP-TITRATION** for severe pain in younger, fitter patients. This is the FASTEST rate of up-titration recommended.

Gabapentin SLOW UP-TITRATION

DAY	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6
1 to 2	100 mg daily^	100 mg three times daily	200 mg three times daily	300 mg three times daily	400 mg three times daily	600 mg three times daily. Continue on this dose
3 to 4	100 mg twice daily	100 mg three times daily				
5 to 7	100 mg three times daily	100 mg three times daily				

Gabapentin FAST UP-TITRATION

DAY	WEEK 1	WEEK 2	WEEK 3
1 to 2	300 mg daily^	300 mg morning 300 mg midday 600 mg at night	600 mg three times daily. Continue on this dose.
3 to 4	300 mg twice daily	300 mg morning 600 mg midday 600 mg at night	
5 to 7	300 mg three times daily	600 mg three times daily	

^after 6pm as a test dose. If tolerated, continue:

- If side effects occur, step down dosing by one stage and continue treatment.
- Although the licensed maximum daily dose is 3600 mg, local Specialists advise that due to gabapentin's non-linear pharmacokinetics, tolerability becomes significantly less reliable with increased side effects after 1800 mg daily. Therefore they advise using a maximum dose of 1800 mg daily.
- For frail, elderly patients, only titrate up to 300 mg PO three times daily prior to referral. For younger, fitter patients, titrate up to 600 mg three times daily.
- QUANTITY to prescribe for the first 28 to 30 days: FAST up-titration: 140 x 300 mg capsules; LOW up-titration: 140 x 100 mg capsules.

Gabapentin doses based upon renal function

Creatinine clearance (CrCl) (ml/min)	Total daily dose (mg/day) in divided doses
≥80	**900 to 3600**
50 to 79	**600 to 1800**
30 to 49	**300 to 900**
15 to 29	**150 to 600 mg (150 mg = 300 mg on alternate days)**
<15	**150 to 300 mg (150 mg = 300 mg on alternate days)**

Gabapentin DOWN-TITRATION / WITHDRAWAL

- **Total daily dose ≤900 mg:** Reduce total daily dose by 100 mg every 4 days.
- **Total daily dose >900 mg:** Reduce total daily dose by 300 mg every 4 days unless observations of emergent symptoms are required, in which case more gradual dose tapering is needed, as seen in table below:

	Week 1	Week 2	Week 3
Morning	300 mg	300 mg	
Midday	300 mg		
Night	300 mg	300 mg	300 mg

- When cross tapering from gabapentin to either duloxetine or pregabalin, the dose of gabapentin should be reduced in accordance with the above table until the patient is taking gabapentin 300 mg daily.

Side effects:
Diarrhoea, dry mouth, reduced concentration dyspepsia, nausea and vomiting, abdominal pain, weight gain, memory loss.

Pregabalin **AMBER INITIATION**

Pregabalin is initiated by Specialist team and continued by GPs.
Specialist responsibilities:

- Prescribe the first 28 days' supply.
- Provide a Patient Advice sheet which summarises dosing, adverse effects and requests the patient to contact the Specialist team by telephone if there is intolerance (normally occurs within the first month).
- Issue a clinic letter to the GP which advises:
  - the date of the next clinic review (follow-up at 3 and 6 months)
  - to prescribe acutely, and not put on as a repeat
  - to stop prescribing after 3 months if feedback from the Specialist about efficacy and dosing has not been received.
- Review the patient at 3 and 6 months.
- Advise on dose reduction if withdrawal is appropriate.

Cautions: See gabapentin. Also: Conditions that may precipitate encephalopathy; severe congestive heart failure.

Drug interactions: Pregabalin with opioids or TCAs: CNS depression

Time to response: 2 weeks

Dose

Pregabalin UP-TITRATION

	Week 1	**Week 2**	**Week 3**
Morning	50 mg	75 mg	150 mg
Evening	50 mg	75 mg	150 mg

- The patient may start treatment using 25 mg in the morning and 50 mg at night to improve tolerability.
- Pregabalin is more cost effective if prescribed TWICE DAILY.
- When the patient is stabilised on long term treatment, pregabalin should be prescribed as a single strength as a twice daily dose (after using up existing stock at home from titration doses).
- Dosing in the elderly and in renal impairment:
  For older patients (>75 years) or those with renal impairment: initially 25 mg PO twice daily. If CrCl <30 ml/min, it may be appropriate to give this as a single daily dose of 25 mg as per table below:

Pregabalin doses according to renal function

Creatinine clearance (ml/min)	**Total daily dose**		**Dose regimes**
	Starting dose (mg/day)	**Max dose (mg/day)**	
≥60	150	600	BD or TDS
30 to 60	75	300	BD or TDS
15 to 30	25 to 50	150	OD or BD
<15	25	75	OD

Pregabalin DOWN-TITRATION / WITHDRAWAL

- Reduce total daily dose by 50 to 75 mg per week.
- Suggested withdrawal schedule for a dose of 150 mg twice a day:

	Week 1	**Week 2**	**Week 3**	**Week 4**	**Stop and review patient**
Morning	150 mg	75 mg	50 mg	25 mg	
Night	75 mg	75 mg	50 mg	25 mg	

Side effects:
Appetite changes; blurred vision; confusion; constipation; diplopia; disturbances in muscle control and movement; dizziness; drowsiness; dry mouth; euphoria; flatulence; reduced concentration, impaired memory; insomnia; irritability; malaise; oedema; paraesthesia; sexual dysfunction; speech disorder; visual disturbances; visual field defects; vomiting; weight gain.

Duloxetine — AMBER RECOMMENDATION

Contraindications

Hepatic impairment, severe renal impairment (avoid if CrCl <30 ml/min), uncontrolled hypertension.

Cautions

Bleeding disorders; cardiac disease; elderly; history of mania; history of seizures; hypertension, raised intra-ocular pressure; susceptibility to angle-closure glaucoma.

Drug interactions

- Duloxetine with tramadol - potential for increased serotonergic effects (see BNF).
- Duloxetine with amitriptyline or nortriptyline: Increased risk of hyponatraemia.
- Duloxetine with imipramine: Increased risk of serotonin syndrome.

Time to response: 2 to 4 weeks

Dose

Duloxetine UP-TITRATION

	Week 1	Weeks 2 to 4**
Night	30 mg	60 mg

**dependent upon response to initial dose.

- The licensed maximum dose for diabetic neuropathy is 120 mg in divided doses. Trials have shown no significant superior efficacy of 120 mg daily compared to 6 mg daily (NNT for 50% pain reduction 5.7 and 5.8 respectively).
- Avoid if CrCl <30 ml/min.

Duloxetine DOWN-TITRATION / WITHDRAWAL

- Reduce daily dose by 30 mg each week.
- Following a week of 30 mg daily, 30 mg to be taken on alternate days for 1 week, then stop.

Side effects

- Nausea is a significant side effect, particularly in the first few days of treatment. It is generally a short term side effect.
- Other side effects include insomnia, agitation, anxiety, reduced appetite, blurred vision, headache, tinnitus, somnolence, dizziness, palpitations, flushing, sexual dysfunction and dry mouth.
- Patients can experience nausea, vomiting, headache, anxiety, dizziness and tremor in response to abrupt withdrawal.

Opioids — AMBER RECOMMENDATION

Opioids are used only rarely for neuropathic pain.
They are prescribed on the recommendation of a Specialist and a stop date will always be defined. They are only recommended for SHORT TERM use whilst awaiting the effects of other interventions.

Contraindications, cautions, side effects: See SPCs and BNF.

Tramadol short term use (eight weeks) — GREEN

Initiated for acute rescue therapy only. To be initiated at the point of referral to the Specialist whilst awaiting an appointment.

Dose

Tramadol UP-TITRATION

- Initially 50 mg PO twice daily (50 mg at night in the elderly) with increments of 50 mg/day every 3 days dependent upon response, up to a maximum of 400 mg/day.

Tramadol DOWN-TITRATION / WITHDRAWAL

- Reduce by 50 mg/day every 3 to 4 days.

Capsaicin 0.075% cream: **GREEN**

Cautions: Avoid:

- Contact with broken skin and eyes.
- Hot shower or bath just before or after application (burning sensation enhanced).
- Inhalation of vapours; do not use if patient asthmatic.
- Use under tight bandages.

Wash hands immediately after use (or 30 minutes after application if hands treated).

Dose

- For management of localised neuropathic pain in patients who wish to avoid, or cannot use oral treatments (due to intolerance or contraindications), or where down titration of oral agents is being attempted.
- A pea sized amount should be applied sparingly 3 to 4 times a day; after lesions have healed, do not apply more often than every 4 hours. To be used for 6 to 8 weeks. Sometimes a second course may be needed. It should not be on repeat prescription.

Side effects: Transient burning sensation during initial treatment (particularly if too much used, used less frequently than 3 times per day or if administered more than 4 times daily

Carbamazepine **GREEN**

Contraindications

- AV conduction abnormalities (unless paced), history of bone marrow suppression or acute porphyria.

Cautions

- Cardiac disease; history of haematological reactions to other drugs; may exacerbate absence and myoclonic seizures; skin reactions; susceptibility to angle-closure glaucoma

Drug interactions

- Carbamazepine induces its own metabolism and is metabolised by the cytochrome P450 3A4 enzyme. There are many other enzyme mediated drug interactions. Check the BNF before prescribing.

Dose for trigeminal neuralgia

- Initial dose: 100 mg PO at night. Increase by 100 mg every 2 weeks according to response. Do not increase faster than this. Usual dose 200 mg PO 3 to 4 times a day. Up to a maximum of 1600 mg PO daily.

Side effects

Nausea, ataxia, confusion and agitation, visual disturbances, leucopenia and thrombocytopenia, rash, Stevens-Johnson syndrome. oedema, fluid retention, weight increase, hyponatraemia and blood osmolarity decreased due to an antidiuretic hormone (ADH)-like effect, leading in rare cases to water intoxication accompanied by lethargy, vomiting, headache, confusional state, neurological disorders. Dizziness, drowsiness, fatigue

Counselling

Advise patients on how to recognise signs of blood, liver and skin disorders. Medical advice must be sought if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop.

See also:

Guideline 375FM Chronic Pain Treatment in Adult Spinal Patients

References

1. British National Formulary, available at https://bnf.nice.org.uk/
2. NICE CG173 Neuropathic pain in adults: pharmacological management in non-specialist settings, November 2013. Last updated 19th July 2019.
3. NICE Clinical Knowledge Summary – Neuropathic Pain Drug Treatment, revised June 2015

4. NICE Clinical Knowledge Summary- Trigeminal Neuralgia https://cks.nice.org.uk/trigeminal-neuralgia
5. Public Health England (2014) Advice for prescribers on the risk of the misuse of pregabalin and gabapentin https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf
6. MHRA Drug Safety Update October 2017. Gabapentin (Neurontin®) risk of severe respiratory depression https://www.gov.uk/drug-safety-update/gabapentin-neurontin-risk-of-severe-respiratory-depression
7. Virani A., Bezchlibnyk-Butler K. Clinical Handbook of Psychotropic Drugs 2017
8. NICE NG59 Low back pain and sciatica in over 16s: assessment and management. Nov. 2016 https://www.nice.org.uk/guidance/ng59
9. MHRA Drug Safety Update April 2019 https://www.gov.uk/drug-safety-update/pregabalin-lyrica-gabapentin-neurontin-and-risk-of-abuse-and-dependence-new-scheduling-requirements-from-1-april
10. Bazire Stephen. Psychotropic Drug Directory 2018, The Professionals' Pocket Handbook and Aide.
11. South London and Maudsley NHS Foundation Trust. The Anticholinergic Effect on Cognition Tool www.medichec.com
12. Amitriptyline 10mg tablets. Brown and Buck UK Ltd. Summary of Product Characteristics updated on the EMC Nov 6th 2019. https://www.medicines.org.uk/emc/product/10849
13. Gabapentin 100mg tablets Accord UK Lt. Summary of Product Characteristics updated on the EMC 26th July 2019: https://www.medicines.org.uk/emc/product/4635/smpc
14. Pregabalin 150mg hard capsules Axalid® Summary of Product Characteristics updated on the EMC 25 July 2017 https://www.medicines.org.uk/emc/product/2320/smpc
15. Duloxetine 30mg capsules Cymbalta® Summary of Product Characteristics updated on the EMC 23 August 2019. https://www.medicines.org.uk/emc/product/3880/smpc
16. Tramadol 50mg capsules Accord UK Ltd. Summary of Product Characteristics updated on the EMC 8 Oct 2019 https://www.medicines.org.uk/emc/product/5924/smpc
17. Capsaicin 0.075% Axsain®cream Summary of Product Characteristics updated on the EMC 20 Nov 2019 https://www.medicines.org.uk/emc/product/887/smpc
18. Carbamazepine Carbagen® 100mg capsules Summary of Product Characteristics updated on the EMC 28 Feb 2020 https://www.medicines.org.uk/emc/product/4384/smpc

Title of Guideline	Management of Neuropathic Pain in Adults
Guideline Number	714FM
Version	3
Effective Date	April 2020
Review Date	April 2023
Original Version Produced	November 2009
Approvals:	
MVG Task and Finish Group	November 2019
Medicines Value Group	5th December 2019
Clinical Guidelines Subgroup	25th March 2020
Author/s	v.3 Neuropathic Pain guideline Task and Finish Group: Neal Evans and Bhamini Ramaswamy Pain Consultants, Maire Stapleton, BHT Formulary Manager, Becky BramhanJones and Nicky Vallance, Pain Clinical Nurse Specialists, Shona Lockie, Clinical Director (GP) Medicines Management, Bucks CCG, Lisa Pazik, Lead pharmacist, NSIC
SDU(s)/Department(s) responsible for updating the guideline	Anaesthetics, Pain Team, Pharmacy
Uploaded to BHT Intranet and Bucks Formulary www.bucksformulary.nhs.uk	2nd April 2020
Buckinghamshire Healthcare NHS Trust, Buckinghamshire Clinical Commissioning Group	

Appendix 1: Useful Resources for Patients, including Patient Information Leaflets and eLearning Packages

- British Pain Society resources
  https://www.britishpainsociety.org/about/articles-and-reports/
- Pain assessment tool – see British Pain Society
- Neil Berry's online audio descriptions of pain (http://www.paincd.org.uk)
- Pain Concern- a charity run by patients experiencing pain, providing support for people living with pain and those that care about them.
- Neuropathy Trust - a charitable organisation with a website dedicated to helping people with neuropathic pain.
- Faculty of Pain Medicine - eLearning for healthcare professionals
  https://www.e-lfh.org.uk/programmes/pain-management/
- ESCAPE-pain app – a useful tool for patients in managing their pain
  https://escape-pain.org/escape-pain-app
- Paintoolkit.org - designed for people who live with persistent pain and healthcare teams who support them.
  https://www.paintoolkit.org/
- Anticholinergic Effect on Cognition (AEC) tool. See web-based app at www.medichec.com.

Appendix 2: Dose Tables for Patients

Amitriptyline, imipramine or nortriptyline

Dose up-titration

- Increase daily dose by 10 mg each week.

Dose down-titration/withdrawal

- Reduce daily dose by 10 mg each week over a four week period.

Gabapentin

Gabapentin SLOW UP-TITRATION

DAY	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6
1 to 2	100 mg daily^	100 mg three times daily	200 mg three times daily	300 mg three times daily	400 mg three times daily	600 mg three times daily. Continue on this dose
3 to 4	100 mg twice daily	100 mg three times daily				
5 to 7	100 mg three times daily	100 mg three times daily				

Gabapentin FAST UP-TITRATION

DAY	WEEK 1	WEEK 2	WEEK 3
1 to 2	300 mg daily^	300 mg morning 300 mg midday 600 mg at night	600 mg three times daily. Continue on this dose.
3 to 4	300 mg twice daily	300 mg morning 600 mg midday 600 mg at night	
5 to 7	300 mg three times daily	600 mg three times daily	

^after 6pm as a test dose. If tolerated, continue.

If side effects occur, step down dosing by one stage and continue treatment.

Dose down - titration / withdrawal

- **Total daily dose ≤900 mg:** Reduce total daily dose by 100 mg every 4 days
- **Total daily dose >900 mg:** Reduce total daily dose by 300 mg every 4 days unless observations of emergent symptoms are required, in which case more gradual dose tapering is needed, as seen in table below:
-

	Week 1	Week 2	Week 3
Morning	300 mg	300 mg	
Midday	300 mg		
Night	300 mg	300 mg	300 mg

Pregabalin

Dose up – titration

	Week 1	Week 2	Week 3	Week 4	Stop and review patient
Morning	150 mg	75 mg	50 mg	25 mg	
Night	75 mg	75 mg	50 mg	25 mg	

- The patient may start treatment using 25 mg in the morning and 50 mg at night to improve tolerability.
- Dosing in the elderly and in renal impairment:
  For older patients (>75 years) or those with renal impairment: initially 25 mg twice daily. If CrCl <30 ml/min, it may be appropriate to give this as a single daily dose of 25 mg.

Dose down – titration/withdrawal

- Reduce total daily dose by 50 to 75 mg per week.
- Suggested withdrawal schedule for a dose of 150 mg twice a day:

	Week 1	Week 2	Week 3	Week 4	Stop and review patient
Morning	150 mg	75 mg	50 mg	25 mg	
Night	75 mg	75 mg	50 mg	25 mg	

Duloxetine

Dose up-titration

	Week 1	Weeks 2 to 4**
Night	30 mg	60 mg

**dependent upon response to initial dose.

Dose down - titration/withdrawal

- Reduce daily dose by 30 mg each week.
- Following a week of 30 mg daily, 30 mg to be taken on alternate days for 1 week, then stop.

Tramadol short term use (eight weeks)

Dose up-titration

- Initially 50 mg TWICE A DAY (50 mg at night in the elderly) with increments of 50 mg/day every 3 days dependent upon response, up to a maximum of 400 mg/day.

Dose down-titration/withdrawal

- Reduce by 50 mg/day every 3 to 4 days.

Capsaicin 0.075% cream

Cautions: Avoid:

- Contact with broken skin and eyes.
- Hot shower or bath just before or after application (burning sensation enhanced).
- Inhalation of vapours; do not use if patient asthmatic.
- Use under tight bandages.

Wash hands immediately after use (or 30 minutes after application if hands treated).

Dose

A pea sized amount should be applied sparingly 3 to 4 times a day; after lesions have healed, do not apply more often than every 4 hours. To be used for 6 to 8 weeks. Sometimes a second course may be needed. It should not be on repeat prescription.