Neuropathic Pain Syndromes

Philippine Society of NeuroRehabilitation

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Neuropathic Pain Syndromes

A Technical Drug Class Review for the Treatment of Common Neuropathic Pain Syndromes in the Philippines: Diabetic Painful Neuropathy (DPN), Post Herpetic Neuralgia (PHN), and Central Post Stroke Pain (CPSP)

The technical review on neuropathic pain is an initiative of the Pain Society of the Philippines and the Philippine Society of Neuro-Rehabilitation. The panel is composed of experts on pain medicine, anesthesiology, neurology, rehabilitation medicine, psychiatry and rheumatology.

The purpose of this review is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes for the management of three neuropathic pain syndromes/conditions. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach.

This review and the summary of recommendations have been submitted to the following organizations for consensus building: Pain Society of the Philippines, Philippine Society of Neuro-Rehabilitation, Philippine Neurological Association, Philippine Psychiatric Association, Philippine Society of Endocrinology and Metabolism, Philippine Diabetes Association, Stroke Society of the Philippines, Philippine Academy of Family Physicians, Philippine College of Physicians, Philippine College of Occupational Medicine, Philippine Academy of Rehabilitation Medicine, Philippine Society of Anesthesiologists, Philippine Orthopedic Association, Philippine Rheumatologic Association, Philippine Medical Association, Department of Health (DOH) and Philippine Drug Enforcement Agency (PDEA).

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“This review and the summary of recommendations have been submitted to the following organizations for consensus building: Pain Society of the Philippines, Philippine Society of Neuro-Rehabilitation, Philippine Neurological Association, Philippine Psychiatric Association, Philippine Society of Endocrinology and Metabolism, Philippine Diabetes Association, Stroke Society of the Philippines, Philippine Academy of Family Physicians, Philippine College of Physicians, Philippine College of Occupational Medicine, Philippine Academy of Rehabilitation Medicine, Philippine Society of Anesthesiologists, Philippine Orthopedic Association, Philippine Rheumatologic Association, Philippine Medical Association, Department of Health (DOH) and Philippine Drug Enforcement Agency (PDEA).”
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Algorithm of Grading System for Neuropathic Pain
(Modified from Treede, Jensen et al. Neurology 2008; 70:1630-1635)

[Diagram of the grading system for neuropathic pain]

FIGURE 1
Neuropathic Pain Syndromes

Background
Neuropathic pain is precipitated or caused by a primary lesion or dysfunction in the nervous system. It can be caused by numerous insults, including infection, metabolic disease, and physical trauma. It is characterized by ongoing and/or evoked types of pain in an area of sensory dysfunction.1, 2 A more recent definition of neuropathic pain states "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system."2 This re-definition, according to its proponents, fits into the nosology of the neurologic disorders. The reference to the somatosensory system connotes a wide range of neuropathic pain conditions which involves the peripheral and or central origins.

Neuropathic pain is estimated to affect up to 3% of the population.3 It may occur in diabetic sensorimotor polyneuropathy, the most common type of generalized polyneuropathy, affecting approximately 54% of patients with type 1 diabetes and 45% of patients with type 2 diabetes. Neuropathic pain develops in up to 25% of patients with diabetes.4,5,6 Approximately 800,000 cases of shingles are reported each year in the United States, with 25% to 50% of those cases developing postherpetic neuralgia, a neuropathic pain condition resulting from infection by the herpes zoster virus. Neuropathic pain conditions due to central nervous system diseases (such as stroke, multiple sclerosis, and spinal cord injury) have also been reported.4, 5, 6 We are unaware of epidemiologic data on neuropathic pain conditions, both central and peripheral, published and unpublished, in the Philippines.

The diagnosis of neuropathic pain has been challenging because of the lack of standard diagnostic tests for neuropathic pain (but not for peripheral neuropathy). Symptoms may include spontaneous pain, evoked pain or both. A diagnosis of neuropathic pain is made with the presence of symptoms plus a focused neurologic examination. Several pain scales are available for screening and identification of neuropathic pain. Treede and co-workers have recently proposed a grading system for neuropathic pain based on the revised IASP definition (2008):

Table Grading system for neuropathic pain

Criteria to be evaluated for each patient
1. Pain with a distinct neuroanatomically plausible distribution
2. A history suggestive of a relevant lesion or disease affecting the peripheral or central somatosensory system
3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test
4. Demonstration of the relevant lesion or disease by at least one confirmatory test.

Grading of certainty for the presence of neuropathic pain definite neuropathic pain: all (1 to 4); probable neuropathic pain: 1 and 2, plus either 3 or 4; possible neuropathic pain: 1 and 2, without confirmatory evidence from 3 or 4.

As part of the neurologic examination, these tests confirm the presence of negative or positive neurologic signs concordant with the distribution of pain. Clinical sensory examination may be supplemented by laboratory and objective tests to uncover subclinical abnormalities. As part of the neurologic examination, these tests confirm the presence of negative or positive neurologic signs concordant with the distribution of pain. Clinical sensory examination may be supplemented by laboratory and objective tests to uncover subclinical abnormalities. As part of the neurologic examination, these tests confirm the presence of negative or positive neurologic signs concordant with the distribution of pain. Clinical sensory examination may be supplemented by laboratory and objective tests to uncover subclinical abnormalities. As part of the neurologic examination, these tests confirm the presence of negative or positive neurologic signs concordant with the distribution of pain. Clinical sensory examination may be supplemented by laboratory and objective tests to uncover subclinical abnormalities.

Other neuropathic pain screening tools include the McGill Visual Analog Scale (VAS), the validated Filipino translation of IDpain7,8 and the SIGN-PQ by Vios and co-workers (Vios for the Special Interest Group in Neuropathic Pain, in preparation) The focus of this review will be chronic neuropathic pain conditions specifically diabetic painful neuropathy, post herpetic neuralgia and central post stroke pain.

Despite its recognition, neuropathic pain has remained to be inadequately treated. Several pharmacological and non-pharmacological interventions have been used. Approximately more than 70% of medications used to treat neuropathic pain in the Philippines are agents lacking evidence-based efficacy data in alleviating neuropathic pain conditions. Widely used in the Philippines for the treatment of any neuropathic condition including painful neuropathies are the vitamin B and its combinations representing large proportion of prescription.9 Evidence-based pharmacotherapies including antidepressants; anticonvulsants; opioids and its derivatives, have been used sparingly or not at all. The value of proper treatment options derived from the systematic review of randomized, placebo-controlled clinical trials cannot be underestimated.

The pharmacotherapeutic strategies used to treat neuropathic pain are based on empirical evidence, and by the mechanism of action, while others are derived from clinical trials. There have been several evidence-based treatment algorithms for neuropathic pain published by foreign organizations based on clinical trials, majority of which compare the active drug with placebo. Medications used in the treatment of neuropathic pain include anticonvulsants, antidepressants, opioids and its derivatives and local anesthetics. These medications modify the peripheral and central sensitization through various mechanisms of action.10

The current review sifts through the evidence in literature, both local and foreign for the treatment of the three above-mentioned chronic neuropathic pain conditions. Pain relief is the primary endpoint of pharmacological management. This is presented for purposes of uniformity and comparability by NNT (numbers needed to treat). The quality of life (QOL) and return to activities of daily living (ADLs) and safety data represented by NNH (numbers needed to harm) were considered in this review. The cost of treatment has been considered as well in making the final recommendations, keeping in mind that medical care in the country is largely an out of pocket expense.

Diabetic Painful Neuropathy (DPN)

Diabetes mellitus is a condition often associated with painful neuropathy. Patients often report superficial pain presenting as allodynia, sharp, stabbing, or burning pain in the feet, numbness and tingling sensation of the distal
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extremities. DPN is a chronic and progressive condition that affects many aspects of a patient’s life, including mood, mobility, ability to sleep and work, and interpersonal relationships.

The cause of DPN is not clear, but appears to involve neural degeneration from oxidative stress, which is highly correlated with hyperglycemia. Diagnosis includes ruling out other possible causes (e.g., alcoholism, vitamin deficiencies etc), and the first step in management is ensuring strict glycemic control. Table 1 summarizes the RCT on different drugs used for DPN and Table 3 shows the numbers needed to treat (NNT), numbers needed to harm (NNH) and cost of treatment per day for drugs for DPN.

### Table 1: Numbers Needed to Treat (NNT), Numbers Needed to Harm (NNH) and Cost of treatment per day for drugs for DPN

<table>
<thead>
<tr>
<th>TCA</th>
<th>NNT</th>
<th>NNH</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>2.1</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Imipramine</td>
<td>1.3/2.4/3.0</td>
<td>NS</td>
<td>Concentration response relationship</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>5.3/4.9</td>
<td>Odds Ratio 120/60 mg</td>
<td>NNT for 4.65**</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

** Anticonvulsants

| Gabapentin                   | 3.8/4.0 | 17.8 | High dose;                            |
| Pregabalin                   | 5.9/4.2 | 17.8 | NNT for 600/300 mg                    |
| Carbamazepine                | 2.3    | 21.7 | Poor data quality                    |

** Weak Opioids

| Tramadol                     | 3.1/4.3 | 7.8  |                                       |
| Opioids                      | 2.8     | NS   | As add on therapy                     |
| Fentanyl                     | NS      | NS   |                                       |

Post herpetic neuralgia, persistence of the pain of herpes zoster more than 3 months after resolution of the rash, is relatively common, affecting 10 to 15% of those with herpes zoster. The time interval used in the clinical case definition of postherpetic neuralgia varies in the literature from 1 to 6 months after resolution of the rash. The incidence of postherpetic neuralgia increases with age. The duration of postherpetic neuralgia is highly variable. The natural history of resolution of postherpetic neuralgia over time is a confounder in the evaluation of treatment efficacy and may limit the ability to generalize the results of controlled clinical trials in this population. Administration of antiviral agents within 72 hours of the onset of herpes zoster can reduce the intensity and duration of acute illness, and can prevent postherpetic neuralgia. Efforts at prevention of herpes zoster and postherpetic neuralgia are important in that 40 to 50% of those with postherpetic neuralgia do not respond to any treatment. It is beyond the scope of this review to deal with the acute treatment and prevention of postherpetic neuralgia.

Table 2 shows the NNT, NNH and cost of drugs per day for PHN.

### Table 2. Numbers Needed to Treat (NNT), Numbers Needed to Harm (NNH) and Cost of treatment per day for drugs for PHN

<table>
<thead>
<tr>
<th>Antidepressants</th>
<th>NNT</th>
<th>NNH</th>
<th>Cost of Treatment per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCA/</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>2.64</td>
<td>16.9</td>
<td>Not available locally</td>
</tr>
</tbody>
</table>

** Anticonvulsants

| Gabapentin      | 3.9-4.4 | 12.2 | P 30/100 mg cap           |
| Pregabalin      | 4.9     | NS   | P 52/75 mg cap            |

** Opioids

| Oxycodone       | 2.6    | P 70/ 5 mg tab            |

Central Post Stroke Pain (CPSP)

Approximately 5 per cent of people who have a stroke will develop neuropathic pain from the stroke called central post-stroke pain (CPSP). The pain is often described as an icy burning sensation. The onset of pain may occur at the time of the stroke but more often several months later. The pain is felt in the part of the body affected by the stroke. In 20 per cent of people, the pain gets better over a period of years. In 30 per cent of these, there is a lessening of pain over the first year. The precise cause of the pain is unknown. In some cases it is due to lesions to the thalamus.

Table 3 shows the summary of the corresponding NNT, NNH and cost of the drug per day.

### Table 3. Numbers Needed to Treat (NNT), Numbers Needed to Harm (NNH) and Cost of treatment per day for drugs for CPSP

<table>
<thead>
<tr>
<th>CPSP</th>
<th>NNT</th>
<th>NNH</th>
<th>Cost of Treatment per unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>3.0</td>
<td>NS</td>
<td>Not available locally</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>3.0</td>
<td>NS</td>
<td>P 34/200 mg tab</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>3.0</td>
<td>-</td>
<td>P 75/100 mg tab</td>
</tr>
</tbody>
</table>

Vitamin B and Vitamin B Combinations

The 2007 IMS data for the Philippines on medications used for the treatment of neuropathic pain conditions showed that Vitamin B and its combinations corner 45% of usage. The availability and relative affordability of vitamin B complex make this drug a frequent choice for treating peripheral neuropathy. Evidence is lacking in the literature on the effectiveness of vitamin B complex.

The vitamin B complex includes: thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pyridoxine (vitamin B6), biotin, pantothenic acid (vitamin B5), folic acid (vitamin B9), cyanocobalamin (vitamin B12), para-aminobenzoic acid, inositol, and choline. The required daily intake of vitamin B for a normal adult is as follows: thiamine 1.0 to 1.5 mg, riboflavin 1.2 to 1.7 mg, pyridoxine 1.4 to 2.0 mg, and niacin 13 to 19 niacin equivalents; cobalamin 3 to 5 mg and folic acid 50 mg.
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The therapeutic dose of vitamin B is higher for the treatment of certain deficiency states with neuropathy, such as: 40 mg oral thiamine per day for thiamine deficiency, 10 to 20 mg pyridoxine per day for peripheral neuritis induced by isoniazid.

A number of studies have shown that vitamin B6, specifically vitamin B6, in megadoses may be toxic to the nervous system.

Summary of Recommendations by the Technical Review Panel

DIABETIC PAINFUL NEUROPATHY (DPN)

I. Among patients with painful neuropathies, specifically painful diabetic polyneuropathy (DPN), how do non-invasive pharmacotherapies affect the probability of reducing pain, or inducing the probability of adverse events?

1) Among the anticonvulsants, pregabalin and gabapentin are effective in reducing pain due to painful diabetic neuropathy. The most common adverse effects are dizziness, somnolence and peripheral edema. which are transient and dose dependent, and thus, dose can be titrated. Based on the benefits of pain relief versus harm, we recommend the use of pregabalin and gabapentin to reduce pain from painful diabetic neuropathy (DPN) (Recommendation: Grade A)

2) Among the antidepressants, duloxetine and venlafaxine are effective in reducing pain from DPN. Most common adverse effects of duloxetine are somnolence, nausea, and constipation, which are usually mild to moderate in intensity, and severity is dose related. For venlafaxine, the most common adverse effects are nausea, vomiting, impotence, dyspepsia, and increased sweating. We recommend the use of duloxetine and venlafaxine to reduce pain from DPN (Recommendation: Grade A)

3) Amitriptyline is effective in reducing pain from DPN (class I). It is associated with anticholinergic adverse effects, such as dry mouth and urinary retention, as well as central effects including sedation, somnolence, dizziness and postural hypotension. This is not available locally (Recommendation: Grade A)

4) There is insufficient evidence for the use other antidepressants (fluoxetine, paroxetine, citalopram) in reducing pain from DPN (Recommendation: Grade U).

5) Oxycodone and fentanyl are effective in reducing pain in DPN. There is limited evidence for the use of morphine in DPN. Common adverse effects include sedation, nausea, vomiting and constipation. Long term use may cause erectile dysfunction. We recommend the use of oxycodone and fentanyl as second line treatment to reduce pain for DPN (Recommendation: Grade A) These are regulated medicines requiring S2 license and a pain specialist or doctors deemed competent to use these medicines are needed.

II. Among patients with post-herpetic neuralgia (PHN), how do non-invasive pharmacotherapies affect the probability of reducing pain, or inducing the probability of adverse events?

1) Among anticonvulsants, gabapentin and pregabalin are effective in reducing pain of PHN. The most common adverse effects are dizziness, somnolence and peripheral edema, which are transient and dose dependent, and thus, dose can be titrated. We recommend the use of pregabalin and gabapentin to reduce pain from PHN (Recommendation: Grade A)

2) Tricyclic antidepressants (amitriptyline, desipramine and nortriptyline) are effective in reducing pain due to postherpetic neuralgia. Adverse effects include sedation, anticholinergic side effects like dry mouth, constipation, fatigue and cardiac dysrhythmias. However, these drugs are not available locally (Recommendation: Grade A)

3) There are no studies on the use of SSRI and SNRI for PHN (Recommendation: Grade U)

4) Oxycodone is shown to be effective in reducing pain from PHN. We recommend the use of oxycodone as second line treatment for PHN. This is a regulated medicine and a pain specialist or doctors deemed competent to use this medicine is needed. (Recommendation: Grade A)

5) Topical Lidocaine patch is effective in reducing pain from PHN. However, it is not locally available (Recommendation: Grade A)

6) There is a single trial on the use of Tramadol for PHN (class II). Adverse events include dizziness,
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PROPOSED SUMMARY OF FIRST AND SECOND LINE DRUGS

<table>
<thead>
<tr>
<th>Disease Entity</th>
<th>Grade A</th>
<th>Grade B</th>
<th>Grade C</th>
<th>Grade U</th>
<th>1st Line</th>
<th>2nd Line</th>
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<tbody>
<tr>
<td>DPN</td>
<td>Pregabalin/GBP</td>
<td>SSRI</td>
<td>Capsaicin</td>
<td>Pregabalin</td>
<td>Duloxetine</td>
<td>Venlafaxine</td>
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<tr>
<td></td>
<td>Duloxetine/venlafaxine</td>
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<tr>
<td></td>
<td>Oxycodeone and Fentanyl</td>
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<td></td>
<td>Tramadol</td>
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<td>Tramadol</td>
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<td>not available locally</td>
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<tr>
<td>CPSP</td>
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<tr>
<td></td>
<td>(not effective)</td>
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<td></td>
<td>SSRI/SNRI</td>
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</tbody>
</table>
* Recommendations for the first and second line drugs are based on strength of evidence, adverse events, costs, and local availability

For medications with Grade U recommendations, we cannot recommend their use at the present time.

CENTRAL POST STROKE PAIN (CPSP)

III. Among patients with central neuropathic pain, specifically central post-stroke pain (CPSP), how do non-procedural pharmacotherapies affect the probability of reducing pain, or inducing the probability of adverse events?

1) Among the anticonvulsants, lamotrigine has modest evidence for reducing pain for CPSP (two class 2) Adverse effects include rash with rapid dose escalation. (Recommendation: Grade B) Gabapentin (class 3) and Zonisamide (class 4) show insufficient evidence in reducing pain for CPSP. (Recommendation: Grade U) Carbamazepine is not effective in reducing pain for CPSP (class 2). Adverse effects include rash, dizziness, gait disturbance, sedation, hepatic and hematologic abnormalities. (Recommendation: Grade B) In general, except for lamotrigine, there is insufficient evidence for the use of most anticonvulsants in reducing pain for CPSP.

2) Amitriptyline has modest evidence in reducing pain for CPSP (one class 2). (Recommendation: Grade B)

3) There are no studies on the use of SSRI and SNRI for CPSP. (Recommendation: Grade U).

4) There is insufficient evidence for the use of opioids for central post stroke pain. (Recommendation: Grade U)

5) Intravenous morphine has been shown to be not effective in reducing pain for CPSP (one class 2). We do not recommend that use of intravenous reducing pain for CPSP (Recommendation: Grade B)

6) Intravenous lidocaine has modest evidence in short term pain relief in CPSP (one class 2). (Recommendation: Grade B)

* For medications with Grade U recommendations, we cannot recommend their use at the present time.
Common Dosages of Medications used for Neuropathic Pain in the Philippines*

<table>
<thead>
<tr>
<th>Anticonvulsants</th>
<th>Usual Adult Dosage; preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>200-800 mg/day; 200/400 mg/tab</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>300-1200 mg/day; 100/300/400/600 mg/cap</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>50-200 mg/day; 50/100 mg/tab</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>300-1200 mg/day; 300/600 mg/tab</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>75-300 mg/day; 50/75/150 mg/cap</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>250-1000 mg/day 250/500 mg/tab</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>100-600 mg/day; 100 mg/tab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti Depressants</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine</td>
<td>60-120 mg/ day; 30/60 mg/tab</td>
</tr>
<tr>
<td>Imipramine</td>
<td>0.2-0.4 mg/kg/day 10/25 mg/tab</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>25-75 mg/day 25/50 mg/tab</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>150-300 mg/day 25/50/75 mg/tab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid Analgesics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>50-100 ug IV/I/M</td>
</tr>
<tr>
<td>Morphine</td>
<td>15-30 mg q 8h 30 mg/tab;</td>
</tr>
<tr>
<td>Oxycodeone</td>
<td>2.5-10 mg SC/IV/IM q 2-6h 10/15 mg/cc</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>10 mg q 12h; 10 mg/tab</td>
</tr>
<tr>
<td>Tramadol</td>
<td>50-100 mg q 4-6h 50 mg/tab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Others</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical Lidocaine</td>
<td>5% ointment</td>
</tr>
</tbody>
</table>

* At this point we cannot recommend dosages for Filipinos

REFERENCES:

2. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hannson P Hughes R, Nurmikko T, Serra J, (What is the title of this article?) Neurology 2008;70:1630-1635

**Neuropathic Pain Syndromes**

15. Nanna B. Finnerup, MD; Marit Otto, MD; Troels S. Jensen, MD, PhD; Soren H. Sindrup, MD, PhD An Evidence-Based Algorithm for the Treatment of Neuropathic Pain Medscape General Medicine. 2007; 24:3-36.
# Recommended Therapeutics

The following index lists therapeutic classifications as recommended by the treatment guideline. For the prescriber’s reference, available drugs are listed under each therapeutic class. For drug information, please refer to the Philippine Drug Directory System (PPD, PPDr, PPD Text, PPD Tabs).

## CNS Drugs

### Anticonvulsants

- **Carbamazepine**
  - Carbilepp
  - Epikor
  - Tegretol
  - Zynaps

- **Gabapentin**
  - Calmpent
  - Gabix
  - Neurontin
  - Neuropin
  - Reinin

- **Lamotrigine**
  - Lamictal

- **Oxcarbazepine**
  - Trileptal

- **Pregabalin**
  - Lyrica

- **Valproic Acid**
  - Depacon
  - Depakene Syrup

- **Zonisamide**

## Psychotropic Drugs

### Antidepressants

- **Tricyclic & Other Norepinephrine-Reuptake Inhibitors**
  - Amitriptyline
  - Desipramine
  - Duloxetine
  - Cymbalta
  - Imipramine
  - Tofranil
  - Trimipramine
  - Surmontil

- **Selective Norepinephrine Reuptake Inhibitor**
  - Venlafaxine

### Vitamin B-complex

- *Vit. B1, B6, B12*
- B3B Capsule
- Balance B-50
- Bernacine
- Blox
- Cetravim
- Cramin Forte
- Drugmaker’s Biotech Vitamin B1 + B6 + B12
- Jaga
- Meganerve 1000
- Meganerve - 300
- Nervit-B Plus
- Nervite
- Neuro - Ace
- Neuro-B’s
- Neurobase
- Neurobexol/Neurobexol Forte
- Neurobion/Neurobion 5000
- Neurogen-E
- Neurolink/Neurolink Forte
- Neuroxel 500
- One-Six-Twelve
- Oranerve Forte
- Pharex Vitamin B-Complex
- Polynerve 1000
- Polynerve 500
- SevenSeas Vitamin B-Complex
- Super B
- Supraneuron
- Valtrex/Valtrex Forte
- Vaneular
- Vibee

### B-Complex/Lysine/Fe

- Crescin

### B-Complex/Paracetamol

- Polynerve Forte

### Fursultiamine/B6/B12

- Nevramin

### Methylcobalamin

- Kaimuco
- Mecovit
- Methycobal

### Pizotifen/Vit. B-Complex

- Mosegor Vita

### Vit. B1/ B6/ B12/ Vit E

- Nuron-E/Hinuron-E