APO-GABAPENTIN
Gabapentin Capsules 100, 300 and 400 mg

THERAPEUTIC CLASSIFICATION
Antiepileptic

ACTIONS AND CLINICAL PHARMACOLOGY
Gabapentin exhibits antiseizure activity in mice and rats both in the maximal electroshock and in the pentylenetetrazol seizure models.

Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid) but does not interact with GABA receptors, it is not metabolized to GABA or to GABA agonists, and it is not an inhibitor of GABA uptake or degradation. Gabapentin at concentrations up to 100µM did not demonstrate affinity for other receptor sites such as benzodiazepine, glutamate, glycine or N-methyl-D-aspatrate receptors nor does it interact with neuronal sodium channels or L-type calcium channels.

The mechanism of action of gabapentin has not yet been established, however, it is unlike that of the commonly used anticonvulsant drugs.

In vitro studies with radiolabelled gabapentin have revealed a gabapentin binding site in rat brain tissues including neocortex and hippocampus. The identity and function of this binding site remain to be elucidated.

PHARMACOKINETICS
Adults
Following oral administration of gabapentin, peak plasma concentrations are observed within 2 to 3 hours. Absolute bioavailability of a 300 mg dose of gabapentin capsules is approximately 59%. At doses of 300 and 400 mg, gabapentin bioavailability is unchanged following multiple dose administration.

Gabapentin elimination from plasma is best described by linear pharmacokinetics. The elimination half-life of gabapentin is independent of dose and averages 5 to 7 hours in subjects with normal renal function.

Plasma gabapentin concentrations are dose-proportional at doses of 300 to 400 mg q8h, ranging between I and 10ug/mL, but are less than dose-proportional above the clinical range (> 600 mg q8h). There is no correlation between plasma levels and efficacy. Gabapentin pharmacokinetics are not affected by repeated administration, and steady-state plasma concentrations are predictable from single dose data.

Gabapentin is not appreciably metabolized in humans, is eliminated solely by renal excretion, and can be removed from plasma by hemodialysis.

Gabapentin does not induce or inhibit hepatic mixed function oxidase enzymes responsible for drug metabolism, does not interfere with the metabolism of commonly coadministered antiepileptic drugs, and is minimally bound to plasma proteins.

Food has no effect on the rate or extent of absorption of gabapentin.

Table 1 summarizes the mean steady-state pharmacokinetic parameters of gabapentin capsules.

Table 1. Summary of gabapentin mean steady-state pharmacokinetic parameters in adults following 8h administration:

PARAM ETER	300 mg (N=7)	400 mg (N=11)
C_{max} (mcg/mL)	4.02	5.50
T_{max} (hr)	2.7	2.1
$T_{1/2}$ (hr)	5.2	6.1
$AUC_{(0-1)}$ (mcg.hr/mL)	24.8	33.3
AE%*	---	63.6

* Amount excreted in urine (% of dose)

In patients with epilepsy, gabapentin concentrations in cerebrospinal fluid are approximately 20% of corresponding steady-state trough plasma concentrations.

Elderly
Apparent oral clearance (CL/F) of gabapentin decreased as age increased, from about 225 mL/min in subjects under 30 years of age to about 125 mL/min in subjects over 70 years of age. Renal clearance (CLr) of gabapentin also declined with age, however, this decrease can largely be explained by the decline in renal function. Reduction of gabapentin dose may be required in patients who have age-related comprised renal function (see **DOSAGE AND ADMINISTRATION**).

Renal Impairment
In patients with impaired renal function, gabapentin clearance is markedly reduced and dosage adjustment is necessary (see Table 5 in **DOSAGE AND ADMINISTRATION**)

Hemodialysis
In a study in anuric subjects (N = 11), the apparent elimination half-life of gabapentin on non-dialysis days was about 1 32 hours, dialysis three times a week (4 hours duration) lowered the apparent half-life of gabapentin by about 60%, from 132 hours to 51 hours. Hemodialysis thus has a significant effect on gabapentin elimination in anuric subjects.

Dosage adjustment in patients undergoing hemodialysis is necessary (see Table 5 in **DOSAGE AND ADMINISTRATION**).

Pediatric
In general, pediatric subjects between 1 month and < 5 years of age achieved approximately 30% lower exposure (AUC) than that observed in those 5 years of age and older. Accordingly, oral clearance normalized to per body weight was higher in the younger children. Apparent oral clearance of gabapentin was directly proportional to creatine clearance. Gabapentin elimination half-life averaged 4.7 hours and was similar across the age groups studied.

Higher oral clearance values were observed in children <5 years of age compared to those observed in children 5 years of age and older, when normalized per body weight. The normalized oral clearance values observed in pediatric patients 5 years of age and older were consistent with values observed in adults after a single dose.

These pharmacokinetic data indicate that the effective daily dose in pediatric patients with epilepsy aged 3 and 4 years should be 40mg/kg/day to achieve average plasma concentrations similar to those achieved in patients 5 years of age and older receiving gabapentin at 30mg/kg/day.

Hepatic Impairment
Because gabapentin is not appreciably metabolized in humans, no study was performed in patients with hepatic impairment.

INDICATIONS AND CLINICAL USE
APO-GABAPENTIN (gabapentin) is indicated as adjunctive therapy for the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy.

CONTRAINDICATIONS
APO-GABAPENTIN (gabapentin) is contraindicated in patients who have demonstrated hypersensitivity to the drug or to any of the components of the formulation.

PRECAUTIONS
General;
Gabapentin has been associated with severe respiratory depression. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants and the elderly might be at higher risk of experiencing this severe adverse reaction. Dose adjustments might be necessary in these patients.

Although there is no evidence of rebound seizures with gabapentin, abrupt withdrawal of anticonvulsants in epileptic patients may precipitate status epilepticus.

Gabapentin is not considered effective in the treatment of absence seizures.

Patients who require concomitant treatment with opioids may experience increases in gabapentin concentrations. Patients who require concomitant treatment with central nervous system (CNS) depressants, including opioids should be carefully observed for signs of CNS depression, such as somnolence, sedation and respiratory depression and the dose of gabapentin or concomitant treatment with CNS depressants including opioids should be reduced appropriately.

Caution is advised when prescribing gabapentin concomitantly with opioids due to risk of CNS depression. In a population-based, observational, nested case-control study of opioid users, co-prescription of opioids and gabapentin was associated with an increased risk for opioid-related death compared to opioid prescription use alone (adjusted odds ratio [aOR], 1.49 [95% CI, 1.18 to 1.88, p<0.001]).

Suicidal ideation and behavior have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomized placebo controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behavior. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for gabapentin.

Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behavior emerge.

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

It is important to note that early manifestation of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Gabapentin should be discontinued if an alternative etiology for the signs or symptoms cannot be established.

Information for Patients:
To assure safe and effective use of gabapentin, the following information and instructions should be given to patients:

1. Inform your physician about any prescription or non-prescription medications, alcohol, or drugs you are now taking or plan to take during your treatment with gabapentin.
2. You should inform your physician if you are pregnant, or if you are planning to become pregnant, or if you become pregnant while you are taking gabapentin.
3. Gabapentin is excreted in human milk, and the effect on the nursing infant is unknown. You should inform your physician if you are breast feeding an infant. (See **USE IN LACTATION**)
4. Gabapentin may impair your ability to drive a car or operate potentially dangerous machinery. Until it is known that this medication does not affect your ability to engage in these activities, do not drive a car or operate potentially dangerous machinery.
5. You should not allow more than 12 hours between gabapentin doses to prevent breakthough convulsions.
6. Prior to initiation of treatment with gabapentin, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity such as fever or lymphadenopathy may herald a serious medical event and that the patient should report any such occurrence to a physician immediately.

Neuropsychiatric adverse events – pediatric patients 3-12 years of age:
Gabapentin use in pediatric patients with epilepsy 3-12 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: 1) emotional lability (primarily behavioral problems) 2) hostility including aggressive behaviors, 3) thought disorder, including concentration problems and change in school performance, and 4) hyperkinesia (primarily restlessness and hyperactivity). Among the gabapentin-treated patients, most of the events were mild to moderate in intensity.

Drug Discontinuation
As with other anticonvulsant agents, abrupt withdrawal is not recommended because of the possibility of increased seizure frequency. When in the judgement of the clinician there is a need for dose reduction, discontinuation of substitution with alternative medication, this should be done gradually over a minimum of one week.

Effect on Ability to Drive and Operate Machines
Patients should be advised not to drive or operate machinery until it is known that the medication does not affect their ability to engage in such activities.

PRE-CLINICAL SAFETY DATA
Carcinogenesis
Gabapentin was given in the diet to mice at 200, 800 and 2000mg/kg/day and to rats at 250, 1000 and 2000mgmg/kg/day for 2 years. A statistically significant increase in the incidence of pancreatic acinar cell tumors was found only in male rats at the highest dose. Peak plasma drug concentrations in rats at 2000mg/kg/day are 10 times higher than plasma concentrations in humans given 3600mg/day. The pancreatic acinar cell tumors in male rats are low-grade malignancies, did not affect survival, did not metastasize or invade surrounding tissue, and were similar to those seen in concurrent controls. The relevance of these pancreatic acinar cell functions in male rats to carcinogenic risk in humans is unclear.

Mutagenesis:
Gabapentin demonstrated no genotoxic potential. It was not mutagenic in vitro in standard assays using bacterial or mammalian cells. Gabapentin did not induce structural chromosome aberrations in mammalian cells in vitro or in vivo, and did not induce micronucleus formation in the bone marrow of hamsters.

Impairment of fertility:
No adverse events on fertility or reproduction were observed in rats at doses up to 2000mg/kg (approximately five times the maximum daily human dose on a mg/m^2 basis)

Teratogenesis:
Gabapentin did not increase the incidence of malformations compared to controls in the offspring of mice, rats or rabbits at doses up to 50, 30 and 25 times respectively the human doses of 3600mg (four, five or eight times respectively the human daily dose of a mg/m^2 basis)

Gabapentin induced delayed ossification in the skull vertebrae, forelimbs and hindlimbs in rodents, indicative of fetal growth retardation. These effects occurred when pregnant mice received oral doses of 1000 or 3000mg/kg/day during organogenesis and in rates given 500, 1000 or 2000mg/kg prior to and during mating and throughout gestation. These doses are approximately 1 to 5 times the human dose of 3600mg on a mg/m^2 basis.

No effects were observed in pregnant mice given 500mg/kg/day (approximately ½ of the daily human dose on a mg/m^2 basis)

An increased incidence of hydroureter and/or hydronephrosis was observed in rats given 2000mg/kg/day in a fertility and general reproduction study, 1500mg/kg/day in a teratology study and 500, 1000 and 2000mg/kg/day in a perinatal and postnatal study. The significance of these findings is unknown, but they have been associated with delayed development. These doses are also approximately 1 to 5 times the human dose of 3600mg on a mg/m^2 basis.

In a teratology study in rabbits, an increased incidence of post-implantation fetal loss occurred in doses given 60, 300 and 1500mg/kg/day during organogenesis. These doses are approximately ¼ to 8 times the daily human dose of 3600mg a on mg/m^2 basis

DRUG INTERACTIONS

Antiepileptic Agents
There is no interaction between gabapentin and phenytoin, valproic acid, carbamazepine, or phenobarbital. Consequently, gabapentin may be used in combination with other commonly used antiepileptic drugs without concern for alteration of the plasma concentrations of gabapentin or the other antiepileptic drugs.

Gabapentin steady-state pharmacokinetics are similar for healthy subjects and patients with epilepsy receiving antiepileptic agents.

Oral Contraceptives
Coadministration of gabapentin with the oral contraceptive containing norethindrone and/or ethinyl estradiol does not influence the steady-state pharmacokinetics of norethindrone or ethinyl estradiol.

Antacids
Coadministration of gabapentin with an aluminum and magnesium-based antacid reduces gabapentin bioavailability up to 20%. It is recommended that gabapentin be taken about 2 hours following antacid administration.

Probenecid
Renal excretion of gabapentin is unaltered by probenecid.

Cimetidine
A slight decrease in renal excretion of gabapentin observed when it is coadministered with cimetidine is not expected to be of clinical importance.

Morphine
In a study involving healthy volunteers (N=12), when a 50mg controlled-release morphine capsule was administered 2 hours prior to a 600mg gabapentin capsule, mean gabapentin AUC increased by 44% compared to gabapentin administered without morphine. This was associated with an increased pain threshold (cold pressor test). The clinical significance of such changes has not been defined. Morphine pharmacokinetic parameter values were not affected by administration of gabapentin 2 hours after morphine. The observed opioid-mediated side effects associated with morphine plus gabapentin did not differ significantly from morphine plus placebo. The magnitude of interaction at other doses is not known

CNS Depressants, including Opioids
There are spontaneous and literature case reports of respiratory depression, sedation and death associated with gabapentin when co-administered with CNS depressants, including opioids. In some of these reports, the authors considered the combination of gabapentin with opioids to be a particular concern in frail patients, in the elderly, in patients with serious underlying respiratory disease, with polypharmacy, and in those patients with substance abuse disorders.

USE IN PREGNANCY
There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should only be used during pregnancy if the potential benefit to the mother justifies the potential risk to the fetus.

USE IN LACTATION
Gabapentin is excreted in human milk. Because the effect on the nursing infant is unknown, caution should be exercised when gabapentin is administered to a nursing mother. Gabapentin should be used in nursing mothers only if the potential benefit outweighs the potential risks.

USE IN RENAL IMPAIRMENT
Gabapentin clearance is markedly reduced in this patient population and dosage reduction is necessary (see Table 5 in **DOSAGE AND ADMINISTRATION**).

LABORATORY TESTS
For urinary protein determination the sulfosalicylic acid precipitation procedure is recommended, as false positive readings were reported with the Ames N-Multistix SG® dipstick test, when gabapentin or placebo was added to other anticonvulsant drugs.

ADVERSE REACTIONS
Epilepsy
Gabapentin has been evaluated for safety in more than 2000 subjects and patients in adjunctive therapy studies and was well tolerated. Of these, 543 patients participated in controlled clinical trials. Since gabapentin was most often administered in combination with other antiepileptic agents, it was not possible to determine which agent(s), if any, was associated with adverse events.

Incidence in controlled adjunctive therapy clinical trials:
Table 2 list treatment-emergent signs and symptoms that occurred in at least 1% of patients with partial seizures participating in placebo-controlled adjunctive therapy studies. In these studies, either gabapentin or placebo was added to the patient's current antiepileptic drug therapy. Adverse events were usually reported as mild to moderate.

Table 2. Treatment-emergent adverse event incidence in placebo-controlled add-on trials (events in at least 1% of gabapentin patients and numerically more frequent than in the placebo group).

BODY SYSTEM/ADVERSE EVENT (AE)	Gabapentin* N=543 %	Placebo) N=378 %
BODY As A WHOLE		
Fatigue	11.0	5.0
Weight Increase	2.9	1.6
Back Pain	1.8	0.5
Peripheral Edema	1.7	0.5
CARDIOVASCULAR		
Vasodilation	1.1	0.3
DIGESTIVE SYSTEM		
Dyspepsia	2.2	0.5
Mouth or Throat Dry	1.7	0.5
Constipation	1.5	0.8
Dental Abnormalities	1.5	0.3
Increased Appetite	1.1	0.8
HEMATOLOGIC AND LYMPHATIC SYSTEM		
Leukopenia	1.1	0.5
MUCOSKELETAL SYSTEM		
Myalgia	2.0	1.9
Fracture	1.1	0.8
NERVOUS SYSTEM		
Somnolence	19.3	8.7
Dizziness	17.1	6.9
Ataxia	12.5	5.6
Nystagmus	8.3	4.0
Tremor	6.8	3.2
Nervousness	2.4	1.9
Dysarthria	2.4	0.5
Amnesia	2.2	0.0
Depression	1.8	1.8
Thinking Abnormal	1.7	1.3
NERVOUS SYSTEM		
Twitching	1.3	0.5
Coordination Abnormal	1.1	0.3
RESPIRATORY SYSTEM		
Rhinitis	4.1	3.7
Pharyngitis	2.8	1.6
Coughing	1.8	1.3
SKIN AND APPENDAGES		
Abrasion	1.3	0.0
Pruritus	1.3	0.5
UROGENITAL SYSTEM		
Impotence	1.5	1.1
SPECIAL SENSES		
Diplopia	5.9	1.9
Amblyopia	4.2	1.1
LABORATORY DEVIATIONS		
WBC Decrease	1.1	0.5

* Includes concomitant antiepileptic drug therapy.

Other Adverse Events Observed in all Clinical Trials
Adverse events that occurred in at least 1% of the 2074 individuals who participated in all clinical trials are described below, except those already listed in the previous table:

Body As A Whole: Aesthenia, malaise or facial edema.

Cardiovascular System: Hypertension.

Digestive System: Anorexia, flatulence or gingivitis.

Hematologic And Lymphatic System: Purpura most often described as bruises resulting from physical trauma.

Musculoskeletal System: Arthralgia.

Nervous System: Vertigo, hyperkinesia, parasthesia, anxiety, hostility, and increased, decreased or absent reflexes.

Respiratory System: Pneumonia.

Urogenital System: Urinary tract infection.

Special Senses: Abnormal vision.

Use in the Elderly:
Adverse clinical events reported among 59 patients over the age of 65 years in pre-marketing clinical trial treated with gabapentin did not differ from those reported for younger individuals.

As gabapentin is eliminated primarily by renal excretion, dosage adjustment may be required in elderly patients because of declining renal function (see **DOSAGE AND ADMINISTRATION**).
Pediatric use:
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 in equal frequency among placebo-treated patients, were viral infection, fever, nausea and/or vomiting and somnolence.

Table 3. Treatment-emergent adverse event incidence in children age 3 to 12 years in controlled add-on trials (events in at least 2% of gabapentin patients and numerically more frequent than in the placebo group)

Body System/ Adverse Events	Gabapentin[a] N=119 %	Placebo[a] N=128 %
Body as a Whole		
Viral infection	10.9	3.1
Fever	10.1	3.1
Weight increase	3.4	0.8
Fatigue	3.4	1.6
Digestive System		
Nausea and/or vomiting	8.4	7.0
Nervous System		
Somnolence	8.4	4.7
Hostility	7.6	2.3
Emotional lability	4.2	1.6
Dizziness	2.5	1.6
Hyperkinesia	2.5	0.8
Respiratory System		
Bronchitis	3.4	0.8

Respiratory infection	2.5	0.8

[a] includes concomitant antiepileptic drug therapy

Other events in more than 2% of children that occurred equally or more frequent in the placebo group included: pharyngitis, upper respiratory infection, headache, rhinitis, convulsions, diarrhea, anorexia, coughing and otitis media

Withdrawal from Treatment due to Adverse Events

Adjunctive Therapy:

Approximately 7% of the more than 2000 healthy volunteers and patients with epilepsy, spasticity or migraine who received gabapentin in clinical studies withdrew due to adverse events.

In all clinical studies the most frequently occurring events that contributed to discontinuation of gabapentin included somnolence, ataxia, dizziness, fatigue, nausea and/or vomiting. Almost all participants had multiple complaints, none of which could be characterized as primary.

Pediatric:

Approximately 8% of the 292 children age 3 to 12 years who received gabapentin in clinical trials discontinued treatment because of an adverse event. The adverse events most commonly associated with withdrawal in children were somnolence, hyperkinesia and hostility.

Post-marketing experience:

Sudden, unexplained deaths have been reported where a causal relationship to treatment with gabapentin has not been established. Additional post-marketing adverse events reported include respiratory depression, acute kidney failure, allergic reaction including urticaria, alopecia, angioedema, blood glucose fluctuations in patients with diabetes, chest pain, elevated liver function tests (LFTs), erythema muliforme, hallucinations, movement disorders such as choreoathetosis, dyskinesia and dystonia, palpitation, pancreatitis, Stevens-Johnson syndrome, thrombocytopenia, tinnitus, urinary incontinence, hepatitis and jaundice.

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

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Acute, life-threatening toxicity has not been observed with gabapentin overdoses of up to 49 grams ingested at one time. In these cases, dizziness, double vision, slurred speech, drowsiness, lethargy and mild diarrhea were observed. All patients recovered with supportive care. Reduced absorption of gabapentin at higher doses may limit drug absorption at the time of overdosing and, hence, reduce toxicity from overdoses.

Although gabapentin can be removed by hemodialysis, based on prior experience, it is usually not required. However, in patients with severe renal impairment, hemodialysis may be indicated.

An oral lethal dose of gabapentin was not identified in mice and rats given doses as high as 8000mg/kg. Signs of acute toxicity in animals included ataxia, laboured breathing, ptosis, hypoactivity, or excitation.

DOSAGE AND ADMINISTRATION

APO-GABAPENTIN (gabapentin) is given orally with or without food.

When in the judgement of the clinician there is a need for dose reduction, discontinuation or substitution with an alternative medication, this should be done gradually over a minimum of one week.

Epilepsy:

Adults and Pediatric Patients Over 12 Years of Age:

In clinical trials, the effective dosing range was 900 to 1800mg/day. Therapy may be initiated by administering 300mg three times a day (TID) on Day 1, or by titrating the dose as described in Table 3. Thereafter, the dose can be increased in three equally divided doses up to a maximum dose of 1800mg/day. Dosages up to 2400mg/day have been well tolerated in long-term open-label clinical studies. Doses up to 3600mg/day have been administered to a small number of patients for a relatively short duration, and have been well tolerated. The maximum time between doses in the three times a day (TID) schedule should not exceed 12 hours to prevent breakthrough convulsions.

Table 3. Titration schedule

DOSE	DAY 1	DAY 2	DAY 3
900mg/day	300mg QD[a]	300mg BID[b]	300mg TID[c]

[a] QD = once a day
[b] BID = two times a day
[c] TID = three times a day

Pediatric patients age 3-12 years

The starting dose should range from 10 to 15 mg/kg/day given in equally divided doses (three times a day), and the effective dose reached by upward titration over a period of approximately 3 days. The effective dose of gabapentin in pediatric patients age 5 years and older is 25 to 35 mg/kg/day given in equally divided doses (3 times a day). The effective dose in pediatric patients aged 3 to less than 5 years is 40mg/kg/day given in equally divided doses (3 times a day). Dosages up to 50mg/kg/day have been well tolerated in a long-term clinical study. The maximum time interval between doses should not exceed 12 hours.

It is not necessary to monitor gabapentin plasma concentrations to optimize gabapentin therapy. Further, because there are no significant pharmacokinetics interactions among gabapentin and other commonly used antiepileptic drugs, the addition of gabapentin does not alter the plasma levels of these drugs appreciably.

If gabapentin is discontinued and/or an alternate anticonvulsant medication is added to the therapy, this should be done gradually over a minimum of one week.

Dosage adjustment in impaired renal function for patients with epilepsy.

Dosage adjustment in patients with compromised renal function or undergoing hemodialysis is recommended in table 4.

Table 4. Maintenance dosage of APO-GABAPENTIN in adults with reduced renal function

RENAL FUNCTION CREATININE CLEARANCE (mL/MIN)	TOTAL DAILY DOSE (mg/DAY)[a]
> 80	900 - 3600
50 to 79	600 – 1800
30 to 49	300 – 900
15 to 29	150[b] – 600
< 15	150[b] - 300

[a] Total daily doses should be administered as a TID regimen. Doses used to treat patients with normal renal function (creatinine clearance > 90mL/min) range from 900 to 3600mg/day. Reduced dosages are for patients with renal impairment (creatinine clearance < 79mL/min)
[b] To be administered as 300mg every other day.

Pediatric patients with renal insufficiency have not been studied

Dosage adjustment in patients undergoing hemodialysis

For patients undergoing hemodialysis who have never received gabapentin, a loading dose of 300 to 400mg is recommended, then 200 to 300mg of gabapentin following each 4 hours of hemodialysis.

AVAILABILITY OF DOSAGE FORMS

APO-GABAPENTIN 100mg CAPSULES

Each white opaque cap with white opaque body hard gelatin capsule, with white to off-white powder fill, imprinted "APO 100", contains 100 mg of gabapentin. Available in unit dose blister packages of 100 (10x10) capsules and in HDPE bottles of 100 and 500 capsules.

APO-GABAPENTIN 300mg CAPSULES:

Each yellow opaque cap with yellow opaque body hard gelatin capsule, with white to off-white powder fill, imprinted "APO 300", contains 300 mg of gabapentin. Available in unit dose blister packages of 100 (10xl0) capsules and in HDPE bottles of 100 and 500 capsules.

APO-GABAPENTIN 400mg CAPSULES:

Each orange opaque cap with orange opaque body hard gelatin capsule, with white to off-white powder fill, imprinted "APO 400", contains 400 mg of gabapentin. Available in unit dose blister packages of 100 (10xl0) capsules and in HDPE bottles of 100 and 500 capsules.

Not all presentations may be available locally.

LIST OF EXCIPIENTS

Croscarmellose Sodium, Magnesium Stearate, Talc USP 500 Mesh, Glob Yellow Iron oxide E172 (Capsule Shell), Titanium Dioxide E171 (Capsule Shell), Gelatin (Capsule Shell).

STABILITY AND STORAGE RECOMMENDATIONS

Store at or below 30°C, in tightly closed and light resistant containers.

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