ข้อความบนเอกสารกำกับยา

ข้อความเหมือนกันทุกขนาดบรรจุ

เอกสารกำกับยาภาษาอังกฤษ

TOPRELIN

1. Product Name

TOPRELIN 25

TOPRELIN 75

TOPRELIN 150

2. Name and Strength of Active Ingredient

TOPRELIN 25: each hard capsule contains 25 mg of pregabalin.

TOPRELIN 75: each hard capsule contains 75 mg of pregabalin.

TOPRELIN 150: each hard capsule contains 150 mg of pregabalin.

3. Product Description

TOPRELIN 25: white powder filled in white capsule no. 4. with black letter TO and figure 25.

TOPRELIN 75: white powder filled in maroon-white capsule no.4 with black letter TO and figure 75.

TOPRELIN 150: white powder filled in orange-white capsule no.2 with black letter TO and figure 150.

4. Pharmacodynamics/Pharmacokinetics

4.1 Pharmacodynamics [1-10],[2-22]

Pregabalin binds with high affinity to the $\alpha_2 - \delta$ site (an auxiliary subunit of voltage-gated calcium channels) in CNS tissues. Although the exact mechanism of action of pregabalin is unknown, binding to the $\alpha_2 - \delta$ site may be related to pregabalin's analgesic and anticonvulsant effects. *In vitro*, pregabalin reduces the calcium-dependent release of various neurotransmitters, including glutamate, norepinephrine, calcitonin gene-related peptide, and substance P, possibly by modulation of calcium channel function.

Pregabalin is a structural derivative of the inhibitory CNS neurotransmitter gamma-aminobutyric acid (GABA). Although pregabalin was developed as a structural analog of GABA, the drug dose not bind directly to $GABA_A$, $GABA_B$ or benzodiazepine receptors; dose not augment $GABA_A$ responses in cultured neuron; and does not alter brain concentrations of GABA in rats or affect GABA uptake or degradation. However, in cultured neurons, prolonged application of pregabalin increases the density of GABA transport protein and increase the rate of functional GABA transport.

[1-10] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1832 หมายเลข 10

[2-22] เอกสารอ้างอิง 2 :AHFS Drug Information 2012 หน้า 2304 หมายเลข 22

4.2 Pharmacokinetics

Absorption [1-11], [1-13]

Pregabalin is well absorbed after oral administration. Following oral administration of pregabalin capsules under fasting conditions, peak plasma concentrations occur within 1.5 hours. Pregabalin oral bioavailability is 90% or more and is independent of dose. Following single-dose (25 to 300 mg) and multiple-dose (75 to 900 mg/day) administration, maximum plasma concentrations (C_{max}) and area under the curve (AUC) values increase linearly. Following repeated administration, steady state is achieved within 24 to 48 hours. Multiple-dose pharmacokinetics can be predicted from single-dose data.

The rate of pregabalin absorption is decreased when given with food, resulting in a decrease in C_{max} of approximately 25% to 30% and an increase in time of maximal concentration (T_{max}) to approximately 3 hours. However, administration of pregabalin with food has no clinically relevant effect on the total absorption of pregabalin. Therefore, pregabalin can be taken with or without food.

Distribution [1-12]

Pregabalin does not bind to plasma proteins. The apparent volume of distribution of pregabalin following oral administration is approximately 0.5 L/kg. Pregabalin is a substrate for system L transporter, which is responsible for the transport for the large amino acids across the blood brain barrier. Although there are no data in humans, pregabalin crossed the blood brain barrier in mice, rats, and monkeys. In addition, pregabalin crossed the placenta in rats and was present in the milk of lactating rats.

Metabolism [1-14]

Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabeled pregabalin, approximately 90% of the administered dose was recovered in the urine as unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of the dose. In preclinical studies, pregabalin (S-enantiomer) did not undergo racemization to the R-enantionmer in mice, rats, rabbits, or monkeys.

Excretion [1-15]

Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug, with a mean elimination half-life of 6.3 hours in subjects with healthy renal function. Mean renal clearance was estimated to be 67 to 80.9 mL/min in young, healthy subjects. Pregabalin elimination is nearly proportional to CrCl.

[1-11]-[1-15] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1832-3 หมายเลข 11-15 ตามลำดับ

Special Populations

Renal function impairment [1-16]

Pregabalin clearance is nearly proportion to CrCl. Dosage reduction in patients with renal impairment is necessary. Pregabalin is effectively removed from plasma be hemodialysis. Following a 4-hour hemodialysis treatment, plasma pregabalin concentrations are reduced approximately 50%. For patients on hemodialysis, dosing must be modified. (See section 6 recommended dose-table 1)

Elderly [1-17]

Pregabalin oral clearance tended to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with age-related decreases in CrCl. Reduction of the pregabalin dose may be required in patients who have age-related compromised renal reduction. (See section 6 recommended dose-table 1)

[1-16]-[1-17] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1833 หมายเลข 16-17 ตามลำดับ

5. Indications [1-1], [2-1],[3-1]

Neuropathic pain

Pregabalin is indicated for the treatment of central and peripheral neuropathic pain in adults which includes diabetic peripheral neuropathy and post herpetic neuralgia.

Epilepsy

Pregabalin is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalization.

Generalized Anxiety Disorder

Pregabalin is indicated for the treatment of Generalized Anxiety Disorder (GAD) in adults.

Fibromyalgia

Pregabalin is indicated for the treatment of fibromyalgia in adult.

[1-1] เอกสารอ้างอิง 1 : Drug Facts and Comparison 2012 หน้า 1832 หมายเลข 1

[2-1] เอกสารอ้างอิง 2 : AHFS Drug Information 2012 หน้า 2301-2 หมายเลข 2

[3-1] เอกสารอ้างอิง 3 : เอกสารกำกับยาต้นแบบที่ได้รับอนุมัติจากอย. หมายเลข 1

6. Recommended Dose

The dose range of pregabalin is 150 to 600 mg daily administered in 2 or 3 divided doses. [3-2]

Adult dosage

Neuropathic Pain [3-2/1]

Pregabalin treatment can be started at a dose of 150 mg per day. Based on individual patient response and tolerability, the dosage may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval.

Epilepsy [3-2/2]

Pregabalin treatment can be started with a dose of 150 mg per day. Based on individual patient response and tolerability, the dosage may be increased to 300 mg per day after 1 week. The maximum dosage of 600 mg per day may be achieved after an additional week.

Generalized Anxiety Disorder [3-3]

The recommended dose range is 150-600 mg daily administered 2 or 3 divided doses. The need for treatment should be reassessed regularly.

Dosing should begin at 150 mg daily and may be increased to 300 mg daily within 1 week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg daily may be further increase to 450 mg daily after 1 week. If needed, in some patients, based on individual response and tolerability, the dose may be increased to maximum dosage of 600 mg daily after an additional week.

Fibromyalgia [3-3/1]

The recommendation dosage of pregabalin is 300-450 mg daily. Pregabalin therapy generally is initiated at a dosage of 150 mg daily (75 mg twice daily); dosage may be increased to 300 mg daily (150 mg twice daily) within 1 week based on efficacy and tolerability. Patients who do not experience adequate benefit with pregabalin 300 mg daily may have dosage further increased to the maximum recommended dosage of 450 mg daily (225 mg twice daily). The maximum dosage of 600 mg per day may be achieved after an additional week.

[3-2] - [3-3/1] เอกสารอ้างอิง 3 : เอกสารกำกับยาต้นแบบที่ได้รับอนุมัติจากอย. หมายเลข 2-3/1 ตามลำดับ

Discontinuous of pregabalin [1-8], [2-3]

It is recommended that this should be tapered gradually over a minimum of 1 week.

Use in special populations

Patients with renal impairment [3-3/2]

Dosage reduction in patients with compromised renal function must be individualized according to creatinine clearance (CL_{cr}), (see section 4.2 Pharmacokinetics, Special populations, Renal function impairment), as indicated in Table 1 determined using the following formula:

$$CL_{cr}\ (ml/min) = \frac{[140 - age\ (years)] \times weight\ (kg)}{72 \times serum\ creatinine\ (mg/dl)}\ (\times 0.85\ for\ female\ patients)$$

For patients receiving hemodialysis, the pregabalin daily dose should be adjusted based on renal function. In addition to the daily dose, a supplementary dose should be given immediately following every 4-hour hemodialysis treatment (see Table 1).

Table 1 Pregabalin dosage adjustment based on renal function

Creatinine Clearance (CL_{cr}) (ml/min)	Total Pregabalin Daily Dose *		Dose Regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
≥ 60	150	600	BID or TID
≥ 30 - < 60	75	300	BID or TID
≥ 15 - < 30	25-50	150	QD or BID
< 15	25	75	QD
Supplementary dosage following hemodialysis (mg)			
	25	100	Single dose†

TID = Three divided doses; BID = Two divided doses; QD = Single daily dose

*Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose.

†Supplementary dose is a single additional dose

Elderly [1-6]

Dosage reduction required in elderly patients with renal impairment. (see section 4.2 Pharmacokinetics, Special populations, Elderly)

[1-6], [1-8] เอกสารอ้างอิง 1 : Drug Facts and Comparison 2012 หน้า 1832 หมายเลข 6, 8

[2-3] เอกสารอ้างอิง 2 : AHFS Drug Information 2012 หน้า 2302 หมายเลข 3

[3-3/2] เอกสารอ้างอิง 3 : เอกสารกำกับยาต้นแบบที่ได้รับอนุมัติจากอย. หมายเลข 3/2

7. Mode of Administration [1-9], [2-2]

The total daily dose is 150 to 600 mg administered orally in either two or three divided dose. The capsule should be taken with or without food.

8. Contraindication [1-18], [2-9]

Hypersensitivity to pregabalin or any of its components.

[1-9], [1-18] เอกสารอ้างอิง 1 : Drug Facts and Comparison 2012 หน้า 1832-3 หมายเลข 9, 18

[2-2], [2-9] เอกสารอ้างอิง 2 : AHFS Drug Information 2012 หน้า 2302-3 หมายเลข 2, 9

9. Warnings and Precautions

Warnings

1 Avoid driving or operating machinery and alcohol-containing beverages because of pregabalin-related dizziness and somnolence.

2 Pregabalin may cause hematologic abnormalities.

3 Do not use pregabalin during pregnancy because of the possible teratogenic effects.

4 Use pregabalin with caution in patients with liver or kidney disease.

Precautions

Should not use in patients with rare hereditary problem of galactose intolerance, the Lapp lactose deficiency, or galactose malabsorption. **[3-4]**

Use with caution in patients with diabetes because pregabalin may cause weight gain. Some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycemic mediations. **[1-24],[2-15],[3-5]**

Should be immediately discontinued in patients with hypersensitivity reaction i.e., skin redness, blisters, hives, rash, dyspnea, wheezing. **[1-29],[2-11]**

Use with caution in patients who have had a previous episode of angioedema. Specific symptoms included swelling of the face, mouth (e.g., tongue, lips, gums) and neck (e.g., throat, larynx). In addition, patients who are using other drugs associated with angioedema (e.g., angiotensin-converting enzymes (ACE) inhibitors) may be at increased risk of developing angioedema. Pregabalin should be immediately discontinued in patient with these symptoms. **[1-19],[2-10]**

Avoid driving or operating machinery while taking pregabalin until experience is gained with the drug's effects. Pregabalin may cause dizziness, somnolence, blurred vision, and neuropsychiatric effects. **[2-23]**

Inform your clinician if changes in vision occur (i.e., blurred vision, decreased visual acuity, visual field changes). If visual disturbance persists, consider further assessment. Discontinuation of pregabalin may result in resolution or improvement of these visual symptoms. **[1-25],[2-16]**

There are insufficient data for the withdrawal of concomitant antiepileptic drugs, once seizure control with pregabalin in the add-on situation has been reached, in order to reach monotherapy on pregabalin. **[3-6]**

Should withdraw pregabalin gradually and reduce dosage slowly over at least 1 week because abrupt or rapid discontinuance of pregabalin has been associated with insomnia, nausea, headache, or diarrhea. **[1-20],[2-12]**

Use with caution in elderly and patients with renal impairment. The dosage of pregabalin should be adjusted according to the degree of renal impairment. **[2-20]**

Use with caution in patients with New York Heart Association (NYHA) class III or IV congestive heart failure because there are limited data on these patients. **[1-23],[2-14]**

Concomitant administration with a thiazolidinedione antidiabetic agent should be used with caution because co-administration increases risk of edema and weight gain and, particularly in patients with pre-existing cardiac conditions, risk of heart failure. **[1-22],[2-24]**

Inform clinicians promptly of the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm because the increased risk of suicidal thoughts or behavior with pregabalin or other antiepileptic drugs (AEDs) may be observed as early as 1 week after starting drug treatment with AEDs. **[1-21],[2-13]**

Inform clinicians promptly of any unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Pregabalin treatment should be discontinued if myopathy is diagnosed or suspected or if markedly elevated CK (CPK) concentrations occur. **[1-26],[2-17]**

Pregabalin may decrease platelet count. **[1-27],[2-18]**

Pregabalin may cause PR interval prolongation.**[1-28],[2-19]**

[1-19]-[1-29] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1833 หมายเลข 19-29

[2-10]-[2-20],[2-23],[2-24] เอกสารอ้างอิง 2 :AHFS Drug Information 2012 หน้า 2302-4 หมายเลข 10-20,23,24 ตามลำดับ

[3-4]-[3-6] เอกสารอ้างอิง 3 : เอกสารกำกับยาต้นแบบที่ได้รับอนุมัติจากอย. หมายเลข 4-6

10. Interactions with Other Medicaments [1-32],[2-21]

Based on results of *in vitro* studies, pregabalin does not appear to inhibit cytochrome P450 (CYP) isoenzymes 1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4 or induce CYP1A2 or CYP3A4. According to the original manufacturer, an increase in metabolism of concomitantly administered CYP1A2 substrates (e.g., caffeine, theophylline) or CYP3A4 substrates (e.g., midazolam, testosterone) is not anticipated.

Since pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans and does not bind to plasma proteins, its pharmacokinetics are unlikely to be affected by other agents through metabolic interactions or protein binding displacement.

ACE-inhibitors: Coadministration of these agents may increase the risk of swelling and hives.
Antiepileptic drugs (carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital, topiramate, gabapentin and tiagabine): Pharmacokinetic interactions are unlikely to occur.

Ethanol, lorazepam, oxycodone: Although no pharmacokinetic interactions were seen, additive effects on cognitive and gross motor functioning occurred. No clinically important effects on respiration were seen. Instruct patients to avoid alcohol.

Oral contraceptives (norethindrone and/or ethinyl estradiol): Pharmacokinetic interactions are unlikely to occur.

Oral antidiabetics (glyburide and metformin), diuretic (furosemide) and insulin: These drugs do not appear to affect the pharmacokinetics of pregabalin.

Thiazolidinedione antidiabetic agents (e.g., pioglitazone, rosiglitazone): Co-administration of pregabalin and a thiazolidinedione may lead to additive effect on edema and weight gain, possibly exacerbating or leading to heart failure. If an interaction is suspected, it may need to adjust the dose of one or both agents.

Drug/Food Interactions [1-33]

The rate of pregabalin absorption is decreased when given with food, resulting in a decrease in C_{max} of approximately 25-30% and an increase in T_{max} to approximately 3 hours. However, administration of pregabalin with food has no clinically relevant effect on the total absorption of pregabalin. Therefore, pregabalin can be taken with or without food.

[1-32],[1-33] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1834 หมายเลข 32,33 ตามลำดับ

[2-21] เอกสารอ้างอิง 2 :AHFS Drug Information 2012 หน้า 2304 หมายเลข 21

11. Pregnancy and Lactation [1-31]

11.1 Pregnancy

Category C: Increased incidences of fetal structural abnormalities and other manifestations of developmental toxicity, including lethality, growth retardation, and nervosa and reproductive system functional impairment, were observed in the offspring of rats and rabbits given pregabalin during pregnancy at does that produced plasma pregabalin exposures (AUC) at least 5 times human exposure at the maximum recommended human dose of 600 mg/day.

There are no adequate and well-controlled studies in pregabalin woman. It is not known if pregabalin crosses the human placenta. The low molecular weight (approximately 159), minimal metabolism, lack of plasma protein binding, and the moderately long elimination half-life suggest that the drug will reach the embryo and fetus. Use pregabalin during pregnancy only if the potential benefit justifies the potential risk to the fetus.

11.2 Labor and delivery

The effects of pregabalin on labor and delivery in pregnant woman are unknown. In the prenatal-postnatal study in rats, pregabalin prolonged gestation and induced dystocia at exposures of 50 times or more the mean human exposure ($AUC_{(0-24)}$ of 123 mcg*h/mL) at the maximum recommended clinical dosage of 600 mg/day.

11.3 Lactation

It is not known if pregabalin is excreted in human milk; it is, however, present in the milk of rats. The low molecular weight (approximately 159), minimal metabolism, lack of plasma protein binding, and the moderately long elimination half-life (6 hours) suggest that the drug will also be excreted into breast milk. Because it is freely soluble in water, the highest concentrations of the drug are found in foremilk. Because many drugs are excreted into human milk and because of the potential for tumorigenicity shown for pregabalin in animal studies, decide whether to discontinuous breast-feeding or the drug, taking into account the importance of the drug to the mother.

[1-31] เอกสารอ้างอิง 1 : Drug Facts and Comparison 2012 หน้า 1833-4 หมายเลข 31

12. Undesirable Effects [3-7]

Very common effects (≥ 1:10):

Nervous system disorders: Dizziness, somnolence

Common (≥ 1:100 to **<1:10):**

Metabolism and nutrition disorders: Appetite increased

Psychiatric disorders: Confusion, disorientation, irritability, euphoric mood, libido decreased, insomnia

Nervous system disorders: Ataxia, coordination abnormal, balance disorder, amnesia, disturbance in attention, memory impairment, tremor, dysarthria, paraesthesia, sedation, lethargy

Eye disorders: Vision blurred, diplopia

Ear and labyrinth disorders: Vertigo

Gastrointestinal disorders: Vomiting, abdominal distension, constipation, dry mouth, flatulence

Reproductive system and breast disorders: Erectile dysfunction

General disorders and administration site conditions: Oedema peripheral, oedema, gait abnormal, feeling drunk, fatigue

Investigations: Weight increased

Uncommon (≥1:1,000 to **< 1:100):**

Infections and infestations: Nasopharyngitis

Metabolism and nutrition disorders: Anorexia

Psychiatric disorders: Depersonalisation, anorgasmia, restlessness, agitation, depression, mood swings, depressed mood, word finding difficulty, hallucination, abnormal dreams, libido increased, panic attack, apathy

Nervous system disorders: Cognitive disorder, hypoaesthesia, nystagmus, speech disorder, myoclonus, hyporeflexia, dyskinesia, psychomotor hyperactivity, postural dizziness, hyperaesthesia, ageusia, burning sensation, intention tremor, stupor, syncope

Eye disorders: Visual disturbance, visual field defect, dry eye, eye swelling, visual acuity reduced, eye pain, asthenopia, lacrimation increased

Ear and labyrinth disorders: Hyperacusis

Cardiac disorders: Atrioventricular block first degree, tachycardia

Vascular disorders: Hypotension, hypertension, flushing, hot flushes, peripheral coldness

Respiratory, thoracic and mediastinal disorders: Dyspnoea, cough, nasal dryness

Gastrointestinal disorders: Salivary hypersecretion, gastrooesophageal reflux disease, oral hypoaesthesia

Skin and subcutaneous tissue disorders: Sweating, papular rash

Musculoskeletal and connective tissue disorders: Muscle twitching, joint swelling, muscle cramp, myalgia, arthralgia, back pain, pain in limb, muscle stiffness

Renal and urinary disorders: Dysuria, urinary incontinence

Reproductive system and breast disorders: Ejaculation delayed, sexual dysfunction

General disorders and administration site conditions: Chest tightness, fall, generalized oedema, pain, chills, asthenia, thirst

Investigations: Alanine aminotransferase increased, blood creatine phosphokinase increased, aspartate aminotransferase increased, platelet count decreased

Rare (<1:1,000):

Blood and lymphatic system disorders: Neutropenia

Metabolism and nutrition disorders: Hypoglycaemia

Psychiatric disorders: Disinhibition, elevated mood

Nervous system disorders: Hypokinesia, parosmia, dysgraphia

Eye disorders: Photopsia, eye irritation, mydriasis, oscillopsia, altered visual depth perception, peripheral vision loss, strabismus, visual brightness

Cardiac disorders: Sinus tachycardia, sinus arrhythmia, sinus bradycardia

Respiratory, thoracic and mediastinal disorders**:** Nasal congestion, epistaxis, rhinitis, snoring, throat tightness

Gastrointestinal disorders: Ascites, dysphagia, pancreatitis

Skin and subcutaneous tissue disorders: Cold sweat, urticaria

Musculoskeletal and connective tissue disorders: Cervical spasm, rhabdomyolysis, neck pain

Renal and urinary disorders: Oliguria, renal failure

Reproductive system and breast disorders: Amenorrhoea, breast discharge, breast pain, dysmenorrhoea, breast enlargement

General disorders and administration site conditions: Pyrexia

Investigations: Blood glucose increased, blood creatinine increased, blood potassium decreased, weight decreased, white blood cell count decreased

Unknown frequency:

Immune system disorders: Angioedema, allergic reaction, hypersensitivity

Nervous system disorders: Headache, loss of consciousness, mental impairment

Eye disorders: Keratitis

Cardiac disorders: Congestive heart failure

Respiratory, thoracic and mediastinal disorders: Pulmonary oedema

Gastrointestinal disorders: Swollen tongue, diarrhea, nausea

Skin and subcutaneous tissue disorders: Face swelling, pruritus

Renal and urinary disorders: Urinary retention

Reproductive system and breast disorders: Gynaecomastia

General disorders and administration site conditions: Malaise

Effects on ability to drive and use machine [1-30]

Pregabalin may cause dizziness and somnolence. Pregabalin-related dizziness and somnolence may impair abilities to perform tasks such as driving or operating machinery.

[1-30] เอกสารอ้างอิง 1 :Drug Facts and Comparison 2012 หน้า 1833-4 หมายเลข 30

[3-7] เอกสารอ้างอิง 3 : เอกสารกำกับยาต้นแบบที่ได้รับอนุมัติจากอย. หมายเลข 7

13. Overdose and Treatment [1-34]

There is limited experience with overdose of pregabalin. The highest reported accidental overdose of pregabalin during the clinical development program was 8,000 mg, and there were no notable clinical consequences.

There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by gastric lavage; observe usual precautions to maintain the airway. General supportive care of the patient is indicated, including monitoring of vital signs and observation of the clinical status of the patient. Although hemodialysis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal function impairment.

[1-34] เอกสารอ้างอิง 1 : Drug Facts and Comparison 2012 หน้า 1837 หมายเลข 34

14. Storage Condition

Store in tight containers at temperatures below 30°C.

15. Dosage Forms and Packaging Available

TOPRELIN 25 : Aluminium-clear colorless PVC/PVdC blister of 14 hard capsules packed in paper carton

TOPRELIN 75 : Aluminium-clear colorless PVC/PVdC blister of 14 hard capsules packed in paper carton

TOPRELIN 150 : Aluminium-clear colorless PVC/PVdC blister of 14 hard capsules packed in paper carton

16. Name and Address of Manufacturer

T.O. CHEMICALS(1979) Ltd.

280 Soi Sabaijai, Suthisarn Road, Bangkok 10310 Thailand

Tel. 02-2756053-9 Fax. 02-2777350

17. Date of Revision of Package Insert

19 April 2016