Nuring NT
Tablets

1. **Generic Name**
   Nortriptyline + Pregabalin

2. **Qualitative and Quantitative Composition**

Nortriptyline 10 mg

Pregabalin 75 mg

3. **Dosage form and strength**

Oral tablets are available in the strength of Nortriptyline 10 mg, Pregabalin 75mg .

4. **Clinical particulars**

4.1 Therapeutic indication

Nuring NT Tablets is indicated in treatment of:

- Diabetic Peripheral Neuropathy
- Low Back Pain
- Post Herpetic Neuralgia
- Fibromyalgia
- Spinal Cord Injury

4.2 Posology and method of administration

Recommended oral dose of Nuring NT Tablets is twice a day. It is advised to consult doctor for the dosage, as the frequency also depends on the patient's condition.

4.3 Contraindication

Nuring NT Tablets is contraindicated in patient with hypersensitivity to any component of tablets and history of urinary retention – BPH

4.4 Special warnings and precautions for use

- Do not drink alcohol while taking Nuring NT Tablets. It can increase the effects of alcohol, which could be dangerous.
- Grapefruit and grapefruit juice may also interact with this medicine and cause unwanted side effects.

- Use of Nuring NT tablets can make patient more prone to sunburns. Hence avoid exposure to sunlight or tanning beds. Wear protective clothing and use sunscreen when outdoors during daytime.

4.5 Drug interactions

- Nortriptyline

✓ Some products that may interact with Nortriptyline include: arbutamine, "blood thinners" (such as warfarin), disulfiram, thyroid supplements, anticholinergic drugs (such as benztropine, belladonna alkaloids), certain drugs for high blood pressure (drugs that work in the brain such as clonidine, guanabenz).

✓ Taking MAO inhibitors with Nortriptyline may cause a serious (possibly fatal) drug interaction. Avoid taking MAO inhibitors (isocarboxazid, linezolid, methylene blue, moclobemide, phenelzine, procarbazine, rasagiline,safinamide,selegiline, tranylcypromi ne) during treatment with this medication.

✓ The risk of serotonin syndrome/toxicity increases if taken with other drugs that increase serotonin. Examples include street drugs such as MDMA/"ecstasy," St. John's wort, certain antidepressants (including SSRIs such as fluoxetine/paroxetine, SNRIs such as duloxetine/venlafaxine), among others.

✓ Other medications can affect the removal of nortriptyline from body, thereby affecting how nortriptyline works. These drugs include cimetidine, terbinafine, drugs to treat irregular heart rate (such as quinidine/propafenone/flecainide). This is not a complete list.

- Pregabalin

Pregabalin has no known severe interactions with other drugs.

Serious interactions of Pregabalin include:

- ✓ benazepril
- ✓ captopril
- ✓ enalapril
- ✓ everolimus
- ✓ fosinopril
- ✓ imidapril
- ✓ lisinopril
- ✓ moexipril
- ✓ perindopril

- ✓ quinapril
- ✓ ramipril
- ✓ sirolimus
- ✓ temsirolimus
- ✓ trandolapril

Moderate interactions of Pregabalin include:

- ✓ clobazam
- ✓ deutetrabenazine
- ✓ lurasidone
- ✓ orlistat

4.6 Use in special population

- Pediatric: safety and efficacy has not been evaluated in children.
- Geriatric: safety and efficacy has not been evaluated in old patients.
- Liver impairment: Not recommended.
- Renal failure: Use with caution.
- Pregnancy and lactation:Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

4.7 Effects on ability to drive and use machine

Nuring NT Tablets may impair thinking or reactions. Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Nuring NT Tablets is known.

4.8 Undesirable effects

- Sedation, Drowsiness and Dizziness
- Weight Gain
- Dry mouth, blurred vision, increased intraocular pressure, constipation
- Hypotension, Syncope, Palpitations, Myocardial Infarction & Arrhythmias

4.9 Overdose

There is limited experience of overdose with Nuring NT. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

It is believed that nortriptyline either inhibits the reuptake of the neurotransmitter serotonin at the neuronal membrane or acts at beta-adrenergic receptors. It displays a more selective reuptake inhibition for noradrenaline, which may explain the relief and improvement of biological symptoms with nortriptyline therapy. Tricyclic antidepressants do not inhibit monoamine oxidase nor do they affect dopamine reuptake. As with other TCAs, nortriptyline displays affinity for other receptors including mACh receptors, histamine receptors and 5-HT receptors. Antimuscarinic effects upon binding to mAChR are responsible for various side effects of TCAs.

By binding presynaptically to the alpha2-delta subunit of voltage-gated calcium channels in the central nervous system, Pregabalin modulates the release of several excitatory neurotransmitters including glutamate, substance-P, norepinephrine, and calcitonin gene related peptide. In addition, Pregabalin prevents the alpha2-delta subunit from being trafficked from the dorsal root ganglia to the spinal dorsal horn, which may also contribute to the mechanism of action.Although Pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), it does not bind directly to GABA or benzodiazepine receptors.

5.2 Pharmacodynamic properties

Nortriptyline is a tricyclic antidepressant of the dibenzocycloheptene type and is the active metabolite of amitriptyline. It is an inhibitor of pre-synaptic noradrenaline reuptake than of serotonin, and is less anticholinergic than amitriptyline whilst having stronger antihistaminergic effects. Nortriptyline has been observed to increase the pressor effect of norepinephrine but blocks the pressor response of phenethylamine.

Although the structure of pregabalin is similar to gamma-aminobutyric acid (GABA), it does not bind to GABA receptors. Instead, it binds the alpha2-delta subunit of presynaptic voltage-gated calcium channels in the central nervous system. Pregabalin does not modulate dopamine receptors, serotonin receptors, opiate receptors, sodium channels or cyclooxygenase activity.

5.3 Pharmacokinetic properties

- **Nortriptyline**

<u>Absorption</u>

As with other TCAs, notriptyline is well absorbed from the GI tract. Peak plasma concentrations occur within 4-8.8 hours following oral administration, with the mean time of 5.5 hours. The mean oral bioavailability is 51%

Protein binding

Plasma protein binding is approximately 93%

Metabolism

Nortriptyline undergoes hepatic metabolism via the same pathway as other TCAs, where it is metabolized via demethylation and hydroxylation followed by conjugation with glucuronic acid. The metabolism is subject to genetic polymorphism (CYP2D6). The main active metabolite is 10-hydroxynortriptyline exists in a cis and a trans form, where the trans form is dominant and more pharmacologically potent. N-demethylnortriptyline is also formed to some extent. The metabolites have the same pharmacological profile as nortiptyline, but are weaker. 10-hydroxynortriptyline dominates in the plasma, but most of the metabolites are conjugated

Excretion

Nortriptyline and its metabolites are mainly excreted in the urine, where only small amounts (2%) of the total drug is recovered as unchanged parent compound . Approximately one-third of a single orally administered dose is excreted in urine within 24 hours. Small amounts are excreted in feces via biliary elimination.

- **Pregabalin**

Absorption

After oral dosing administered in the fasted state, pregabalin absorption is rapid, and extensive.Pregabalin oral bioavailability is reported to be ≥90% regardless of the dose. Cmax is attained within 1.5 hours after single or multiple doses, and steady state is attained within 24-48 hours with repeated administration. Both Cmax and AUC appear to be dose proportional.

Protein binding

Pregabalin is not plasma protein bound.

Metabolism

Less than 2% of pregabalin is metabolized and it is excreted virtually unchanged in the urine

Excretion

Pregabalin is almost exclusively eliminated in the urine

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Not required.

7. Description

- **Nortriptyline**

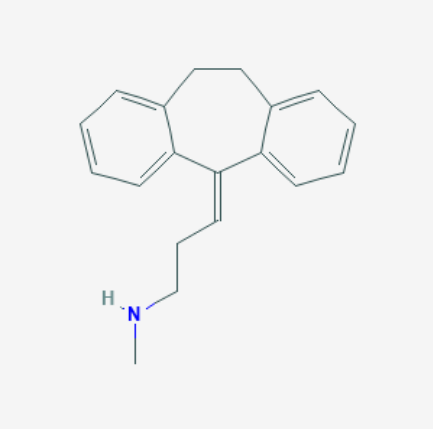
Nortriptyline is a tricyclic antidepressant agent used for short-term treatment of various forms of depression.

Chemical Name- *N*-methyl-3-(2-tricyclo[9.4.0.0^{3,8}]pentadeca-1(15),3,5,7,11,13-hexaenylidene)propan-1-amine

Molecular Weight- 277.4 g/mol

Molecular Formula- $C_{19}H_{21}N$

Structure-



- . **Pregabalin**

Pregabalin is a 3-isobutyl derivative of gamma-amino butyric acid (GABA) with anti-convulsant, anti-epileptic, anxiolytic, and analgesic activities.

Chemical Name- *N*-methyl-3-(2-tricyclo[9.4.0.0^{3,8}]pentadeca-1(15),3,5,7,11,13-hexaenylidene)propan-1-amine

Molecular Weight- 263.4 g/mol

Molecular Formula- $C_{19}H_{21}N$

Structure-

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Nuring NT Tablets are available in pack of 10 tablets

8.4 Storage and handling instructions

Store in a cool and dry place. Store out of sight and reach of the children.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patients are advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

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11. Details of permission or license number with date

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12. Date of revision: January 2021