



PRODIGY Guidance - Shingles and postherpetic neuralgia



Have I got the right guidance ?

Applies to:
Patients over 192 months (16 years)

This guidance covers the management of shingles (herpes zoster) and postherpetic neuralgia.

There is separate Prodigy guidance on *Chickenpox*, *Herpes simplex - oral* (cold sores), *Herpes simplex - ocular*, *Herpes simplex - genital*, and *Trigeminal neuralgia*.

Changes

Last revised in April 2002

[www.prodigy.nhs.uk/guidance.asp?gt=Shingles/postherpetic pain](http://www.prodigy.nhs.uk/guidance.asp?gt=Shingles/postherpetic%20pain)

August 2003 - minor formatting update.

December 2001 - reviewed and guidance renamed *Shingles and postherpetic neuralgia* (previously called *Herpes zoster*). Validated in March 2002 and issued in April 2002.

August 1998 - written.

Goals and Outcome Measures

Goals

- To relieve the symptoms of shingles
- To minimize the risk of progression to postherpetic neuralgia
- To reduce symptoms and aid early recovery from postherpetic neuralgia

Background Information

- What is it?
- How common is it?
- How do I know my patient has it?
- What else might it be?
- Complications and prognosis?

What is it?

Shingles (herpes zoster) is an acute infection caused by reactivation of latent varicella zoster virus. Following primary chickenpox infection, the virus lies dormant in the dorsal root ganglia of the spinal cord. When reactivated, it travels along the sensory nerve to affect one or more dermatomes, causing the characteristic shingles rash. Reactivation of the virus probably occurs following a decrease in cell-mediated immunity (e.g. with increasing age, HIV infection, illness).

Postherpetic neuralgia is pain that persists following resolution of shingles. Definitions vary: from pain persisting after the shingles rash heals to pain persisting for more than 30 days or 6 months after the onset or healing of the rash. In this guidance, it is suggested that postherpetic neuralgia should be considered as a possibility if pain persists for more than 4-6 weeks (and as definite if pain lasts for more than 3 months).

How common is it?

Shingles

Elderly people and people who are immunocompromised are most at risk of developing shingles.

An annual incidence of just over 3/1000 was estimated in a retrospective UK study that considered people who had attended their general practitioner with a diagnosis of shingles. In people younger than 50 years, the incidence was less than 2/1000. In people aged 50-79 years this rose to 7/1000, and in people aged 80 years or older to 11/1000 [Hope-Simpson, 1975].

Lifetime risk of shingles is 20%. The risk of a second attack is less than 5% [Cunningham and Dworkin, 2000].

Postherpetic neuralgia

The incidence of postherpetic neuralgia (PHN) varies depending on the definition used.

Overall, PHN complicated shingles in 14% of people, in a UK general practice-based study that retrospectively reviewed the notes of 321 people who had been diagnosed as having shingles. PHN was diagnosed if there was a record of subsequent consultation for pain more than a month after onset of the shingles rash. PHN rarely occurred in people younger than 50 years, but occurred in 21% of people with shingles aged 60-69 years and in 34% of people older than 80 years [Hope-Simpson, 1975].

A general practice-based study in Iceland followed 421 people with a first episode of shingles [Helgason et al, 2000]. Only 4% of these were treated with antiviral drugs. Overall, 7% of people had pain 3 months after the start of the shingles rash and 3% at 12 months.

In people younger than 60 years, 2% had pain at 3 months (which was mild in all cases) and 0.6% at 12 months.

In people 60 years and older, 20% had pain at 3 months (or 7% for pain of moderate to severe severity) and 9% at 12 months (with no cases of severe pain).

How do I know my patient has it?

Prodromal phase of shingles

Paraesthesia and pain over the affected dermatome may occur between 2 days to 3 weeks prior to the onset of the shingles rash.

The pain varies from a superficial itching, tingling, or burning discomfort to a severe deep boring pain or a sharp, stabbing, lancinating pain. It may be constant or intermittent [Wallace and Oxman, 1997].

Acute shingles

Erythematous, maculopapular lesions evolve into a vesicular rash.

New lesions continue to form over 3-5 days, with scabbing after 4-7 days.

The extent of the rash varies, but it is partially or completely confined to one or more dermatomes. The rash is almost always unilateral. The thoracic dermatomes are most commonly involved, particularly T5 and T6.

Pain over the affected area is the most common complaint.

Mild systemic illness may occur (e.g. low-grade pyrexia, malaise).

Postherpetic neuralgia

Continuing pain despite resolution of shingles is experienced by people with postherpetic neuralgia (PHN). Definitions of PHN vary from pain persisting after the shingles rash heals to pain persisting for more than 30 days or 6 months after the onset or healing of the rash.

Pain is typically localized to the dermatome that was affected by the shingles rash. It may be a steady burning, aching pain; a paroxysmal, jabbing pain; or a combination of both. Pain may be triggered by usually innocuous stimuli (allodynia), such as clothing moving against the skin. There may be associated hypoaesthesia.

Scarring or hypopigmentation of the skin affected by the previous shingles rash may occur.

What else might it be?

Differential diagnosis for the rash of shingles includes:

Bacterial impetigo
Herpes simplex
Eczema herpeticum (caused by herpes simplex)
Coxsackie virus (e.g. hand, foot, and mouth disease)
Pemphigoid and other blistering conditions

Differential diagnosis for the pain of shingles or postherpetic neuralgia includes:

Pathology in underlying bone, muscle, or viscera (e.g. trauma, fracture, inflammation, infection, neoplasm)
Vertebral pathology (e.g. prolapsed intervertebral disk, crush fractures, neoplasm)
Diabetic mononeuritis
Cardiac ischaemia
Pleurisy
Tabes dorsalis (a form of neurosyphilis)

Complications and prognosis

Complications

Complications of shingles

Postherpetic neuralgia (the most common complication)
Ophthalmic zoster (may cause conjunctivitis, keratitis, and rarely uveitis, acute retinal necrosis, and cataract)
Motor zoster (includes facial nerve paralysis)
Autonomic zoster (may progress to urinary retention)
Zoster encephalomyelitis
Purpura fulminans (tissue loss may be extensive)
Disseminated zoster (more common in people who are immunocompromised; it can be life-threatening)
Acute retinal necrosis (can lead to retinal detachment)
Bacterial superinfection

Complications of postherpetic neuralgia

Disruption of sleep and work, with impaired quality of life
Depression and anxiety

Prognosis

It is unusual for a person to develop shingles more than once (less than 5% have recurrence).

About 2% of people had pain for more than 5 years following an episode of shingles according to a UK general practice-based study [Hope-Simpson, 1975]. In a general practice-based study in Iceland, just over 3% of people had pain 12 months after a first episode of shingles, and less than 2% of people had pain after 6 years [Helgason et al, 2000].

Older age is most strongly associated with the risk of developing postherpetic neuralgia. Other factors that seem to be important are: greater acute pain severity; greater rash severity; sensory dysfunction in the affected dermatome during shingles; and the presence of a painful prodrome preceding the rash [Kanazi et al, 2000].

Management Issues

Shingles (acute herpes zoster)

General issues

Effectiveness of oral antiviral drugs

When to use oral antiviral drugs

Tricyclic antidepressant drugs

Treatments that are not recommended

Postherpetic neuralgia

General issues

Tricyclic antidepressant drugs

Anticonvulsant drugs

Topical capsaicin

Topical anaesthesia

Treatments that are not recommended

Shingles (acute herpes zoster)

General issues

Skin hygiene is important for preventing secondary bacterial infection.

There is little available data on which to guide choice of symptomatic treatment.

Physical measures such as calamine lotion, wet dressings, and ice packs may provide short-term relief of symptoms [Johnson 1997 1248 /id][Wallace and Oxman, 1997; Johnson, 1997].

Effective pain relief is vital. Acute shingles pain can vary from a mild discomfort to a severe debilitating pain. The World Health Organization (WHO) three-step analgesic ladder is a useful model: step 1 is a non-opioid; step 2 is a weak opioid in combination with a non-opioid, and step 3 is a strong opioid with or without a non-opioid. Analgesics should be started at the 'step' most appropriate to the person's level of pain [MeReC, 2000]. An adjuvant analgesic, such as low-dose amitriptyline, may be required at any step. Oral NSAIDs seem to be of little benefit in the treatment of acute shingles pain [Johnson, 1997; Kanazi et al, 2000].

People with shingles can transmit varicella zoster virus to non-immune individuals, resulting in chickenpox. Infectivity lasts until the shingles skin lesions have dried up. If lesions are covered, transmission is unlikely (as the virus is only transmitted by direct contact with vesicles). Over 90% of adults will be immune to varicella zoster virus; however, immigrants from tropical countries are frequently non-immune. In particular, pregnant women and people who are immunocompromised or who are taking systemic corticosteroids should avoid contact with people who have shingles [BSSI, 1995].

Shingles affecting the ophthalmic division of the trigeminal nerve may involve the eye (particularly if the rash is present towards the tip of the nose), with a high risk of ocular complications. Oral antiviral treatment, started within 72 hours of the appearance of the rash, is recommended for all people with ophthalmic shingles. The British Infection Society recommends that, if there is a red eye or other signs of ocular involvement, an urgent ophthalmological opinion is obtained [BSSI, 1995].

Effectiveness of oral antiviral drugs

Oral antiviral drugs, started within 72 hours of onset of the shingles rash, reduce the duration of rash and associated pain, and reduce the risk of developing postherpetic neuralgia (PHN) [DTB, 1998b; Alper and Lewis, 2000; Yaphe and Lancaster, 2000]. Although the results from individual studies are conflicting, systematic reviews have found that aciclovir nearly halves the risk of postherpetic pain at 6 months. Famciclovir gives similar results when compared with placebo. Evidence from a single randomized controlled trial comparing valaciclovir with aciclovir suggests that valaciclovir may be slightly more effective at preventing PHN [Beutner et al, 1995]. Valaciclovir has been compared with famciclovir, with no difference found for the risk of PHN [Tyring et al, 2000].

When to use oral antiviral drugs

Only start antiviral treatment (if indicated) in people who present within 72 hours of the onset of rash.

Oral antiviral drugs are not indicated in healthy young adults with shingles, as they are unlikely to have severe symptoms and are at very low risk of developing postherpetic neuralgia [BSSI, 1995; Helgason et al, 2000].

Oral antiviral drugs are indicated in people who are elderly (60 years or older), have ophthalmic involvement, or who are immunocompromised. Such individuals have a higher risk of severe acute disease or progression to postherpetic neuralgia.

Aciclovir is least expensive but has to be taken five times daily. Valaciclovir and famciclovir have the advantage of easier dosage regimens. Valaciclovir is a pro-drug of aciclovir and can be taken three times a day. Famciclovir is a pro-drug of penciclovir and can be taken either three times a day or as a single daily dose.

Tricyclic antidepressant drugs

Adjuvant treatment with a low-dose tricyclic antidepressant may be indicated for pain control, as described in the *General issues* section above.

Some experts recommend that low-dose tricyclic antidepressants should be started as soon as possible in all people with shingles aged 60 years or more. There is limited evidence that early treatment with amitriptyline may reduce the incidence of postherpetic neuralgia. A systematic review [Alper and Lewis, 2000] found one double-blind randomized controlled trial that compared amitriptyline 25 mg daily with placebo in 80 elderly people (older than 60 years) with shingles [Bowsher, 1997]. Treatment was started within 48 hours of rash onset and continued for 90 days. The prevalence of pain at 6 months in the amitriptyline group was half that of the placebo group, although this was of borderline statistical significance (AR 16% versus 35%; RR 0.45; ARR 0.19, 95% CI -0.01 to +0.39). Larger studies are needed to examine this further.

Treatments that are not recommended

Systemic corticosteroids. These offer only short-term benefit and are not recommended. There is some evidence that high-dose corticosteroids added to antiviral drugs may speed healing of shingles [Yaphe and Lancaster, 2000]. There is no evidence that they reduce the risk of postherpetic neuralgia [Yaphe and Lancaster, 2000]. It is generally felt that any slight benefit is outweighed by the potential for harm.

Topical antiviral agents. Topical idoxuridine may provide short-term pain relief in acute shingles, but there is no evidence that it reduces the risk of postherpetic neuralgia [Yaphe and Lancaster, 2000].

Postherpetic neuralgia

General issues

Postherpetic neuralgia is usually a self-limiting condition; however, in some people it can be prolonged or even persist indefinitely.

Psychological distress is common. Many people become depressed and may require specific management of this (see *Prodigy Depression* guidance). Psychological services (e.g. based at pain clinics) may be able to help people develop pain-coping strategies.

Measures to reduce stimulation of the skin may be beneficial, as skin hypersensitivity (allodynia) is common. Natural fibre clothing is preferable to artificial fibres. A protective layer over the skin may be helpful (e.g. clingfilm or 'plastic skin') [Kanazi et al, 2000].

Cold pack application may provide short-term relief of pain [Kanazi et al, 2000].

Analgesic drugs may be helpful. Paracetamol alone or in combination with codeine is commonly prescribed and seems to be effective in people with mild to moderate pain [Johnson, 1997]. There is increasing evidence that opioid analgesics are effective in treating the pain of postherpetic neuralgia [DTB, 2000; Yaphe and Lancaster, 2000; Kanazi et al, 2000]. There is concern, however, about the use of strong opioids, as chronic usage is likely to be needed. Strong opioids are therefore best reserved for use in specialist pain clinics. Oral NSAIDs seem to be of little benefit [Johnson, 1997; Kanazi et al, 2000].

Treatments active against neuropathic pain are usually necessary. Those suitable for use in primary care are tricyclic antidepressants and anticonvulsants. If response to these agents is inadequate, then referral to a pain clinic for specialist management is strongly recommended.

Tricyclic antidepressant drugs

Tricyclic antidepressants (TCAs) are effective at relieving the pain of postherpetic neuralgia [DTB, 2000; Collins et al, 2000; Yaphe and Lancaster, 2000; Kanazi et al, 2000]. They reduce pain in up to 80% of people [Yaphe and Lancaster, 2000]. None are specifically licensed for the treatment of neuropathic pain.

The pain-relieving effect of TCAs is independent of their antidepressant effect. It is important to explain this to people, as many will be aware of their use in depression.

Amitriptyline is the drug of choice. If this is not tolerated or is ineffective, evidence most supports the use of nortriptyline [Watson et al, 1998]. Maprotiline and desipramine have also been found to be effective, but maprotiline has a high incidence of rash and desipramine is not available in the UK.

The usual dose of amitriptyline or nortriptyline is 25 mg/day, with weekly 25 mg/day incremental increases until

pain relief or unacceptable adverse effects occur. In elderly or frail people, a starting dose of 10 mg/day with weekly 10 mg/day incremental increases is recommended. It is rarely necessary to exceed 75 mg/day - the maximum recommended dose is 150 mg/day [Bowsher, 1995; BSSI, 1995; DTB, 2000].

Pain relief usually occurs within a few days, but may take 2-3 weeks. Maximum benefit may take several weeks to occur.

Treatment should be continued at full dose for 3 months after the pain has disappeared, then gradually tailed off. Treatment should be restarted (or the dose increased) if pain recurs [Bowsher, 1995].

Anticonvulsant drugs

Gabapentin has been studied in two double-blind randomized placebo-controlled trials. A study of 229 people with postherpetic neuralgia (PHN) found that gabapentin reduced pain by nearly a third [Rowbotham et al, 1998]. However, the dose of gabapentin was titrated up to 3.6 g/day, which is twice the maximum licensed dose in neuropathic pain. In a more recent study of 334 people with PHN, doses of 1.8 g/day or 2.4 g/day were used; approximately 30% of people treated with either dose of gabapentin had a 50% or greater reduction in mean pain score, compared with just over 10% of people treated with placebo [Rice and Maton, 2001]. Similar improvements were found for patient- and clinician-assessed symptoms. Dizziness and sedation were the most common adverse effects of gabapentin, occurring in approximately 30% and 20% of people, respectively.

Carbamazepine has not been specifically studied in the treatment of postherpetic neuralgia. However, there is trial data showing efficacy against other types of neuropathic pain and it is widely used for the treatment of postherpetic neuralgia.

Phenytoin has been less well studied than carbamazepine, but also seems to be effective against neuropathic pain. It is usually poorly tolerated and is therefore less preferred.

Sodium valproate has been studied in only one small trial of people with spinal cord injury, and was found to be ineffective. Although it is widely used in the treatment of neuropathic pain and is reported as being effective, more data is needed before it can be recommended for use in postherpetic neuralgia.

Anticonvulsants are generally reserved for use with a tricyclic antidepressant, if pain relief is inadequate with use of a tricyclic alone. However, there is no trial data to support this approach. If a tricyclic antidepressant drug cannot be taken, then use of an anticonvulsant drug alone should be considered. On the basis of current evidence on the treatment of neuropathic pain, gabapentin or carbamazepine are the preferred anticonvulsants.

[DTB, 2000; Collins et al, 2000; Yaphe and Lancaster, 2000; Tremont-Lukats et al, 2000; Kanazi et al, 2000; Wiffen et al, 2001].

Topical capsaicin

Topical capsaicin seems to provide some pain relief in postherpetic neuralgia [Yaphe and Lancaster, 2000]. The mechanism of action is unknown, but may be due to depletion of substance P in peripheral nerve fibres. Trials are difficult to interpret, as blinding is impossible due to the burning sensation that follows application of capsaicin. This may lead to an overestimate of effect.

It is poorly tolerated because of the intense burning sensation following application, although this effect diminishes with continued use. It is therefore not a first-choice treatment.

Topical anaesthesia

Topical lidocaine (lignocaine) 5% patch provides short-term pain relief in postherpetic neuralgia. It is not currently available in the UK.

There have been two published double-blind randomized controlled trials [Comer and Lamb, 2000]. A crossover study of 35 people with postherpetic neuralgia found that a single application of lidocaine 5% patch significantly reduced pain over 4-12 hours [Rowbotham et al, 1996]. A crossover study of 32 people previously successfully treated with lidocaine 5% patch found that treatment failure occurred sooner in people treated with placebo patches (median 4 days versus 14 days) [Galer et al, 1999].

Systemic absorption is minimal and no systemic adverse effects have been seen.

Mild skin redness or irritation may occur at the application site.

Treatments that are not recommended

Oral antiviral drugs have no effect on established postherpetic neuralgia [Acosta and Balfour, Jr., 2001].

Transcutaneous electrical nerve stimulation (TENS) is of doubtful benefit [Kanazi et al, 2000].
Acupuncture seems to provide little benefit [Kanazi et al, 2000].

References

Cited

1. Acosta, E.P. and Balfour, H.H., Jr (2001) Acyclovir for treatment of postherpetic neuralgia: efficacy and pharmacokinetics. *Antimicrobial Agents and Chemotherapy* **45**(10), 2771-2774.
2. Alper, B.S. and Lewis, P.R. (2000) Does treatment of acute herpes zoster prevent or shorten postherpetic neuralgia? *Journal of Family Practice* **49**(3), 255-264.
3. Beutner, K.R., Friedman, D.J., Forszpaniak, C., et al. (1995) Valaciclovir compared with acyclovir for improved therapy for herpes zoster in immunocompetent adults. *Antimicrobial Agents and Chemotherapy* **39**(7), 1546-1553.
4. BNF 42 (2001) *British National Formulary*. 42nd edn. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain.
5. Bowsher, D. (1995) *Notes for doctors: treatment of post-herpetic neuralgia in the elderly*. Shingles Support Society. www.herpex.org.uk/shingles/bowsher1.htm
6. Bowsher, D. (1997) The effects of pre-emptive treatment of postherpetic neuralgia with amitriptyline. *Journal of Pain & Symptom Management* **13**(6), 327-331.
7. BSSI (1995) Guidelines for the management of shingles. British Society for the Study of Infection (BSSI) Working Party. *Journal of Infection* **30**, 193-200.
8. Charlton, J.E. (1999) Tramadol hydrochloride. *Prescribers' Journal* **39**(2), 109-112.
9. Collins, S.L., Moore, R.A., McQuayHJ, and Wiffen, P. (2000) Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review. *Journal of Pain & Symptom Management* **20**(6), 449-458.
10. Comer, A.M. and Lamb, H.M. (2000) Lidocaine patch 5%. *Drugs* **59**(2), 245-249.
11. Cunningham, A.L. and Dworkin, R.H. (2000) The management of post-herpetic neuralgia. *British Medical Journal* **321**(7264), 778-779.
12. DTB (1998a) Co-proxamol or paracetamol for acute pain. *Drug & Therapeutics Bulletin* **36**(10), 80.
13. DTB (1998b) Update on drugs for herpes zoster and genital herpes. *Drug & Therapeutics Bulletin* **36**(10), 77-79.
14. DTB (2000) Drug treatment of neuropathic pain. *Drug & Therapeutics Bulletin* **38**(12), 89-93.
15. Galer, B.S., Rowbotham, M.C., Perander, J., and Friedman, E. (1999) Topical lidocaine patch relieves postherpetic neuralgia more effectively than a vehicle topical patch: results of an enriched enrollment study. *Pain* **80**(3), 533-538.
16. Helgason, S., Petursson, G., Gudmundsson, S., and Sigurdsson, J.A. (2000) Prevalence of postherpetic neuralgia after a first episode of herpes zoster: prospective study with long term follow up. *British Medical Journal* **321**(7264), 794-796.
17. Hope-Simpson, R.E. (1975) Postherpetic neuralgia. *Journal of the Royal College of General Practitioners* **25**(157), 571-575.
18. Johnson, R.W. (1997) Current and future management of herpes zoster. *Antiviral Chemistry & Chemotherapy* **8**(Suppl. 1), 19-29.
19. Kanazi, G.E., Johnson, R.W., and Dworkin, R.H. (2000) Treatment of postherpetic neuralgia: an update. *Drugs* **59**(5), 1113-1126.
20. MeReC (2000) The use of oral analgesics in primary care. *MeReC Bulletin* **11**(1), 1-4.
21. Moore, R.A. and McQuay, H.J. (1997) Single-patient data meta-analysis of 3453 postoperative patients: oral tramadol versus placebo, codeine and combination analgesics. *Pain* **69**, 287-294.
22. Regional Drug and Therapeutics Centre (1998) *Drug update: Tramadol*. NHS Northern and Yorkshire, Regional Drug and Therapeutics Centre, Wolfson Unit, Claremont Place, Newcastle Upon Tyne.
23. Rice, A.S.C. and Maton, S. (2001) Gabapentin in postherpetic neuralgia: a randomised, double blind, placebo controlled study. *Pain* **94**, 215-224.
24. Rowbotham, M., Harden, N., Stacey, B., et al. (1998) Gabapentin for the treatment of postherpetic neuralgia. *Journal of the American Medical Association* **280**(21), 1837-1842.
25. Rowbotham, M.C., Davies, P.S., Verkempinck, C., and Galer, B.S. (1996) Lidocaine patch: double blind controlled study of a new treatment method for post herpetic neuralgia. *Pain* **65**(1), 39-44.
26. Tremont-Lukats, I.W., Megeff, C., and Backonja, M.M. (2000) Anticonvulsants for neuropathic pain syndromes: mechanisms of action and place in therapy. *Drugs* **60**(5), 1029-1052.
27. Tyring, S.K., Beutner, K.R., Tucker, B.A., et al. (2000) Antiviral therapy for herpes zoster: randomized, controlled clinical

trial of valacyclovir and famciclovir therapy in immunocompetent patients 50 years and older. *Archives of Family Medicine* **9**(9), 863-869.

28. Wallace, M.S. and Oxman, M.N. (1997) Acute herpes zoster and postherpetic neuralgia. *Anesthesiology Clinics of North America* **15**(2), 371-405.

29. Watson, C.P., Vernich, L., Chipman, M., and Reed, K. (1998) Nortriptyline versus amitriptyline in postherpetic neuralgia: a randomized trial. *Neurology* **51**(4), 1166-1171.

30. Wiffen, P., McQuay, H., Carroll, D., et al (2001) *Anticonvulsant drugs for acute and chronic pain (Cochrane Review)*. The Cochrane Library (3). Oxford: Update Software.

31. Yaphe, J. and Lancaster, T. (2000) Postherpetic neuralgia. *Clinical Evidence* **6**, 616-624.

Background

1. DARE (2001) Abstract and commentary for: McQuay, H., Carroll, D., Jadad, A.R., et al. (1995) Anticonvulsant drugs for the management of pain: a systematic review. *British Medical Journal*, **311**, 1047-1052. In: *Database of Abstracts of Reviews of Effectiveness*.

2. DARE (2001) Abstract and commentary for: McQuay, H.J., Tramer, M., Nye, B.A., et al. (1996) A systematic review of antidepressants in neuropathic pain. *Pain*, **68**, 217-227. In: *Database of Abstracts of Reviews of Effectiveness*.

3. DARE (2001) Abstract and commentary for: Volmink, J., Lancaster, T., Gray, S., and Silagy, C. (1996) Treatments for postherpetic neuralgia: a systematic review of randomized controlled trials. *Family Practice*, **13**(1), 84-91. In: *Database of Abstracts of Reviews of Effectiveness*.

4. DARE. (2001) Abstract and commentary for: Zhang, W.Y. and Li Wan Po, A. (1994) The effectiveness of topically applied capsaicin: a meta-analysis. *European Journal of Clinical Pharmacology*, **46**, 517-522. In: *Database of Abstracts of Reviews of Effectiveness*.

5. Lancaster, T., Silagy, C., and Gray, S. (1995) Primary care management of acute herpes zoster: systematic review of evidence from randomized controlled trials. *British Journal of General Practice*, 39-45.

6. MacFarlane, L.L., Simmons, M.M., and Hunter, M.H. (1998) The use of corticosteroids in the management of herpes zoster. *Journal of the American Board of Family Practice*, **11**, 224-228.

7. McQuay, H. (2001) Opioids in chronic non-malignant pain. *British Medical Journal*, **322**, 1134-1135.

8. McQuay, H.J. and Moore, R.A. (1997) Antidepressants and chronic pain. *British Medical Journal*, **314**, 763.

9. Stankus, S.J., Dlugopolski, M., and Packer, D. (2000) Management of herpes zoster (shingles) and postherpetic neuralgia. *Am. Fam. Physician*, **61**, 2437-2438.

Which Scenario ?

Shingles - less than 60 years old: applies to all healthy, young people with shingles.

Shingles - 60 years or older/high risk: applies to people with shingles who are at high risk of severe disease and progression to postherpetic neuralgia. This includes people aged 60 years and older; people with ophthalmic shingles; or people who are immunocompromised.

Postherpetic neuralgia - first-line: applies to people with postherpetic neuralgia who have not yet started with specific treatment for this. There is no widely agreed definition of postherpetic neuralgia, but pain persisting for more than 4-6 weeks suggests the development of postherpetic neuralgia, and pain persisting for more than 3 months confirms the diagnosis.

Postherpetic neuralgia - treatment failure: applies to people who did not respond to treatment in scenario *Postherpetic neuralgia - first-line*.

Scenario - Shingles - less than 60 years old

Which Therapy ?

Oral antivirals are not recommended for young, healthy people, as they are unlikely to have severe symptoms and are at very low risk of developing postherpetic neuralgia

Exceptions are people who have severe symptoms, who are immunocompromised, or who have ophthalmic shingles (see scenario *Shingles 60 years or older/high risk*).

Skin hygiene is important for preventing secondary bacterial infection.

Physical measures such as calamine lotion, wet dressings, and ice packs may provide short-term relief of symptoms.

Analgesics should be started at the 'step' most appropriate to the person's level of pain.

Paracetamol alone or with codeine is often adequate.

Amitriptyline as adjuvant analgesia may be required.

A strong opioid (such as morphine) may be necessary for some people.

Prescribing points

For further information see the *Medicines Compendium* (www.medicines.org.uk) or the *British National Formulary* (www.bnf.org).

Amitriptyline

Driving: the Driver and Vehicle Licensing Authority (DVLA) recommends avoiding drugs that have antimuscarinic effects, such as tricyclic antidepressants (TCAs). All people taking TCAs should be advised not to drive if adversely affected, particularly during the first month of starting the medication or increasing the dose (tolerance develops within a week or two of a stable dose).

Other cautions include: cardiac disease particularly with arrhythmias; epilepsy; pregnancy and breastfeeding; glaucoma; prostatism; bipolar disorder; urinary retention; and suspected risk of overdosing.

Contraindications: recent myocardial infarction, arrhythmias, and hepatic impairment.

Adverse effects: commonly include dry mouth, sedation, constipation, postural hypotension, confusion (particularly in elderly people), urinary retention, and weight gain.

Morphine sulphate

Constipation is a common adverse effect. If morphine is required regularly, then laxatives should be prescribed.

Follow up advice

Pain persisting for more than 4-6 weeks (and definitely for more than 3 months) suggests the possibility of postherpetic neuralgia. Management of this is outlined in the scenario *Postherpetic neuralgia - first-line*.

Should I refer or investigate ?

Refer?

Admission is required if severe complications develop, such as dissemination or encephalitis.

Investigate?

If immunodeficiency is suspected (e.g. recurrent shingles), immunological tests should be done (discuss with local haematologist).

Doctor/patient discussion points

The rash and pain of shingles usually last 2-3 weeks.

Paracetamol alone, or combined with codeine, usually eases the pain.

Stronger painkillers are sometimes needed.

An antidepressant may help if the pain is bad. This is not to treat depression. It is good at easing nerve pains, such as shingles.

Calamine or similar lotions may be soothing.

Ice packs, or wet dressings over the rash, may ease the discomfort.

Soft cotton clothing is the most comfortable.

Antiviral medicine is not recommended if you are healthy, and under the age of 60. It is unlikely to have much effect on the rash and outcome.

If you still have pain after the rash clears, come back to see a doctor.

Drug Rationale

Drugs not included

Oral antivirals are not indicated in young (less than 60 years) healthy adults, as such individuals are unlikely to have severe symptoms and are at very low risk of developing postherpetic neuralgia. However, oral antiviral treatment should be offered to people presenting within 72 hours of the shingles rash who are at high risk, e.g. 60 years or older, have ophthalmic shingles, or are immunocompromised (see the scenario, *Shingles 60 years or older/ high risk*).

Topical idoxuridine may provide short-term pain relief in acute shingles, but there is no evidence that it reduces the risk of postherpetic neuralgia [Yaphe and Lancaster, 2000].

Oral NSAIDs seem to be of little benefit in the treatment of shingles pain [Kanazi et al, 2000].

Systemic corticosteroids are not included, as any slight benefit is outweighed by the potential for harm. There is some evidence that high-dose corticosteroids added to antiviral drugs may speed healing of shingles, but there is no evidence that they reduce the risk of postherpetic neuralgia [Alper and Lewis, 2000; Yaphe and Lancaster, 2000].

Low-dose weak opioids with paracetamol (combination products), e.g. co-codamol 8/500 mg. There is no evidence that these offer any clinical benefit over paracetamol alone and they are likely to lead to opioid adverse effects [DTB, 1998a; MeReC, 2000; BNF 42, 2001].

High-dose weak opioids with paracetamol (combination products), e.g. co-codamol 30/500 mg. These fixed-dose formulations do not allow titration to the most effective and safe analgesic dose to match the person's requirements.

Strong opioids other than morphine sulphate 10 mg/5 ml solution will require handwritten prescriptions.

Tramadol is expensive and there is a lack of evidence for its superiority over other analgesics. Tramadol has the potential to produce opioid adverse effects [Moore and McQuay, 1997; Regional Drug and Therapeutics Centre, 1998; Charlton, 1999].

Drugs included

Calamine lotion may provide short-term relief of symptoms [Kanazi et al, 2000].

Paracetamol with or without codeine is often adequate for relief of shingles pain.

Amitriptyline is offered as an adjuvant to paracetamol, with or without codeine, if additional pain relief is required.

Morphine sulphate 10 mg/5 ml solution is a further option for some individuals with acute severe shingles pain.

PILs attached to this guidance

[Herpes Viruses Association](#)
[Shingles](#)
[Shingles - Post Herpetic Neuralgia](#)
[Shingles Support Society](#)

Therapy Groups

Therapy Group: Analgesia: use when required

Paracetamol 1g up to four times a day

NHS Prescription for age: 192 to 719
Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Add on if required: codeine 30-60mg up to four times a day

NHS Prescription for age: 192 to 719
Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Paracetamol 500mg tablets + codeine 30mg tablets

Patient Info: You may find it best to take your paracetamol regularly to start with.

Paracetamol 500mg tablets

NHS Prescription for age: 192 to 719
Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Codeine 30mg tablets

NHS Prescription for age: 192 to 719
Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Therapy Group: Calamine Lotion

Calamine lotion: apply when required to relieve itching

NHS Prescription for age: 192 to 719
Calamine lotion

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
m313.	200 ml	Licensed	£0.64	£1.13	No CSM warning in BNF	OK

Usage Instructions: Apply to the affected area(s) when required to relieve itching

Patient Info: You may buy calamine lotion from a pharmacy.

Therapy Group: Start amitriptyline as an adjuvant analgesic: titrate up

Amitriptyline: titrate up from 25mg daily until pain settles

NHS Prescription for age: 192 to 719
Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	63 tablets	Not Licensed	£1.80		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take up to a maximum of three tablets (75mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Therapy Group: Morphine solution for acute severe shingles pain

Morphine sulphate solution: 10mg every 4 hours when required

NHS Prescription for age: 192 to 719
Morphine sulphate 10mg/5ml sol

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj1L.	200 ml	Licensed	£4.16		No CSM warning in BNF	OK

Usage Instructions: Take one 5ml spoonful every 4 hours when required for pain relief

Patient Info:

Scenario - Shingles - 60 years or older/high risk

Which Therapy ?

Oral antiviral medication (aciclovir, famciclovir, valaciclovir) is recommended for all people with shingles who are aged 60 years or older, who are immunocompromised, or who have ophthalmic shingles. Such individuals are at high risk of severe shingles, complications, and the development of postherpetic neuralgia.

Treatment should be started within 72 hours of the rash onset.

Skin hygiene is important for preventing secondary bacterial infection.

Physical measures such as calamine lotion, wet dressings, and ice packs may provide short-term relief of symptoms.

Analgesics should be started at the 'step' most appropriate to the person's level of pain.

Paracetamol alone or with codeine is often adequate.

Amitriptyline as adjuvant analgesia may be required.

A strong opioid (such as morphine) may be necessary for some people.

Low-dose amitriptyline is also recommended by some experts for use in all people with shingles aged 60 years or more, as there is some evidence that early treatment with amitriptyline may reduce the incidence of postherpetic neuralgia. If used for this purpose, it should ideally be prescribed in a dose of at least 25 mg/day and continued for 3 months.

Prescribing points

For further information see the *Medicines Compendium* (www.medicines.org.uk) or the *British National Formulary* (www.bnf.org).

Antivirals

Renal failure: the dose should be reduced in moderate to severe renal failure.

Amitriptyline

Driving: the Driver and Vehicle Licensing Authority (DVLA) recommends avoiding drugs that have antimuscarinic effects, such as tricyclic antidepressants (TCAs). All people taking TCAs should be advised not to drive if adversely affected, particularly during the first month of starting or increasing the dose (tolerance develops within a week or two of stabilizing the dose).

Other cautions include: cardiac disease particularly with arrhythmias; epilepsy; pregnancy and breastfeeding; glaucoma; prostatism; bipolar disorder; urinary retention; and suspected risk of overdosing.

Contraindications: recent myocardial infarction, arrhythmias, and hepatic impairment.

Adverse effects: commonly include dry mouth, sedation, constipation, postural hypotension, confusion (particularly in elderly people), urinary retention, and weight gain.

Morphine sulphate

Constipation is a common adverse effect. If morphine is required regularly, then laxatives should be prescribed.

Follow up advice

Review in 4-6 weeks, or earlier if pain is poorly controlled. If the person has persistent pain, then the possibility of postherpetic neuralgia should be considered (although some would only diagnose this if pain persists for more than 3 months). Refer to the scenario *Postherpetic neuralgia - first-line*.

If low-dose amitriptyline is started with the aim of reducing the risk of subsequent postherpetic neuralgia, it should ideally be continued at a dose of at least 25 mg/day for 3 months.

Should I refer or investigate ?

Refer?

It is advisable to seek specialist advice with people who are immunocompromised. People with severe immunosuppression may require admission for intravenous aciclovir, as they are at high risk of disseminated zoster and complications.

Ophthalmic shingles requires urgent ophthalmological referral if a red eye or other sign of ocular involvement develops.

Admission is required if severe complications develop, such as dissemination or encephalitis.

Investigate?

If immunodeficiency is suspected (e.g. recurrent attacks of shingles in a person who is not already known to be immunocompromised), immunological tests should be done (discuss with local haematologist).

Doctor/patient discussion points

The rash and pain of shingles usually last 2-3 weeks.

Paracetamol alone, or combined with codeine, usually eases the pain.

Stronger painkillers are sometimes needed.

An antidepressant may help if the pain is bad. This is not to treat depression. It is good at easing nerve pains, such as shingles. Some experts say that all people over 60 should take an antidepressant to help prevent persistent pain from developing.

Antiviral medicine should be started within 72 hours of the rash appearing. It reduces the chance of pain persisting after the rash has gone.

Calamine or similar lotions may be soothing.

Ice packs or wet dressings over the rash may ease the discomfort.

Soft cotton clothing is the most comfortable.

If you still have pain after the rash clears come back to see a doctor.

Drug Rationale

Drugs not included

Oral NSAIDs seem to be of little benefit in the treatment of shingles pain [Kanazi et al, 2000].

Systemic corticosteroids are not included as any slight benefit is outweighed by the potential for harm. There is some evidence that high-dose corticosteroids added to antiviral drugs may speed healing of shingles, but there is no evidence that they reduce the risk of postherpetic neuralgia [Alper and Lewis, 2000; Yaphe and Lancaster, 2000].

Topical idoxuridine may provide short-term pain relief in acute shingles, but there is no evidence that it reduces the risk of postherpetic neuralgia [Yaphe and Lancaster, 2000].

Low-dose weak opioids with paracetamol (combination products), e.g. co-codamol 8/500 mg. There is no evidence that these offer any clinical benefit over paracetamol alone and they are likely to lead to opioid adverse effects [DTB, 1998a; MeReC, 2000; BNF 42, 2001].

High-dose weak opioids with paracetamol (combination products), e.g. co-codamol 30/500 mg. These fixed dose formulations do not allow titration to the most effective and safe analgesic dose to match the person's requirements.

Strong opioids other than morphine sulphate 10 mg/5 ml solution will require handwritten prescriptions.

Tricyclic antidepressants (TCAs) other than amitriptyline are not included: there is limited data available on the use of other TCAs in this situation.

Tramadol is expensive and there is a lack of evidence for its superiority over other analgesics. Tramadol has the potential to produce opioid adverse effects [Moore and McQuay, 1997; Regional Drug and Therapeutics Centre, 1998; Charlton, 1999].

Famciclovir 500 mg three times a day is not offered. It is licensed at this dosage for the treatment of people who are immunocompromised, but alternative less expensive regimens are available for this purpose.

Drugs included

Calamine lotion may provide short-term relief of symptoms [Kanazi et al, 2000].

Paracetamol with or without codeine is often adequate for relief of shingles pain.

Amitriptyline is offered as an adjuvant to paracetamol with or without codeine if additional pain relief is required. There is also limited evidence that early treatment with amitriptyline may reduce the incidence of postherpetic neuralgia in people with shingles aged 60 years or more [Bowsher, 1997].

Morphine sulphate 10 mg/5 ml solution is a further option for some individuals with acute severe shingles pain.

Oral antivirals (aciclovir, famciclovir, valaciclovir) are recommended for all people who are at high risk of severe shingles or the development of postherpetic neuralgia. Treatment should be started within 72 hours of the rash onset. Aciclovir is least expensive but has to be taken five times daily. Valaciclovir and famciclovir have the advantage of easier dosage regimens. Valaciclovir is a pro-drug of aciclovir and can be taken three times a day. Famciclovir is a pro-drug of penciclovir and can be taken either as 250 mg three times a day or as a 750 mg single daily dose.

PILs attached to this guidance

[Herpes Viruses Association](#)
[Shingles](#)
[Shingles - Post Herpetic Neuralgia](#)
[Shingles Support Society](#)

Therapy Groups

Therapy Group: Analgesia: use when required

Paracetamol 1g up to four times a day

NHS Prescription for age: 192 to 3060

Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Add on if required: codeine 30-60mg up to four times a day

NHS Prescription for age: 192 to 3060

Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Paracetamol 500mg tablets + codeine 30mg tablets

Patient Info: You may find it best to take your paracetamol regularly to start with.

Paracetamol 500mg tablets

NHS Prescription for age: 192 to 3060

Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Codeine 30mg tablets

NHS Prescription for age: 192 to 3060

Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Therapy Group: Calamine Lotion

Calamine lotion: apply when required to relieve itching

NHS Prescription for age: 192 to 3060

Calamine lotion

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
m313.	200 ml	Licensed	£0.64	£1.13	No CSM warning in BNF	OK

Usage Instructions: Apply to the affected area(s) when required to relieve itching

Patient Info: You may buy calamine lotion from a pharmacy.

Therapy Group: Start amitriptyline as an adjuvant analgesic: titrate up

Amitriptyline: titrate up from 10mg daily until pain settles

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	70 tablets	Not Licensed	£1.95		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take three tablets at night for 7 nights, then take a maximum of four tablets (40mg) at night. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Amitriptyline: titrate up from 25mg daily until pain settles

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	63 tablets	Not Licensed	£1.80		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take up to a maximum of three tablets (75mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Therapy Group: Morphine solution for acute severe shingles pain

Morphine sulphate solution: 10mg every 4 hours when required

NHS Prescription for age: 192 to 3060

Morphine sulphate 10mg/5ml sol

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj1L.	200 ml	Licensed	£4.16		No CSM warning in BNF	OK

Usage Instructions: Take one 5ml spoonful every 4 hours when required for pain relief

Patient Info:

Therapy Group: Antivirals for 7 days

Aciclovir 800mg five times a day

NHS Prescription for age: 192 to 3060

Aciclovir 800mg disp tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
ei1d.	35 tablets	Licensed	£21.91		No CSM warning in BNF	OK

Usage Instructions: Take one tablet five times a day for 7 days

Famciclovir 250mg three times a day

NHS Prescription for age: 192 to 3060

Famciclovir 250mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
ei92.	21 tablets	Licensed	£118.08		No CSM warning in BNF	OK

Usage Instructions: Take one tablet three times a day for 7 days

Famciclovir 750mg once a day

NHS Prescription for age: 192 to 3060

Famciclovir 750mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
ei95.	7 tablets	Licensed	£112.72		No CSM warning in BNF	OK

Usage Instructions: Take one tablet once a day for 7 days

Valaciclovir 1g three times a day

NHS Prescription for age: 192 to 3060

Valaciclovir 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
eiC1.	42 tablets	Licensed	£98.50		No CSM warning in BNF	OK

Usage Instructions: Take two tablets three times a day for 7 days

Scenario - Postherpetic neuralgia - first line

Which Therapy ?

Reassure that postherpetic neuralgia is usually a self-limiting condition (but unfortunately in some people it can be prolonged or even persist indefinitely).

Measures to reduce stimulation of the skin may be beneficial, as skin hypersensitivity (allodynia) is common. Natural fibre clothing is preferable to artificial fibres. A protective layer over the skin may be helpful (e.g. clingfilm or 'plastic skin').

Cold pack application may provide short-term relief of pain.

Paracetamol alone or with codeine may be effective in people with mild to moderate pain.

Treatments active against neuropathic pain are usually necessary. A tricyclic antidepressant (TCA) is the preferred first choice. Evidence best supports the use of **amitriptyline**. Alternative treatments are offered in the scenario *Postherpetic neuralgia - second-line*. (These should be considered if amitriptyline is ineffective, poorly tolerated, or contraindicated, or if it only partially relieves symptoms and add-on treatment is being considered).

The usual starting dose of amitriptyline is 25 mg/day, but a starting dose of 10 mg/day may be preferred in people who are elderly or frail.

The pain-relieving effect of TCAs is independent of their antidepressant effect. It is important to explain this to people, as many will be aware of their use in depression and will be concerned that the doctor thinks the pain is 'all in their mind'.

Pain relief with TCAs is often rapid, but may take 2-3 weeks to occur and maximum benefit may occur only after several weeks of treatment.

Prescribing points

For further information see the *Medicines Compendium* (www.medicines.org.uk) or the *British National Formulary* (www.bnf.org).

Amitriptyline

Driving: the Driver and Vehicle Licensing Authority (DVLA) recommends avoiding drugs that have antimuscarinic effects, such as TCAs. All people taking TCAs should be advised not to drive if adversely affected, particularly during the first month of starting or increasing the dose (tolerance develops within a week or two of stabilizing the dosage).

Other cautions include: cardiac disease particularly with arrhythmias; epilepsy; pregnancy and breastfeeding; glaucoma; prostatism; bipolar disorder; urinary retention; and suspected risk of overdosing.

Contraindications: recent myocardial infarction, arrhythmias, and hepatic impairment.

Adverse effects: commonly include dry mouth, sedation, constipation, postural hypotension, confusion (particularly in elderly people), urinary retention, and weight gain.

Morphine sulphate

Constipation is a common adverse effect. If morphine is required regularly, then laxatives should be prescribed.

Follow up advice

Review regularly to ensure treatment is tolerated and pain control is achieved.

Amitriptyline should be continued for 3 months, at the dose found to be effective, then gradually tailed off. Treatment should be restarted (or the dose increased) if pain recurs.

If amitriptyline is poorly tolerated or is ineffective (most people should gain benefit at 75 mg/day, but doses up to 150 mg/day may be tried) then additional or alternative treatment should be tried (see scenario *Postherpetic neuralgia - treatment failure*).

Should I refer or investigate ?

Refer?

If pain relief is inadequate, despite treatment with amitriptyline, referral to a pain clinic should be considered.

While waiting for the person to be seen, an alternative treatment may be considered (see scenario *Postherpetic neuralgia - treatment failure*).

Doctor/patient discussion points

In some cases of shingles, the pain persists for several weeks after the rash has gone. Sometimes the pain lasts months or longer.

Ice packs, or a layer of clingfilm, placed over the painful area may ease the discomfort.

Soft cotton clothing is the most comfortable.

Paracetamol, alone or combined with codeine, taken regularly, may help.

An antidepressant is often effective. It is not used here to treat depression. Certain antidepressants, such as amitriptyline, are also good at easing nerve pains.

A low dose is used at first, and the dose gradually increased if needed.

It usually eases the pain within a few days, but it may take 2-3 weeks.

It can take several weeks before you get maximum benefit.

You should take it for a further 3 months after the pain has gone or eased.

Drug Rationale

Drugs not included

Alternatives to amitriptyline for the pain of postherpetic neuralgia are offered in the scenario *Postherpetic neuralgia - treatment failure*.

Tricyclic antidepressants other than amitriptyline

Nortriptyline was found to be as effective as amitriptyline in a small double-blind, randomized controlled trial, and may be better tolerated [Watson et al, 1998]. It is an alternative tricyclic antidepressant for people intolerant to amitriptyline. It should also be considered if response to amitriptyline is inadequate. Prescriptions are offered in *Postherpetic neuralgia - second-line*.

Maprotiline and desipramine have also been found to be effective, but maprotiline has a high incidence of rash and desipramine is not available in the UK.

Other antidepressants have not been adequately studied in the treatment of postherpetic neuralgia.

Analgesics

Oral NSAIDs seem to be of little benefit [Johnson, 1997; Kanazi et al, 2000].

Low-dose weak opioids with paracetamol (combination products), e.g. co-codamol 8/500 mg. There is no evidence that these offer any clinical benefit over paracetamol alone and they are likely to lead to opioid adverse effects [DTB, 1998a; MeReC, 2000; BNF 42, 2001].

High-dose weak opioids with paracetamol (combination products), e.g. co-codamol 30/500 mg. These fixed-dose formulations do not allow titration to the most effective and safe analgesic dose to match the person's requirements.

Strong opioids (e.g. morphine) should generally be avoided due to the risk of dependence if used inappropriately. They are best reserved for use in specialist pain clinics, as there is a high risk of chronic usage in this situation. Strong opioids are usually reserved for moderate to severe pain of a visceral origin but there is increasing evidence that they are effective in treating the pain of postherpetic neuralgia [DTB, 2000; Yaphe and Lancaster, 2000; Kanazi et al, 2000].

Tramadol is expensive and there is a lack of evidence for its superiority over other analgesics. Tramadol has the potential to produce opioid adverse effects [Moore and McQuay, 1997; Regional Drug and Therapeutics Centre, 1998; Charlton, 1999].

Drugs included

Paracetamol alone or with codeine may be effective in people with mild to moderate pain.

Amitriptyline is widely considered to be the first-choice treatment for postherpetic neuralgia. If this is contraindicated, ineffective, or poorly tolerated, alternative treatments are offered in the scenario *Postherpetic neuralgia - treatment failure*.

PILs attached to this guidance

Herpes Viruses Association
Shingles
Shingles - Post Herpetic Neuralgia
Shingles Support Society

Therapy Groups

Therapy Group: Analgesia: use when required

Paracetamol 1g up to four times a day

NHS Prescription for age: 192 to 3060

Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Add on if required: codeine 30-60mg up to four times a day

NHS Prescription for age: 192 to 3060

Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Patient Info:

Paracetamol 500mg tablets + codeine 30mg tablets

Patient Info: You may find it best to take your paracetamol regularly to start with.

Paracetamol 500mg tablets

NHS Prescription for age: 192 to 3060

Paracetamol 500mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
di21.	100 tablets	Licensed	£0.75	£1.32	No CSM warning in BNF	OK

Usage Instructions: Take two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Codeine 30mg tablets

NHS Prescription for age: 192 to 3060

Codeine 30mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dj42.	56 tablets	Licensed	£2.90		No CSM warning in BNF	OK

Usage Instructions: Take one to two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.

Therapy Group: Start amitriptyline: titrate up

Amitriptyline: titrate up from 10mg daily until pain settles

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	70 tablets	Not Licensed	£1.95		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take three tablets at night for 7 nights, then take a maximum of four tablets (40mg) at night. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Amitriptyline: titrate up from 25mg daily until pain settles

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	63 tablets	Not Licensed	£1.80		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take up to a maximum of three tablets (75mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Further titration from 50mg to 80mg per day, if needed

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one amitriptyline 50mg tablet at night for 7 days. If pain persists, take ONE amitriptyline 50mg tablet together with ONE amitriptyline 10mg tablet at night for 7 days. The dose can be increased by ONE amitriptyline 10mg tablet at night every 7 days up to a maximum of THREE amitriptyline 10mg tablets in addition to ONE amitriptyline 50mg tablet at night. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking ONE amitriptyline 50mg tablet at night, there is no need to increase the dose any further.

Amitriptyline 50mg tablets

NHS Prescription for age: 192 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	28 tablets	Not Licensed	£1.20		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Amitriptyline 10mg tablets

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	42 tablets	Not Licensed	£1.17		CSM advice in BNF	OK

Usage Instructions: Take as directed on the right hand side of the prescription

Further titration from 100mg to 150mg per day, if needed

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	126 tablets	Not Licensed	£3.60		CSM advice in BNF	OK

Usage Instructions: Take four tablets at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take four tablets at night for 7 nights, then take five tablets at night for 7 nights, then take up to a maximum of six tablets (150mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 5 tablets at night, there is no need to increase the dose any further.

Therapy Group: Maintenance doses: amitriptyline 10mg to 50mg at night

Amitriptyline 10mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	28 tablets	Not Licensed	£0.78		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Patient Info:

Amitriptyline 20mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	56 tablets	Not Licensed	£1.56		CSM advice in BNF	OK

Usage Instructions: Take two tablets at night

Patient Info:

Amitriptyline 25mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	28 tablets	Not Licensed	£0.80		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Patient Info:

Amitriptyline 30mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	84 tablets	Not Licensed	£2.34		CSM advice in BNF	OK

Usage Instructions: Take three tablets at night

Patient Info:

Amitriptyline 40mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	112 tablets	Not Licensed	£3.12		CSM advice in BNF	OK

Usage Instructions: Take four tablets at night

Patient Info:

Amitriptyline 50mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	28 tablets	Not Licensed	£1.20		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Patient Info:

Therapy Group: Maintenance doses: amitriptyline 60mg to 150mg at night

Amitriptyline 60mg at night

Patient Info: You need to take 60mg of amitriptyline at night, so take ONE amitriptyline 50mg tablet together with ONE amitriptyline 10mg tablet at night.

Amitriptyline 50mg tablets

NHS Prescription for age: 720 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	28 tablets	Not Licensed	£1.20		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Amitriptyline 10mg tablets

NHS Prescription for age: 720 to 3060

Amitriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d711.	28 tablets	Not Licensed	£0.78		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Amitriptyline 75mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	84 tablets	Not Licensed	£2.40		CSM advice in BNF	OK

Usage Instructions: Take three tablets at night

Patient Info:

Amitriptyline 100mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	56 tablets	Not Licensed	£2.40		CSM advice in BNF	OK

Usage Instructions: Take two tablets at night

Patient Info:

Amitriptyline 125mg at night

Patient Info: You need to take 125mg of amitriptyline at night, so take TWO amitriptyline 50mg tablets together with ONE amitriptyline 25mg tablet at night.

Amitriptyline 50mg tablets

NHS Prescription for age: 192 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	56 tablets	Not Licensed	£2.40		CSM advice in BNF	OK

Usage Instructions: Take two tablets at night

Amitriptyline 25mg tablets

NHS Prescription for age: 192 to 3060

Amitriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d712.	28 tablets	Not Licensed	£0.80		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night

Amitriptyline 150mg at night

NHS Prescription for age: 192 to 3060

Amitriptyline 50mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d713.	84 tablets	Not Licensed	£3.60		CSM advice in BNF	OK

Usage Instructions: Take three tablets at night

Patient Info:

Scenario - Postherpetic neuralgia - treatment failure

Which Therapy ?

Referral to a pain clinic should be considered if pain relief is inadequate despite treatment with an adequate dose of a tricyclic antidepressant (TCA). While waiting for the person to be seen, an alternative treatment may be considered.

For people taking amitriptyline, ensure that an adequate dose is being taken. Most people will gain benefit with 75 mg/day, but up to 150 mg/day may be tried.

Nortriptyline is an alternative TCA if amitriptyline is poorly tolerated. It should also be considered if response to amitriptyline is inadequate. The usual starting dose is 25 mg/day, but a starting dose of 10 mg/day may be preferred in people who are elderly or frail.

Gabapentin or carbamazepine may be useful as add-on treatments, if amitriptyline or nortriptyline alone give inadequate pain relief. They may also be used as monotherapy if tricyclic antidepressants are not tolerated, are contraindicated, or are ineffective.

Psychosocial and behavioural approaches should be considered (e.g. pain-coping strategies, management of co-existing depression).

Prescribing points

For further information see the *Medicines Compendium* (www.medicines.org.uk) or the *British National Formulary* (www.bnf.org).

Nortriptyline

Driving: the Driver and Vehicle Licensing Authority (DVLA) recommends avoiding drugs that have antimuscarinic effects, such as tricyclic antidepressants (TCAs). All people taking TCAs should be advised not to drive if adversely affected, particularly during the first month of starting the medication or increasing the dose (tolerance develops within a week or two of stabilizing the dose).

Other cautions include: cardiac disease particularly with arrhythmias; epilepsy; pregnancy and breastfeeding; glaucoma; prostatism; bipolar disorder; urinary retention; and suspected risk of overdosing.

Contraindications: recent myocardial infarction, arrhythmias and hepatic impairment.

Adverse effects: commonly include dry mouth, sedation, constipation, postural hypotension, confusion (particularly in elderly people), urinary retention, and weight gain.

Gabapentin

Adverse effects are most commonly sedation, fatigue, dizziness and ataxia.

Antacids reduce the absorption and consequent bioavailability of gabapentin. If antacids are necessary, they should be taken at a different time of the day.

In renal impairment, the dose of gabapentin should be reduced (see datasheet for detailed information regarding this).

Carbamazepine

Adverse effects are most commonly sedation, diplopia, headache, nausea and vomiting.

Rash occurs in up to 10% of people who take carbamazepine. If the rash is persistent or severe, treatment must be stopped.

Agranulocytosis is a rare idiosyncratic reaction and is not predictable by routine blood monitoring.

Symptoms such as fever, sore throat, mouth ulcers, bruising: people should be advised to immediately report such symptoms.

History of bone marrow suppression: carbamazepine is not advised in people with such a history.

Carbamazepine reduces the effectiveness of oral contraceptives, and alternative forms of contraception should be considered. Gabapentin may be a better option in this situation. If carbamazepine is prescribed, then a combined oral contraceptive pill with at least 50 micrograms of oestrogen should be used. If the progestogen-only pill is used then double the usual dose should be taken (see *Prodigy Contraception* guidance for further information).

Carbamazepine interacts with a large number of drugs and possible interactions should be checked for prior to

starting this medication. (See *British National Formulary*, Appendix 1: Interactions, for full details.)

Follow up advice

Review regularly to ensure treatment is tolerated and pain control is achieved.

Treatment should be continued for at least 3 months, at the dose found to be effective for pain control, then gradually tailed off. Treatment should be restarted (or the dose increased) if pain recurs.

Should I refer or investigate ?

Refer?

Consider early referral to a pain clinic if pain relief is inadequate despite treatment with an adequate dose of a tricyclic antidepressant. While waiting for the person to be seen, an alternative treatment may be considered.

Refer to a pain clinic if pain control is inadequate despite management in general practice.

Doctor/patient discussion points

Your pain from shingles is still persisting.

Ice packs, or a layer of clingfilm over the rash, may ease the discomfort.

Soft cotton clothing is the most comfortable.

Paracetamol, alone or combined with codeine, taken regularly, may help. You may already be taking these, but carry on with them.

Some antidepressants are good at easing nerve pains. You may be taking one, but the dose may need to be increased. If you are on maximum dose, or side effects are troublesome, a change to a different type is an option.

An anticonvulsant medicine is another option. One can be taken in addition, or as an alternative to, an antidepressant. This is not because you have epilepsy. Some anticonvulsants ease nerve pains too.

Referral to a pain clinic is an option if the above does not help much.

Drug Rationale

Drugs not included

Tricyclic antidepressants other than nortriptyline

Amitriptyline is offered as the first-choice treatment of postherpetic neuralgia in the scenario *Postherpetic neuralgia - first-line*. Titration doses are available in that scenario.

Maprotiline and **desipramine** have also been found to be effective [Johnson, 1997; Kanazi et al, 2000], but maprotiline has a high incidence of rash and desipramine is not available in the UK.

Other antidepressants have not been adequately studied.

Anticonvulsants other than carbamazepine and gabapentin

Phenytoin has been less well studied than carbamazepine, but also seems to be effective against neuropathic pain. However, it is generally poorly tolerated and has a narrow therapeutic index.

Sodium valproate has only been studied in one small trial of people with spinal cord injury, and was found to be ineffective. However, it is widely used in the treatment of neuropathic pain and is reported as being effective. It might be considered if carbamazepine or gabapentin cannot be taken, but should generally be reserved for specialist use.

Newer anticonvulsants (other than gabapentin) have been inadequately studied.

[DTB, 2000; Collins et al, 2000; Yaphe and Lancaster, 2000; Tremont-Lukats et al, 2000; Kanazi et al, 2000; Wiffen et al, 2001].

Strong opioids

Strong opioids are best reserved for use in specialist pain clinics, as there is a high risk of chronic usage in this situation. There is increasing evidence that opioid analgesics are effective in treating the pain of postherpetic

neuralgia [DTB, 2000; Yaphe and Lancaster, 2000; Kanazi et al, 2000].

Topical treatments

Topical capsaicin is a licensed product which seems to provide some pain relief in postherpetic neuralgia [Yaphe and Lancaster, 2000]. However, it is poorly tolerated due to the intense burning sensation following application, although this effect diminishes with continued use. It is therefore not a first-choice treatment.

Topical lidocaine (lignocaine) 5% patch is not currently available in the UK. There is trial evidence of short-term relief of postherpetic neuralgia [Rowbotham et al, 1996; Galer et al 1999; Comer and Lamb, 2000].

Drugs included

Tricyclic antidepressants

Nortriptyline was found to be as effective as amitriptyline in a small double-blind, randomized controlled trial, and may be better tolerated [Watson et al, 1998]. It is an alternative tricyclic antidepressant for people intolerant of amitriptyline. It should also be considered if response to amitriptyline is inadequate.

Anticonvulsant drugs

Gabapentin has been studied in two double-blind randomized placebo-controlled trials. The first study found that gabapentin reduced pain by nearly a third [Rowbotham et al, 1998]. However, the dose of gabapentin was titrated up to 3.6 g/day, which is twice the maximum licensed dose in neuropathic pain. A more recent study used doses of 1.8 g/day or 2.4 g/day: approximately 30% of people treated with either dose of gabapentin had a 50% or greater reduction in mean pain score, compared with just over 10% of people treated with placebo [Rice and Maton, 2001]. We offer doses up to the maximum licensed dose - if pain relief is inadequate once this dose is reached, specialist opinion should be sought.

Carbamazepine is a well-established drug, with trial data for efficacy against neuropathic pain. It has not been specifically studied in people with postherpetic neuralgia

[DTB, 2000; Collins et al, 2000; Yaphe and Lancaster, 2000; Tremont-Lukats et al, 2000; Kanazi et al, 2000; Wiffen et al, 2001].

PILs attached to this guidance

[Herpes Viruses Association](#)
[Shingles](#)
[Shingles - Post Herpetic Neuralgia](#)
[Shingles Support Society](#)

Therapy Groups

Therapy Group: Start nortriptyline: titrate up

Nortriptyline: titrate up from 10mg daily until pain settles

NHS Prescription for age: 192 to 3060

Nortriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c6.	70 tablets	Not Licensed	£8.68		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take three tablets at night for 7 nights, then take a maximum of four tablets (40mg) at night. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Nortriptyline: titrate up from 25mg daily until pain settles

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	63 tablets	Not Licensed	£15.89		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take one tablet at night for 7 nights, then take two tablets at night for 7 nights, then take up to a maximum of three tablets (75mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 2 tablets at night, there is no need to increase the dose any further.

Further titration from 50mg to 80mg per day, if needed

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take two nortriptyline 25mg tablets at night for 7 days. If pain persists, take TWO nortriptyline 25mg tablets together with ONE nortriptyline 10mg tablet at night for 7 days. The dose can be increased by ONE nortriptyline 10mg tablet at night every 7 days up to a maximum of THREE nortriptyline 10mg tablets in addition to TWO nortriptyline 25mg tablets at night. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking TWO nortriptyline 25mg tablets at night, there is no need to increase the dose any further.

Nortriptyline 25mg tablets

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	56 tablets	Not Licensed	£14.13		CSM advice in BNF	OK

Usage Instructions: Take two tablets at night for 7 days, then take as instructed (see the right hand side of the prescription).

Nortriptyline 10mg tablets

NHS Prescription for age: 192 to 3060

Nortriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c6.	42 tablets	Not Licensed	£4.35		CSM advice in BNF	OK

Usage Instructions: Take as directed on the right hand side of the prescription

Further titration from 100mg to 150mg per day, if needed

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	126 tablets	Not Licensed	£31.78		CSM advice in BNF	OK

Usage Instructions: Take four tablets at night for 7 days, then take as instructed (see the right hand side of the prescription).

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take four tablets at night for 7 nights, then take five tablets at night for 7 nights, then take up to a maximum of six tablets (150mg) at night and continue. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking 5 tablets at night, there is no need to increase the dose any further.

Therapy Group: Maintenance doses: nortriptyline 10mg to 150mg at night

Nortriptyline 10mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 10mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c6.	28 tablets	Not Licensed	£3.47		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night**Patient Info:**

Nortriptyline 25mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	28 tablets	Not Licensed	£7.06		CSM advice in BNF	OK

Usage Instructions: Take one tablet at night**Patient Info:**

Nortriptyline 50mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	56 tablets	Not Licensed	£14.12		CSM advice in BNF	OK

Usage Instructions: Take two tablets at night**Patient Info:**

Nortriptyline 75mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	84 tablets	Not Licensed	£21.19		CSM advice in BNF	OK

Usage Instructions: Take three tablets at night**Patient Info:**

Nortriptyline 100mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	112 tablets	Not Licensed	£28.25		CSM advice in BNF	OK

Usage Instructions: Take four tablets at night**Patient Info:**

Nortriptyline 125mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	140 tablets	Not Licensed	£35.32		CSM advice in BNF	OK

Usage Instructions: Take five tablets at night

Patient Info:

Nortriptyline 150mg at night

NHS Prescription for age: 192 to 3060

Nortriptyline 25mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
d7c8.	168 tablets	Not Licensed	£42.38		CSM advice in BNF	OK

Usage Instructions: Take six tablets at night

Patient Info:

Therapy Group: Start carbamazepine: titrate up

Carbamazepine:titrate up from 100mg daily until pain settles

NHS Prescription for age: 192 to 3060

Carbamazepine 100mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn31.	70 tablets	Not Licensed	£2.95		No CSM warning in BNF	OK

Usage Instructions: Take one tablet once a day for 7 days, then increase the dose as instructed (see the right hand side of the prescription) until the pain settles.

Patient Info: Unless your doctor tells you otherwise the dose may be increased as follows until the pain settles. After 7 days, increase the dose to one tablet twice a day. After a further 7 days, increase to one tablet three times a day. After a further 7 days, increase the dose to one tablet four times a day. If you are on 2 or more tablets a day, take the tablets in evenly spaced doses through the day. Tell your doctor if you are taking any other medicines.

Carbamazepine:titrate up from 200mg daily until pain settles

NHS Prescription for age: 192 to 3060

Carbamazepine 100mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn31.	91 tablets	Not Licensed	£5.27		No CSM warning in BNF	OK

Usage Instructions: Take one tablet twice a day for 7 days, then increase the dose as instructed (see the right hand side of the prescription) until the pain settles.

Patient Info: Unless your doctor tells you otherwise the dose may be increased as follows until the pain settles. After 7 days increase to one tablet three times a day. After a further 7 days increase the dose to one tablet four times a day. If you take 2 or more tablets a day, you should not take them all at once. Take your tablets in evenly spaced doses through the day. Tell your doctor if you are taking any other medicine.

Therapy Group: Maintenance doses: carbamazepine 200mg to 800mg per day

Carbamazepine 200mg per day (100mg twice a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 100mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn31.	56 tablets	Not Licensed	£1.62		No CSM warning in BNF	OK

Usage Instructions: Take one tablet twice a day

Patient Info:

Carbamazepine 300mg per day (100mg three times a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 100mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn31.	84 tablets	Not Licensed	£2.43		No CSM warning in BNF	OK

Usage Instructions: Take one tablet three times a day**Patient Info:**

Carbamazepine 400mg per day (100mg four times a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 100mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn31.	112 tablets	Not Licensed	£3.24		No CSM warning in BNF	OK

Usage Instructions: Take one tablet four times a day**Patient Info:**

Carbamazepine 600mg per day (200mg three times a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 200mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn32.	84 tablets	Not Licensed	£4.50		No CSM warning in BNF	OK

Usage Instructions: Take one tablet three times a day**Patient Info:**

Carbamazepine 800mg per day (200mg four times a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 200mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn32.	112 tablets	Not Licensed	£3.62		No CSM warning in BNF	OK

Usage Instructions: Take one tablet four times a day**Patient Info:**

Carbamazepine m/r 400mg per day (200mg twice a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 200mg m/r tabs

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn3a.	56 tablets	Not Licensed	£5.26		No CSM warning in BNF	OK

Usage Instructions: Take one tablet twice a day**Patient Info:**

Carbamazepine m/r 800mg per day (400mg twice a day)

NHS Prescription for age: 192 to 3060

Carbamazepine 400mg m/r tabs

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dn3b.	56 tablets	Not Licensed	£10.34		No CSM warning in BNF	OK

Usage Instructions: Take one tablet twice a day

Patient Info:

Therapy Group: Gabapentin: titrate up or maintenance

Gabapentin: initial titration from 300mg to 900mg per day

NHS Prescription for age: 216 to 3060

Gabapentin 300mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj2.	39 capsules	Licensed	£20.67		No CSM warning in BNF	OK

Usage Instructions: Take one capsule on day 1. Take one capsule twice a day on day 2. Take one capsule three times a day from day 3 onwards.

Patient Info:

Gabapentin further titration from 1.2g to 1.8g per day

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take ONE Gabapentin 300mg capsule with ONE Gabapentin 100mg capsule (total dose 400mg) three times a day for 5 days. Then take ONE Gabapentin 300mg capsule with TWO Gabapentin 100mg capsules (total dose 500mg) three times a day for 5 days. Then take ONE Gabapentin 300mg capsule three times a day with THREE Gabapentin 100mg capsules (total dose 600mg) three times a day for 4 days. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking ONE Gabapentin 300mg capsule with ONE Gabapentin 100mg capsule (total dose 400mg) three times a day, there is no need to increase the dose any further.

Gabapentin 300mg capsules

NHS Prescription for age: 216 to 3060

Gabapentin 300mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj2.	42 capsules	Licensed	£22.26		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day, then take as instructed (see the right hand side of the prescription) until pain settles.

Gabapentin 100mg capsules

NHS Prescription for age: 216 to 3060

Gabapentin 100mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj1.	81 capsules	Licensed	£18.52		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day for 5 days, then take as instructed (see the right hand side of the prescription) until pain settles.

Gabapentin: initial titration from 300mg to 1.8g per day

Patient Info: Unless your doctor tells you otherwise, the dose may be increased as follows until the pain settles. Take ONE Gabapentin 300mg capsule on day 1. Take ONE Gabapentin 300mg capsule twice a day on day 2. Take ONE Gabapentin 300mg capsules three times a day on day 3. Then take ONE Gabapentin 300mg capsule together with ONE Gabapentin 100mg capsule (total dose 400mg) three times a day on days 4 to 7. Then take ONE Gabapentin 300mg capsule together with TWO Gabapentin 100mg capsules (total dose 500mg) three times a day on day 8. Then take TWO Gabapentin 300mg capsules (total dose 600mg) three times a day on days 9 to 14. You do not have to increase the dose any further once the pain has settled, so, for example, if the pain is controlled by taking ONE Gabapentin 300mg capsule three times a day, there is no need to increase the dose any further.

Gabapentin 300mg capsules

NHS Prescription for age: 216 to 3060

Gabapentin 300mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj2.	57 capsules	Licensed	£30.21		No CSM warning in BNF	OK

Usage Instructions: Take as directed on the right hand side of the prescription

Gabapentin 100mg capsules

NHS Prescription for age: 216 to 3060

Gabapentin 100mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj1.	18 capsules	Licensed	£4.11		No CSM warning in BNF	OK

Usage Instructions: Take as directed on the right hand side of the prescription**Gabapentin 900mg per day (300mg three times a day)**

NHS Prescription for age: 216 to 3060

Gabapentin 300mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj2.	84 capsules	Licensed	£44.52		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day**Patient Info:****Gabapentin 1200mg per day (400mg three times a day)**

NHS Prescription for age: 216 to 3060

Gabapentin 400mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj3.	84 capsules	Licensed	£51.52		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day**Patient Info:****Gabapentin 1500mg per day (500mg three times a day)****Patient Info:** You need to take 1500mg of Gabapentin each day, so take one 400mg capsule together with one 100mg capsule (total dose 500mg) three times a day.**Gabapentin 100mg capsules**

NHS Prescription for age: 216 to 3060

Gabapentin 100mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj1.	84 capsules	Licensed	£19.20		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day**Gabapentin 400mg capsules**

NHS Prescription for age: 216 to 3060

Gabapentin 400mg capsules

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnj3.	84 capsules	Licensed	£51.52		No CSM warning in BNF	OK

Usage Instructions: Take one capsule three times a day**Gabapentin 1800mg per day (600mg three times a day)**

NHS Prescription for age: 216 to 3060

Gabapentin 600mg tablets

Read Code	Quantity	Licence	NHS Cost	OTC Cost	CSM	Bioavailability
dnjy.	84 tablets	Licensed	£89.04		No CSM warning in BNF	OK

Usage Instructions: Take one tablet three times a day**Patient Info:**

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