SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Neurorubine™-Forte Lactab,

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances
Each Neurorubine™-Forte Lactab, coated tablet contains: thiamine nitrate (vitamin B_1) 200 mg, pyridoxine hydrochloride (vitamin B_6) 50 mg, cyanocobalamin (vitamin B_{12}) 1000 mg

Excipients
Colouring agent: E127 (erythrosine); excipients for coated tablets (for a full list of excipients, see section 6.1.)

3. PHARMACEUTICAL FORM

Film-coated tablet (Lactab)

Neurorubine™-Forte is pink, round, biconvex, film coated tablet embossed “TP” on one side

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

As an adjuvant in the treatment of neuritis pain: acute or chronic neuritis and polyneuritis, neuralgia, as well as toxic damage to nerve tissue such as due to alcoholism, diabetic polyneuropathy and drug intoxication.

4.2 Posology and method of administration

Adults
One to two tablets daily.

Children
To date, there has been no experience with treatment of children. The product should therefore not be used in children.

For oral administration.

4.3 Contraindications

Neurorubine™-Forte is contraindicated in patients with known hypersensitivity to one or more ingredients, particularly vitamins B_1, B_6 and B_{12}.
Vitamin B_{12} is contraindicated in the case of psoriasis, as patients with existing psoriasis may experience a flare reaction to vitamin B_{12}, i.e. a worsening of psoriasis symptoms.

4.4 Special warnings and precautions for use

Neurorubine™-Forte should not be used in individuals under 18, as there are no clinical data available.
Skin reactions, which are signs of hypersensitivity to vitamin B_1, B_6 or B_{12}, may occur during treatment. Vitamin B_6 and high doses of Vitamin B_{12} can trigger or aggravate acne.

4.5 Interaction with other medicinal products and other forms of interaction

Vitamin B_6 in high dosage, as contained in Neurorubine™-Forte, can reduce the effect of L-dopa in Parkinson's disease. Moreover, the toxicity of isoniazid may be increased. Being thiamine antagonists, thiosemicarbazone and 5-fluorouracil abolish the effect of vitamin B_1. Antacids inhibit the absorption of vitamin B_1.

4.6 Fertility, Pregnancy and lactation

Pregnancy Category C. Animal reproduction studies have not been conducted with Neurorubine™-Forte. It is also not known whether daily doses of Neurorubine™-Forte can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Neurorubine™-Forte should be given to a pregnant woman only if clearly needed.

Vitamin B_6 is excreted in breast milk. However, to date no serious adverse consequences are known. Neurorubine™-Forte can be used during breast-feeding only if this is clearly necessary.

4.7 Effects on ability to drive and use machines

No specific study has been carried out with Neurorubine™-Forte on the ability to drive and use machines. It is however rather unlikely that this medicine would have a negative influence in this regard.

4.8 Undesirable effects

Adverse reactions in Table 1 are listed according to MedDRA system organ class and frequency category. Frequency categories are defined using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Tabulated list of adverse reactions

Table 1

Immune system disorders *Rare:* Allergic reactions. *Very rare:* Angioneurotic oedema
Endocrine disorders *Very rare:* Prolactin release is inhibited.
Nervous system disorders *Rare:* Isolated cases of anxiety have been described (especially in sensitive patients). Pyridoxine stimulates the decarboxylisation of levodopa and can reduce its therapeutic effect on Parkinson's disease, unless a decarboxylase inhibitor is given at the same time. In rare cases reversible peripheral sensory neuropathy was observed at high doses over a longer period (> 500 mg/day). *Very rare:* Agitation, anxiety, paraesthesia, somnolence, headache.
Cardiac disorders *Rare:* Tachycardia.
Vascular disorders *Rare:* Circulatory failure (especially in sensitive patients).
Respiratory, thoracic and mediastinal disorders *Very rare:* In isolated cases, cyanosis and pulmonary oedema have been described (especially in sensitive patients).
Gastrointestinal disorders *Very rare:* Nausea and haemorrhages in the gastrointestinal tract have been described (especially in sensitive patients).
Hepatobiliary disorders *Very rare:* High doses can lead to an increase in serum glutamic oxaloacetic transaminase (GOT).
Skin and subcutaneous tissue disorders *Uncommon:* High doses can cause acne. Pyroxidine can trigger or aggravate acne vulgaris or acne-like rash. *Rare:* Allergic reactions. *Very rare:* Skin reactions with pruritus and urticaria have been described (especially in sensitive patients).
General disorders and administration site conditions *Very rare:* Outbreaks of sweating, feeling of weakness, globus symptoms.

To reports any side effect(s):

- ***Saudi Arabia:***

The National Pharmacovigilance and Drug Safety Centre (NPC)
Fax: +966-11-205-7662
Call NPC at +966-11-2038222, Exts: 2317-2356-2353-2354-2334-2340.
Toll free phone: 8002490000
E-mail: npc.drug@sfda.gov.sa
Website: www.sfda.gov.sa/npc

Other GCC States:

Please contact the relevant competent authority

4.9 Overdose

Consumption of excessive daily doses of vitamin B_6 (500 mg or more for longer than 5 months) can in rare cases lead to peripheral sensory neuropathies, which are however generally reversible after discontinuation of the preparation.

In the case of an overdose, symptomatic treatment must be initiated. Toxin removal (induce vomiting, gastric lavage) and measures to reduce resorption (administer charcoal) are indicated.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

ATC code: A11D B

Mechanism of action

B-vitamins are predominantly components of enzyme systems that regulate protein, fat and carbohydrate metabolism. All B-vitamins each fulfil a specific biological function. Their presence in equilibrated amounts is essential for trouble-free metabolic processes.
Neurorubine™-Forte combines three vitamins at high dose that are important for the function of the nervous system. Each of these vitamins is essential for normal metabolic processes in the nerve cell. They show an analgesic effect when administered in pharmacodynamically high doses.

5.2 Pharmacokinetic properties

Cyanocobalamin (vit. B_{12})

Cyanocobalamin is absorbed only to a limited extent in healthy people and depends on the concentration of "intrinsic factor". A fraction of vitamin B12 is absorbed in the free form, but the main quantity is absorbed only after binding to the “intrinsic factor”. After absorption from the intestinal tract, vitamin B12 is bound in the serum to the specific B_{12}-binding-beta-(transcobalamin) and B_{12}-binding-alpha1-globulins. The storage of vitamin B_{12} takes place mainly in the liver. The half-life in plasma is approx. 5 days, in the liver approx. 1 year.

Thiamine (vit. B_1)

Thiamine is absorbed in the duodenum, jejunum and ileum by active transport. After absorption by the intestinal mucosa, thiamine is transported through the portal circulation to the liver. Some of the absorbed thiamine is amenable to the enterohepatic circulation.

The main excretion products of thiamine constitute thiamine carboxylic acid and pyramine (2,5-dimethyl-4-aminopyrimidine), in addition to relatively small amounts of unmodified thiamine.

Pyridoxine hydrochloride (vit. B_6)

Pyridoxine is quickly absorbed from the intestinal tract.
In the organism, it is oxidised to pyridoxal or amidated to pyridoxamine.
Phosphorylation of the CH_2OH-group at position 5 (pyridoxal-5-phosphate, PALP) is a prerequisite for its function as a co-enzyme. In the blood, almost 80% of PALP is bound to protein. Pyridoxine is predominantly stored in muscle as PALP. The main excretion product is 4-pyridoxic acid.

5.3 Preclinical safety data

No relevant preclinical data are available on the current preparation.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients

Table core: Mannitol, Cellulose powdered, Cellulose microcrystalline, Starch pregelatinized, Magnesium stearate & Silica colloidal anhydrous.

Film-coating: Purified water, Hypromellose, Macrogol 6000, Talc, Titanium dioxide (E171) & Erythrosine (E 127).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Do not store above 30 ºC.

6.5 Nature and contents of container

Neurorubine™-Forte is pink, round, biconvex, film coated tablet embossed “TP” on one side.
The film coated tablets are packed in aluminum blister.

Packs of 10, 20 and 100 tablets.
Not all presentations may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

Acino Pharma AG, Liesberg, Switzerland

8. MARKETING AUTHORISATION NUMBER

10-222-99

9. DATE OF FIRST AUTHORISATION

1999

10. DATE OF REVISION OF THE TEXT

10/2018