Berlin

Package Insert

Berlontin

Gabapentin

1. Product Name

Berlontin 100

Berlontin 300

Berlontin 600

2. Name and strength of Active Ingredient

Berlontin 100: Each capsule contains gabapentin 100 mg

Berlontin 300: Each capsule contains gabapentin 300 mg

Berlontin 600: Each tablet contains gabapentin 600 mg

3. Product Description

Capsules and tablets for oral administration

Berlontin 100: Hard gelatin capsule No. 3 imprinting with “B” on opaque white cap and “100” on opaque white body, containing white powder.

Berlontin 300: Yellow size 1 hard gelatin capsule imprinting with "B" on cap and "300" on body, containing white powder.

Berlontin 600: White oval biconvex film coated tablets with score on one side and score between “BT” and “6” on the other side.

4. Pharmacodynamics/Pharmacokinetics

Mechanism of Action

Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid) but it does not modify $GABA_A$ or $GABA_B$ radioligand binding, it is not converted metabolically into GABA or a GABA agonist, and it is not an inhibitor of GABA uptake or degradation. It is hypothesized that gabapentin antagonizes thrombospondin binding to alpha 2 delta-1 as receptor involved in excitatory synapse formation and suggested that gabapentin may function therapeutically by blocking new synapse formation.

(1- Ref.1, Drug Facts and Comparisons 2014, p.1859)

Pharmacokinetics

Absorption

Gabapentin bioavailability is not dose-proportional (i.e., as dose is increased, bioavailability decreases). Bioavailability of gabapentin is approximately 60%, 47%, 34%, 33% and 27% following 900, 1200, 2400, 3600 and 4800 mg/day given in 3 divided doses, respectively. Food has only a slight effect on the rate and extent of absorption of gabapentin (14% increases in AUC and C_{max}).

(2- Ref.1, Drug Facts and Comparisons 2014, p.1859)

Distribution

Less than 3% of gabapentin circulates unbound to plasma protein. The apparent volume of distribution of gabapentin after 150 mg intravenous administration is 58 ± 6 L (mean ± SD). In patients with epilepsy, steady-state predose (C_{min}) concentrations of gabapentin in cerebro-spinal fluid were approximately 20% of the corresponding plasma concentrations.

(3- Ref.1, Drug Facts and Comparisons 2014, p.1859)

Metabolism

Gabapentin is not metabolized.

(4- Ref.2, Martindale Thirty-ninth edition, p. 534)

Excretion

Gabapentin is eliminated from the systemic circulation by renal extraction as unchanged drug. Gabapentin elimination half-life is 5 to 7 hours and is unaltered by dose or following multiple dosing. Gabapentin elimination rate constant, plasma clearance and renal clearance are directly proportional to creatinine clearance. In elderly patients, and in patients with impaired renal function, gabapentin plasma clearance is reduced. Gabapentin can be removed from plasma by hemodialysis.

(5- Ref.1, Drug Facts and Comparisons 2014, p. 1859-1860)

5. Indications

Epilepsy

Gabapentin is indicated as monotherapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 12 years and above. Safety and effectiveness for monotherapy in pediatric patients below the age of 12 years have not been established.

Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 3 years and above. Safety and effectiveness for adjunctive therapy in pediatric patients below the age of 3 years have not been established.

Neuropathic Pain

Gabapentin is indicated in the treatment of neuropathic pain in adults. Safety and effectiveness of gabapentin in children have not been established.

(6- Ref.2, Martindale Thirty-ninth edition, p.532; Ref.1, Drug Facts and Comparisons 2014, p.1857; Ref. 5, Neurontin Package Insert, p.1)

6. Recommended Dose

Gabapentin is given orally with or without food. If gabapentin is reduced, discontinued or substituted with alternative medication, this should be done gradually over a minimum of one week.

(7- Ref.1, Drug Facts and Comparisons 2014, p.1859)

Epilepsy

Adults and Pediatric Patients over 12 years of age

The effective dose of gabapentin is 900 to 3600 mg/day. The initial dose is 300 mg on the first day of treatment, 300 mg twice daily on the second day, and 300 mg three times daily on the third day; alternatively, gabapentin may be given as 300 mg three times a day on the first day of treatment. Thereafter the dose may be increased in three equally divided doses up to maximum doses of 3600 mg/day. Higher doses up to 4800 mg/day have been reported to be well tolerated. The maximum time between doses in the three times a day schedule should not exceed 12 hours.

(8- Ref.2, Martindale Thirty-ninth edition, p.532; Ref.5, Neurontin Package Insert, p.1)

Pediatric Patients age 3 to 12 years

The starting dose should range from 10 to 15 mg/kg/day in 3 divided doses and the effective dose reached by upward titration over a period of approximately 3 days. *(9a- Ref.1, Drug Facts and Comparisons 2014, p.1859)* The effective dose of gabapentin in patients 5 years of age and older is 25 to 35 mg/kg/day and given in divided doses (3 times a day). *(9b- Ref.1, Drug Facts and Comparisons 2014, p.1859)* Dosages up to 50 mg/kg/day have been well-tolerated in a long-term clinical study. *(9c- Ref.1, Drug Facts and Comparisons 2014, p.1859)* The maximum time interval between does should not exceed 12 hours. *(9d- Ref.1, Drug Facts and Comparisons 2014, p.1859)*

Neuropathic Pain in Adults

Gabapentin therapy may be initiated as a single 300 mg dose on day one, 600 mg per day on day 2 (divided twice daily) and 900 mg per day on day 3 (divided 3 times daily). The dose can subsequently be titrated up as needed for pain relief to a daily dose of 1800 mg (divided 3 times daily). In clinical studies, efficacy was demonstrated over a range of doses from 1800 mg per day to 3600 mg per day with comparable effects across the dose range.

(10- Ref.1, Drug Facts and Comparisons 2014 p.1858; Ref.2, Martindale Thirty-ninth edition, p.534)

Dosage Adjustment in Renal Impairment

Reduced doses of gabapentin are recommended for patients with renal impairment or undergoing hemodialysis. The following maintenance doses based on creatinine clearance (CC) and given as 3 divided doses are recommened:

- CC 50 to 79 ml/minute: 600 to 1800 mg daily
- CC 30 to 49 ml/minute: 300 to 900 mg daily
- CC 15 to 29 ml/minute: 300 mg on alternate days to 600 mg daily
- CC less than 15 ml/minute: 300 mg on alternate days to 300 mg daily

(11- Ref.2, Martindale Thirty-ninth edition, p.532-533)

Dosage Adjustment in Patients Undergoing Hemodialysis

For patients undergoing hemodialysis who have never received gabapentin, the recommended loading dose is 300 to 400 mg followed by 200 to 300 mg after each 4 hours of hemodialysis. On dialysis-free days no doses of gabapentin should be given.

(12- Ref.2, Martindale Thirty-ninth edition, p.533)

7. Mode of Administration

Gabapentin is administered orally. The drug may be administered without regard to meals. If scored tablets containing 600 mg of gabapentin are to be used in patients requiring a 300 or 400 mg dose, the tablets can be halved to allow administration of the appropriate dose. Patients should be instructed to take one-half tablet; the remaining half-tablet should be used for the next dose. Half-tablets that are not used within several days should be discarded.

Patients who are currently receiving or beginning therapy with gabapentin and/or any anticonvulsant for any indication should be closely monitored for the emergence or worsening of depression, suicidal thoughts or behavior and/or any unusual changes in mood or behavior.

(13- Ref. 3, AHFS Drug Information 2017, p. 2365)

8. Contraindications

Hypersensitivity to the drug or its ingredients.

(14- Ref. 1, Drug Facts and Comparisons 2014 p.1860)

9. Warnings and Precautions

Warnings (based on the Ministry of Public Health Announcement)

1. The drug may cause drowsiness, do not drive a car, operate machinery and drink alcoholic beverages while taking this drug.
2. The drug may cause hematologic disorder.
3. Do not use the drug in pregnancy patients because it may cause teratogenesis.
4. Use this drug with caution in patients with liver, kidney disease.

(15- Ref.6, ประกาศกระทรวงสาธารณสุขเรื่อง ยาที่ต้องแจ้งคำเตือนการใช้ยาไว้ในฉลากและที่เอกสารกำกับยา และข้อความของคำเตือน)

Warning/Precautions

Suicidal behavior and ideation

Antiepileptic drugs (AEDs), including gabapentin, increase the risk of suicidal thoughts of behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence of worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

(15a- Ref. 1, Drug Facts and Comparisons 2014, p.1860)

Neuropsychiatric effects

Gabapentin use in pediatric patients with epilepsy 3 to 12 years of age is associated with the occurrence of central nervous system related adverse events. The most significant of these can be classified into the following categories: emotional lability (primarily behavioral problems), hostility (including aggressive behaviors), thought disorder (including concentration problems and change in school performance), hyperkinesia (primarily restlessness and hyperactivity). Among the gabapentin-treated patients, most of the events were mild to moderate in intensity.

(15b- Ref. 1, Drug Facts and Comparisons 2014, p.1860)

Withdrawal precipitated seizure

Antiepiliptic drugs should not be abruptly discontinued because of the possibility of increasing seizure frequency.

(15c- Ref. 1, Drug Facts and Comparisons 2014, p.1860)

Hazardous tasks

Patients should be advised that gabapentin may cause dizziness, somnolence and other symptoms and signs of CNS depression. Accordingly, they should be advised neither to drive a car nor to operate other complex machinery until they have gained sufficient experience on gabapentin to gauge whether or not it affects their mental and/or motor performance adversely.

(15d- Ref. 1, Drug Facts and Comparisons 2014, p.1860)

Elderly

Clinical studies of gabapentin in epilepsy did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

(15e- Ref. 3, AHFS Drug Information 2017, p. 2368)

Drug Rash with Eosinophillia and Systemic Symptoms (DRESS)

Severe life threatening, systemic hypersensitivity reactions such as drug rash with eosinophillia and systemic symptoms (DRESS) have reported in patients taking antiepileptic drugs including gabapentin.

(15f- Ref. 4, Drug Information Handbook with International Trade Names Index 2017-18, p.1055)

10. Interactions with Other Medicaments

Gabapentin is not appreciably metabolized nor does it is interfere with the metabolism of commonly coadministered antiepileptic drugs (Table 1).

Drug/lab test interaction

Because false positive readings were reported with the Ames N-Multistix SG dipstick test for urinary protein when gabapentin was added to other antiepileptic drugs, the more specific sulfosalicylic acid precipitation procedure is recommended to determine the presence of urine protein.

Table 1 Gabapentin drug interaction			
Precipitant drug	**Object drug***		**Description**
Antacids	Gabapentin	↓	Antacids reduced the bioavailability of gabapentin by about 20%. This decrease in bioavailability was about 5% when gabapentin was given 2 hours after the antacid. It is recommended that gabapentin be taken at least 2 hours following antacid administration.
Cimetidine	Gabapentin	↑	The mean apparent oral clearance of gabapentin fell by 14% and CrCl fell by 10% with concurrent cimetidine. Thus, cimetidine seemed to alter the renal excretion of gabapentin and creatinine. This is not expected to be of clinical importance.
Hydrocodone	Gabapentin	↑	Coadministration increases gabapentin AUC values by 14%. Coadministration decreases hydrocodone C_{max} and AUC values in a dose-dependent manner. C_{max} and AUC values were 3% and 4% lower, respectively, after administration of 125 mg gabapentin and 21% to 22% lower, respectively after administration of 500 mg gabapentin. The mechanism for this interaction and the magnitude of interaction at other doses is unknown.
Gabapentin	Hydrocodone	↓	
Morphine	Gabapentin	↑	Coadministration of 60 mg morphine 2 hours prior to administration of 600 mg gabapentin resulted in an increase in gabapentin AUC by 44%. The magnitude of interaction at other doses is unknown.
Naproxen	Gabapentin	↑	Coadministration (n = 18) of naproxen sodium capsules (250 mg) with gabapentin (125 mg) appears to increase the amount of gabapentin absorbed by 12% to 15%. Gabapentin had no effect on naproxen pharmacokinetic parameters. These doses are lower than the therapeutic doses for both drugs. The magnitude of interaction within the recommended dose ranges of either drug is not known.
Gabapentin	Contraceptives, hormonal	↑	The C_{max} of norethindrone was 13% higher when coadministered with gabapentin; this interaction is not expected to be of clinical importance.

- ↑ = object drug increased. ↓ = object drug decreased.

(16- Ref.1, Drug Facts and Comparisons 2014, p.1861)

11. Pregnancy and Lactation

Pregnancy

Category C. It is not known whether gabapentin crosses the human placenta to fetus. Because of its lack of protein binding and low molecular weight (approximately 171), exposure of the embryo and fetus should be expected. There are no adequate and well-controlled studies in pregnant woman. This drug should be used during pregnancy only if the potential benefit justifies the potential risk to fetus.

(17- Ref.1, Drug Facts and Comparisons 2014, p.1860)

Lactation

Gabapentin is secreted into human milk following oral administration. A nursed infant could be exposed to a maximum dose of approximately 1 mg/kg/day of gabapentin. Because the effect on the nursing infant is unknown, gabapentin should be used in women who are nursing only if the benefits clearly outweigh the risks.

(18- Ref. 1, Drug Facts and Comparisons 2014, p.1861)

12. Undesirable Effects

Epilepsy

***Common adverse reaction*:** The most commonly observed adverse reactions associated with the use of gabapentin in combination with other antiepileptic drugs in patients greater than 12 years of age, not seen at an equivalent frequency among placebo-treated patients, were somnolence, dizziness, ataxia, fatigue and nystagmus. The most commonly observed adverse events reported with the use of gabapentin in combination with other antiepileptic drugs in children 3 to 12 years of age, not seen at an equal frequency among placebo-treated patients, were viral infection, fever, nausea and/or vomiting, somnolence and hostility.

***Discontinuation*:** Approximately 7% of the 2074 patients greater than 12 years of age and approximately 7% of the 449 children 3 to 12 years of age who received gabapentin in premarketing clinical trials discontinued treatment because of an adverse reaction. The adverse reaction most commonly associated with withdrawal in patients older than 12 years of age were somnolence (1.2%), ataxia (0.8%), fatigue (0.6%), nausea and/or vomiting (0.6%) and dizziness (0.6%). The adverse reactions most commonly associated with withdrawal in children were emotional lability (1.6%), hostility (1.3%) and hyperkinesia (1.1%)

Adults and children 12 years of age and older

The following Table 2 lists adverse reactions that occurred in at least 1% of gabapentin-treated patients with epilepsy participating in placebo-controlled trails and that were numerically more frequent in the gabapentin group than in the placebo group. Adverse events were usually mild to moderate in intensity.

Table 2		
Gabapentin adverse reactions in add-on epilepsy trials in patient > 12 years of age (≥ 1%)		
Body system/adverse reaction	**Gabapentin[a] (n = 543) %**	**Placebo[a] (n = 378) %**
CNS		
Abnormal coordination	1.1	0.3
Abnormal thinking	1.7	1.3
Amnesia	2.2	0
Ataxia	12.5	5.6
Depression	1.8	1.1
Dizziness	17.1	6.9
Dysarthria	2.4	0.5
Fatigue	11	5
Nervousness	2.4	1.9
Nystagmus	8.3	4
Somnolence	19.3	8.7
Tremor	6.8	3.2
Twitching	1.3	0.5
Dermatologic		
Abrasion	1.3	0
Pruritus	1.3	0.5
GI		
Constipation	1.5	0.8
Dental abnormalities	1.5	0.3
Dyspepsia	2.2	0.5
Increased appetite	1.1	0.8
Mouth or throat dry	1.7	0.5
Body system/adverse reaction	Gabapentin[a] (n = 543) %	Placebo[a] (n = 378) %
Musculoskeletal		
Back pain	1.8	0.5
Fracture	1.1	0.8
Myalgia	2	1.9

Table 2		
Gabapentin adverse reactions in add-on epilepsy trials in patient > 12 years of age (≥ 1%)		
Body system/adverse reaction	**Gabapentin[a] (n = 543) %**	**Placebo[a] (n = 378) %**
Respiratory		
Coughing	1.8	1.3
Pharyngitis	2.8	1.6
Rhinitis	4.1	3.7
Special senses		
Amblyopia[b]	4.2	1.1
Diplopia	5.9	1.9
Miscellaneous		
Impotence	1.5	1.1
Leukopenia	1.1	0.5
Peripheral edema	1.7	0.5
Vasodilatation	1.1	0.3
WBC count decreased	1.1	0.5
Weight increase	2.9	1.6

[a] Plus background antiepileptic drug therapy.

[b] Amblyopia was often described as blurred vision.

Other reactions in greater than 1% of patients older than 12 years of age but equally or more frequent in the placebo group included the following; headache, viral infection, fever, nausea and/or vomiting, abdominal pain, diarrhea, convulsions, confusion, insomnia, emotional lability, rash, acne.

Among the treatment-emergent adverse events occurring at an incidence of at least 10% of gabapentin-treat patients, somnolence and ataxia appeared to exhibit a positive dose-response relationship.

Children 3 to 12 years of age

The Table 3 lists adverse reactions that occurred in at least 2% of gabapentin-treated patient's age 3 to 12 years with epilepsy participating in placebo-controlled trails and were numerically more common in the gabapentin group. Adverse events were usually mild to moderate in intensity.

Table 3		
Gabapentin adverse reactions in add-on epilepsy trials in children 3 to 12 years of age (≥2%)		
Body system/Adverse reaction	**Gabapentin[a] (n = 119) %**	**Placebo[a] (n = 128) %**
CNS		
Dizziness	2.5	1.6
Emotional lability	4.2	1.6
Fatigue	3.4	1.6
Hostility	7.6	2.3
Hyperkinesia	2.5	0.8
Somnolence	8.4	4.7
Respiratory		
Bronchitis	3.4	0.8
Respiratory tract infection	2.5	0.8
Miscellaneous		
Fever	10.1	3.1
Nausea/vomiting	8.4	7
Viral infection	10.9	3.1
Weight increase	3.4	0.8

[a] Plus background antiepileptic drug therapy.

Other reactions in more than 2% of children 3 to 12 years of age but equally or more frequent in the placebo group included the following; pharyngitis, upper respiratory tract infection, headache, rhinitis, convulsion, diarrhea, anorexia, coughing and otitis media.

Additional adverse reactions in epilepsy trial **(frequently occurred in at least 1%):**

Cardiovascular: Hypertension

CNS: Anxiety, decreased or absent reflexes, hostility, hyperkinesias, increased reflexes, paresthesia, vertigo

GI: Anorexia, flatulence, gingivitis

Hemic/lymphatic: Purpura most often described as bruises resulting from physical trauma

Musculoskeletal: Arthralgia

Respiratory: Pneumonia

Special senses: Abnormal vision

Miscelleneous: Asthenia, face edema, malaise

(19a-Ref. 1, Drug Facts and Comparisons 2014, p.1861-1863)

Other adverse reactions which may be rarely occur, but serious effect

Cardiovascular: angina pectoris, hypotension, migraine, murmur, peripheral vascular disorder, tachycardia, atrial fibrilation, bradycardia, cerebrovascular accident, deep thrombophelbitis, heart block, heart failure, hyperlipidemia, myocardial infarction, pericardial effusion, pericardial rub, pericarditis, premature atrial contraction, pulmonary embolus, pulmonary thrombosis, thrombophlebitis, ventricular extrasystoles, angioedema

CNS: aphasia, cerebellar dysfunction, CNS tumors, dystonia, facial paralysis, hallucination, hemiplegia, intracranial hemorrhage, subdural hematoma, syncope, encephalopathy, local myoclonus, meningismus, nerve palsy, movement disorder

Dermatologic: herpes zoster, erythema multiforme, Stevens-Johnson syndrome

Endocrine: cushingoid appearance, hyper/hypothyroid, ovarian failure, hyponatremia

GI: gastroenteritis, fecal incontinence, hepatomegaly, dysphagia, pancreatitis, peptic ulcer, colitis, hiatal hernia, hematemesis, rectal hemorrhage, esophageal spasm

GU: breast cancer, breast hypertrophy, dysmenorrhea, hematuria, vaginal hemorrhage, acute renal failure, glycosuria, nephrosis, renal stone

Hepatic: elevated liver function tests, jaundice

Hemic/lymphatic: anemia, lymphadenopathy, thrombocytopenia, bleeding time increased, lymphocytosis, non-Hodgkin lymphoma

Musculoskeletal: osteoporosis

Respiratory: dyspnea, apnea, aspiration pneumonia, bronchospasm, lung edema

Special senses: cataract, eye hemorrhage, hearing loss, visual field defect, blindness, chorioretinitis, corneal disorders, glaucoma, retinal degeneration, retionopathy

(19a-Ref. 1, Drug Facts and Comparisons 2014, p.1861-1863)

Neuropathic pain:

The Table 4 lists adverse reactions that occurred in at least 1% of gabapentin-treated patients with neuropathic pain participating in placebo-controlled trails and were numerically more common in the gabapentin group. Adverse events were usually mild to moderate in intensity.

Table 4		
Gabapentin adverse reactions in controlled trials in neuropathic pain (≥ 1% and numerically more frequent than with placebo)		
Body system/adverse reaction	**Gabapentin (n = 821) %**	**Placebo (n = 537) %**
CNS		
Abnormal gait	1.1	0.0
Abnormal thinking	1.5	0.0
Amnesia	1.8	0.6
Ataxia	2.3	0.0
Confusion	1.8	0.9
Dizziness	21.1	6.5
Headache	5.5	6.1
Hypesthesia	1.3	0.6
Somnolence	16.1	5.0
Tremor	1.1	1.4
Vertigo	1.0	0.4
Dermatologic		
Rash	1.7	0.7
GI		
Abdominal pain	2.8	3.2
Constipation	2.3	1.7
Diarrhea	5.6	4.5
Dry mouth	3.3	0.9
Dyspepsia	1.9	1.9
Flatulence	1.7	1.1
Nausea	5.5	5.4
Vomiting	1.9	2.4
Metabolic/nutritional		
Peripheral edema	5.4	2.6
Weight gain	1.7	0.0
Musculoskeletal		
Back pain	2.3	1.5
Respiratory		
Dyspnea	1.1	0.6
Pharyngitis	1.8	1.3
Special senses		
Amblyopia	1.8	0.4

Table 4		
Gabapentin adverse reactions in controlled trials in neuropathic pain (≥ 1% and numerically more frequent than with placebo)		
Body system/adverse reaction	**Body system/adverse reaction**	**Body system/adverse reaction**
Miscelleneous		
Accidental injury	3.9	3.2
Asthenia	5.0	4.7
Flu syndrome	2.6	2.6
Infection	4.6	7.4
Pain	3.7	6.7

(19b- Ref.5, Neurontin Package Insert, p.1-2)

Postmarketing Experience:

Sudden, unexplained deaths have been reported where a casual relationship to treatment with gabepentin has not been established.

Additional post-marketing adverse events reported include blood creatine phosphokinase increased, rhabdomyolysis, acute kidney failure, allergic reaction including urticaria, alopecia, angioedema, blood glucose fluctuations in patients with diabetes, breast hypertrophy, chest pain, drug rash with eosinophilia and systemic symptoms, elevated liver function tests (LFTs), erythema multiforme, generalized edema, gynecomastia, hallucinations, hepatitis, hypersensitivity including systemic reactions, jaundice, movement disorders such as choreoathetosis, dyskinesia, and dystonia, myoclonus, palpitation, pancreatitis, Stevens-Johnson syndrome, thrombocytopenia, tinnitus, and urinary incontinence.

Adverse events following the abrupt discontinuation of gabapentin have also been reported. The most frepuently repoted events were anxiety, insomnia, nausea, pain, and sweating.

(19c- *Ref.5, Neurontin Package Insert, p.1*)

13. Overdose and Treatment

Overdose

Acute oral overdoses of gabapentin up to 49 g have been reported. In these cases, double vision, slurred speech, drowsiness, lethargy and diarrhea were observed. All patients recovered with supportive care.

Treatment

Gabapentin can be removed by hemodialysis. Although hemodialysis has not been performed in the few overdose cases reported, it may be indicated by the patient's clinical state or in patients with significant renal impairment.

(20- Ref.1A, Drug Facts and Comparisons 2013, p.1917)

14. Storage Condition

Store below 30°C

15. Dosage Forms Available and Packaging

Capsules or tablets for oral use

Blister of 10 capsules or tablets

16. Name and address of Manufacturer

Manufacturer: Berlin Pharmaceutical Industry Co., Ltd.

222 Romklao Road, Kongsamprawet, Ladkrabang, Bangkok

For further information**:** Tel. 02-252-4650-7 Fax. 02-252-4658

17. Date of revision of Package Insert

7 June 2019