PRESCRIBING INFORMATION

[Pr]PRIMIDONE

Primidone Tablets USP

125 mg and 250 mg

Therapeutic Classification

Anticonvulsant

AA PHARMA INC.
1165 Creditstone Road, Unit #1
Vaughan, Ontario
L4K 4N7

DATE OF REVISION:
June 30, 2015

Control Number: 179553

[Pr]PRIMIDONE

Primidone Tablets USP

THERAPEUTIC CLASSIFICATION

Anticonvulsant

INDICATIONS

For the control of grand mal and psychomotor seizure. May be used alone or in combination with other anticonvulsants.

CONTRAINDICATIONS

- patients who are known to be hypersensitive to barbituric acid derivatives, any ingredient in the formulation or component of the container
- patients with porphyria, severe respiratory depression or pulmonary insufficiency, renal impairment, hepatic impairment, sleep apnea, suicidal potential, alcoholism, drug dependence or in the presence of uncontrolled pain (paradoxical excitement may be produced).

WARNINGS AND PRECAUTIONS

General

Administer PRIMIDONE with caution to patients with myasthenia gravis, central nervous system depression, hepatic or renal impairment and in patients with hyperkinesis tendencies.
Lower doses are required in debilitated patients in order to preclude oversedation.
The abrupt withdrawal of antiepileptic medications may precipitate status epilepticus. Withdrawal should be cautious and gradual.

Bone Disorders

Long-term use of antiepileptics such as carbamazepine, phenobarbital (major metabolite of PRIMIDONE), phenytoin, primidone, oxcarbazepine, lamotrigine and sodium valproate is associated with a risk of decreased bone mineral density that may lead to weakened or brittle bones. In such cases, discontinuation of PRIMIDONE should be considered.
Rarely, rickets and osteomalacia have been reported following prolonged usage of phenobarbital due to increased metabolism of vitamin D (**see ADVERSE REACTIONS).**

Cardiovascular

Administer PRIMIDONE with caution to patients with hypotension or with cardiac impairment.

Concomitant use with other drugs
Concomitant use of the following should be avoided as much as possible because of likely occurrence of adverse reactions: alcohol, anaesthetics and CNS depressants and to a lesser extent, acetaminophen, oral anticoagulants, carbamazepine, oral contraceptives, estrogens, corticosteroids, digitalis, digitoxin, tricyclic antidepressants, cyclophosphamide, doxycycline, griseofulvin, monoamine oxidase inhibitors, phenytoin, quinidine, sodium valproate, and valproic acid.

Dependence/Tolerance
Prolonged use of phenobarbital (the major metabolite of primidone), may result in addiction and physical dependence. Patients may escalate dosage without medical advice. PRIMIDONE should be used with caution in patients with a history of drug addiction/dependence or drug abuse.

Hematologic
Administer PRIMIDONE with caution to patients in hemorrhagic shock or in patients with severe anemia.

Endocrine and Metabolism
Administer PRIMIDONE with caution to patients with myxedema and diabetes mellitus.

Occupational Hazards
PRIMIDONE may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a vehicle or operating machinery. The concomitant use of alcohol or other CNS depressants may have strong additive effect. Patients should be warned accordingly.

Psychiatric Disorders
Suicidal Ideation and Behaviour
Suicidal ideation and behavior have been reported in patients treated with antiepileptic agents in several indications. All patients treated with antiepileptic drugs, irrespective of indication, should be monitored for signs of suicidal ideation and behavior and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge. A FDA meta-analysis of randomized placebo controlled trials, in which antiepileptic drugs were used for various indications, has shown a small increased risk of suicidal ideation and behaviour in patients treated with these drugs. The mechanism of this risk is not known. There were 43892 patients treated in the placebo controlled clinical trials that were included in the meta-analysis. Approximately 75% of patients in these clinical trials were treated for indications other than epilepsy and, for the majority of non-epilepsy indications the treatment (antiepileptic drug or placebo) was administered as monotherapy. Patients with epilepsy represented approximately 25% of the total number of patients treated in the placebo controlled clinical trials and, for the majority of epilepsy patients, treatment (antiepileptic drug or placebo) was administered as adjunct to other antiepileptic agents (i.e., patients in both treatment arms were being treated with one or more antiepileptic drug). Therefore, the small increased risk of suicidal ideation and behavior reported from the meta-analysis (0.43% for patients on antiepileptic drugs compared to 0.24% for patients on placebo) is based largely on patients that received monotherapy treatment (antiepileptic drug or placebo) for non-epilepsy indications. The study design does not allow an estimation of the risk of suicidal ideation and behavior for Patients with epilepsy that are taking antiepileptic drugs, due both to this population being the minority in the study, and the drug-placebo comparison in this

population being confounded by the presence of adjunct antiepileptic drug treatment in both arms.

Respiratory
PRIMIDONE should be used with caution when administered to patients with any respiratory difficulty or after recent administration of other respiratory depressants.

Serious Dermatological Reactions
There have been rare post-marketing reports of serious and sometimes fatal skin reactions, including Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), with PRIMIDONE use. Post-marketing reporting rate is generally accepted to be an underestimate due to under-reporting. Recurrence of serious skin reactions following re- challenge with PRIMIDONE has also been reported. Therefore, if a patient develops a skin reaction during PRIMIDONE treatment, consideration should be given to permanent discontinuation and replacement of PRIMIDONE with alternative treatment.

Special Population

Pregnant Women
Administer PRIMIDONE with caution to pregnant women. Recent reports strongly suggest an association between the use of anticonvulsant drugs by women with epilepsy and elevated incidence of birth defects in children born to these women. Reference has been made to PRIMIDONE in several cases in which it was used in combination with other anticonvulsants, but its teratogenicity has not been demonstrated conclusively. The possibility exists that other factors, e.g. genetic factors of the epileptic condition, may contribute to the higher incidence of birth defects. Data also indicate that the great majority of mothers receiving anticonvulsant medication deliver normal infants. In addition to reports of increased incidence of congenital malformations such as cleft lip/palate and heart malformations in children of women receiving phenobarbital and other antiepileptic drugs, there have been reports of fetal hydantoin syndrome. This consists of prenatal growth deficiency, microcephaly and mental deficiency in children born to mothers who have received phenobarbital, phenytoin, alcohol or trimethadione. However, these features are all interrelated and are frequently associated with intrauterine growth retardation from other causes.

PRIMIDONE should not be discontinued in patients in whom the drugs are administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and risk to both the mother and the unborn child. With regard to drugs given for minor seizures, the risk of discontinuing medication prior to or during pregnancy should be weighed against the risk of congenital defects in the particular case and with the particular family history. However, it is not guaranteed with confidence that even minor seizures do not pose some hazards to the developing embryo or fetus.

If women receiving PRIMIDONE become pregnant, plan to become pregnant, or if the need to initiate treatment with PRIMIDONE arises during pregnancy, the drug's potential benefits must carefully be weighed against its hazards, particularly during the first 3 months of pregnancy.

Neonatal hemorrhage, with coagulation defect resembling vitamin K deficiency, has been described within the first 24 hours in newborns whose mothers were taking PRIMIDONE or other anticonvulsants. Vitamin K has been shown to prevent or correct this defect and has been recommended to be given to the mother before delivery and to the neonate after birth. Pregnant

women under anticonvulsant therapy should receive prophylactic vitamin K therapy for one month prior to, and during delivery as well as the neonate after birth.
Folic acid deficiency is known to occur in pregnancy and can contribute to the increased incidence of birth defects in the offspring of treated epileptic women. Like many other anti-epileptic drugs, PRIMIDONE may contribute to, or aggravate, folic acid deficiency. Folic acid supplementation is recommended before and during pregnancy.

The physician should weigh all of the foregoing considerations when treating and counseling epileptic women of childbearing potential. The total daily dosage of PRIMIDONE should not exceed 2 g. Since PRIMIDONE therapy generally extends over prolonged periods, a complete blood count and sequential multiple analysis test (e.g. SMA-12) should be made every six months.

Phenobarbital (a major active metabolite of PRIMIDONE) withdrawal symptoms have occurred in newborns exposed to the drug in utero and may be characterized by hypotonia, irritability and vomiting.

Nursing Women
There is evidence that in mothers treated with PRIMIDONE, the drug, or its metabolites, appear in the milk in substantial quantities. Therefore, the benefits of breast feeding should be weighed against the possible risks to the infant and a decision should be made whether to discontinue nursing or to discontinue PRIMIDONE, taking into account the importance of the drug to the mother. Since tests for the presence of PRIMIDONE in biological fluids are too complex to be carried out in the average clinical laboratory, it is suggested that the presence of undue somnolence and drowsiness in nursing newborns of PRIMIDONE-treated mothers be taken as an indication that nursing should be discontinued. When breastfeeding is discontinued there is a potential for withdrawal symptoms in infants.

Geriatrics
Lower doses are required in elderly patients in order to preclude oversedation.

ADVERSE REACTIONS

Adverse reactions tend to disappear with continued therapy or reduction of dosage. The occurrence of the following, particularly in the early treatment program, has been reported:

Nervous system disorders
Ataxia, diplopia, nystagmus. Drowsiness is frequent, especially at initiation of therapy. Mild impairment of concentration, judgment, memory, and fine motor skills may occur. Exacerbation of pre-existing pain may occur. Disturbances of sleep, dizziness, vertigo, headache and depression may occur. Patients with uncontrolled pain may experience paradoxical euphoria, elation, excitement and confusion. In children, hyperactivity is not uncommon; behavioural disturbances and cognitive impairment may occur. Geriatric patients may experience excitation, confusion or depression.

Gastrointestinal disorders
Epigastric pain, nausea, vomiting, diarrhea and constipation.

General disorders and administration site conditions
Fatigue, oedema. On rare occasions, persistent or severe side effects may necessitate withdrawal of the drug.

Hematologic
Megaloblastic anemia. The anemia usually responds to folic acid 15 mg daily, without the necessity of discontinuing therapy**.** Agranulocytosis and thrombocytopenia are rare.

Hepatobiliary disorders
Severe allergic reactions may result in jaundice due to degenerative changes in the liver. Toxic hepatitis is rare.

Immune system disorders
Facial edema. Hypersensitivity reactions have a greater tendency to occur in patients with a history of asthma, urticaria or angioedema.

Metabolism and nutrition disorders
Anorexia. Phenobarbital (a major active metabolite of PRIMIDONE) may increase vitamin D requirements, possibly by increasing vitamin D metabolism via enzyme induction. Rarely, rickets and osteomalacia have been reported following prolonged use of phenobarbital(see WARNINGS AND PRECAUTIONS).

Psychiatric disorders
Hyperirritability, emotional disturbances

Respiratory, thoracic and mediastinal disorders
Respiratory depression.

Reproductive system and breast disorders
Impotence

Renal and urinary disorders
Polyuria and thirst occur only rarely.

Skin and subcutaneous tissue disorders
Skin rash (vesicular or erythematous). Exfoliative dermatitis and erythema multiforme are rare. Morbilifom skin eruptions are occasionally seen.

Serious Dermatological Reactions
There have been rare post-marketing reports of serious and sometimes fatal skin reactions, including Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), with PRIMIDONE use. Post-marketing reporting rate is generally accepted to be an underestimate due to under-reporting. Recurrence of serious skin reactions following re - challenge with PRIMIDONE has also been reported .

Miscellaneous
Exacerbation of porphyria (See CONTRAINDICATIONS)

Post-Market Adverse Drug Reactions
There have been reports of decreased bone mineral density, osteopenia, osteoporosis and fractures in patients on long-term therapy with antiepileptic drugs.

DRUG INTERACTIONS

Most drug interactions have been documented with phenobarbital, however, as PRIMIDONE major active metabolite is phenobarbital, the following drug interactions are likely applicable to PRIMIDONE. Phenobarbital is an inducer of cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP2C19 and CYP3A4, and is capable of increasing the clearance of many hepatically metabolized drugs. This can result in: i) decrease in, or loss of, effectiveness of other drug(s); ii) increase in effect, or frank toxicity of, the other drug(s) on discontinuation of PRIMIDONE. When adding or deleting any barbiturate to, or from, the patient's therapeutic regimen, pharmacotherapy must be monitored closely as dosage adjustment may be necessary.

Oral anticoagulants

Metabolism of coumarin anticoagulants may be accelerated, resulting in decreased anticoagulant response. Correspondingly, if PRIMIDONE is discontinued from a stabilized regimen, the hypoprothrombinemic response may be greatly increased, potentially resulting in hemorrhagic complications. Prothrombin times should be monitored closely when PRIMIDONE is added to, or deleted from, a regimen that includes oral anticoagulants.

Anticonvulsants

Phenytoin: When PRIMIDONE is used with phenytoin, concentrations of either phenytoin or phenobarbital may be increased, decreased or remain unchanged. While PRIMIDONE may induce the metabolism of phenytoin, it may also decrease it because both drugs compete for the same metabolic pathway. **Valproic Acid:** Concomitant administration of valproic acid and PRIMIDONE may result in increased levels of phenobarbital and resultant oversedation. **Carbamazepine:** When PRIMIDONE and carbamazepine are used together, the metabolism of carbamazepine can be accelerated and plasma concentrations may be decreased. The clinical significance of this interaction is not known.

Antidepressants

MAO Inhibitors: MAO inhibitors may inhibit PRIMIDONE metabolism, resulting in increased CNS depressant effects. **Tricyclic:** Phenobarbital may increase metabolism of tricyclic antidepressants resulting in their lack of effect. Plasma tricyclic concentrations should be monitored if possible, especially if the patient is not responding to standard dosages of antidepressant. The use of both drugs concomitantly may result in additive respiratory depressant effects.

CNS Depressants

Alcohol, benzodiazepines and other CNS depressants used concurrently with PRIMIDONE may result in excessive CNS depression.

Corticosteroids

PRIMIDONE may increase the metabolism of corticosteroids. Exacerbation of asthma and other conditions may occur if PRIMIDONE is added to regimens containing corticosteroids.

Oral Contraceptives

PRIMIDONE may accelerate the metabolism of both the estrogenic and progestagenic components of the contraceptive, resulting in decreased effectiveness, which may or may not be signalled by breakthrough bleeding. It would be advisable to use some other form of contraception.

Miscellaneous

Phenobarbital has been reported to increase the metabolism and correspondingly reduce the effectiveness of the following: griseofulvin, digitoxin and doxycycline.

DOSAGE AND ADMINISTRATION

Dosing considerations

Lower doses are required in elderly and debilitated patients in order to preclude oversedation.

Recommended Dose and Dosage Adjustment

Week	Adults and Children over 8 years	Children under 8 years
1	250 mg hs (at bedtime)	125 mg hs (at bedtime)
2	250 mg bid (morning & evening)	125 mg bid (morning & evening)
3	250 mg tid	125 mg tid
4	250 mg qid	125 mg qid

The therapeutic efficacy of a dosage regimen takes several days before it can be assessed. If necessary, continue similar weekly increments until seizures are controlled. Dosage exceeding 2 g daily is not recommended. In patients already receiving other anticonvulsants, the usual dosage range of PRIMIDONE in adults and children 8 years and older is between 125 mg and 1500 mg daily in divided doses. The dosage of PRIMIDONE is gradually increased while the dosage of other drug (s) is gradually decreased. When therapy with PRIMIDONE alone is the objective, the transition should not be completed in no less than two weeks.

Missed Dose

If a patient misses one or more doses, it is recommended that they take a single dose as soon as they remember. After taking the missed dose, enough time should elapse before taking the next dose to assure that the recommended maximum daily dose of 2 g is not exceeded. Then, the normal dosing schedule should be resumed.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

As for barbiturate poisoning; general supportive therapy is recommended.

Symptoms

As for phenobarbital (the major metabolite pf Primidone) poisoning, acute overdose with PRIMIDONE primarily affects the CNS and the cardiovascular system. Mild overdose resembles alcohol intoxication. Drowsiness, confusion, stupor, respiratory depression, ataxia, sluggish or absent reflexes, early hypothermia, late fever, cardiovascular depression with hypotension, renal failure, cardiac arrhythmias, pulmonary edema, aspiration pneumonia, bullae over pressure points and decreased gastrointestinal motility are all possible symptoms. Severe overdose may progress to shock, coma and death.

Doses that result in toxicity vary widely among patients and depend on co-ingestion of other drugs and the patient's underlying comorbidities. The lethal dose of phenobarbital is believed to be 5 g.

The lowest dose of phenobarbital reported to have led to fatality is 1.41 g.

According to literature, the highest acute dose of phenobarbital that has not resulted in fatality was 27 g, which corresponded to 253 mcg/mL phenobarbital in human plasma.
Chronic ingestion of phenobarbital results in the development of tolerance and large doses can be ingested without overt toxicity. Serious toxicity can result at lower phenobarbital levels if combined with alcohol or other CNS depressant drugs.

Treatment

General supportive therapy is recommended.

Patients who have ingested phenobarbital in overdose often require respiratory and hemodynamic support. This may include intubation, ventilation, boluses of isotonic IV fluids, and inotrope infusions. Once a patient's airway is protected, activated charcoal should be administered to minimize absorption of orally administered phenobarbital. Administering multiple doses of activated charcoal enhances the clearance of phenobarbital, though there is no evidence that it actually improves clinical outcomes such as duration of intubation. In patients with normal renal and cardiac function, urinary alkalinization also enhances phenobarbital clearance. Likewise, urinary alkalinization has not actually been shown to improve clinical outcomes.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Form and Strength	Medicinal Ingredient	Non-medicinal Ingredients	Description and Packaging
125 mg tablets	PRIMIDONE USP	Colloidal Silicon Dioxide, Croscarmellose Sodium, Magnesium Stearate, Methylcellulose	Round, white, flat-faced, bevelled edge tablets identified "125". Bottles of 100
250 mg tablets	PRIMIDONE USP	Colloidal Silicon Dioxide, Croscarmellose Sodium, Magnesium Stearate, Methylcellulose	Round, white, flat-faced, bevelled edge, scored tablets identified "250". Bottles of 100

PART III: PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

PRPRIMIDONE
Primidone Tablets USP

Read this carefully before you or your child start taking **PRIMIDONE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your or your child's medical condition and treatment and ask if there is any new information about **PRIMIDONE**.

What is PRIMIDONE used for?
PRIMIDONE is used to control grand mal and psychomotor seizures. It may be used alone or in combination with other anti-epileptic drugs.

How does PRIMIDONE work?
It is not completely known how PRIMIDONE works.

What are the ingredients in PRIMIDONE?
Medicinal ingredients: Primidone
Non-medicinal ingredients: methylcellulose, croscarmellose, magnesium stearate and colloidal silicon dioxide

PRIMIDONE comes in the following dosage forms:
Tablets; 125 mg and 250 mg.

Do not use PRIMIDONE if you or your child:
- is allergic to the active ingredient primidone, phenobarbital, or any of the other ingredients
- have the following symptoms or problems:
    - Porphyria (a genetic disorder that can cause nervous system, blood and skin problems)
    - Lung problems or severe respiratory depression
    - Liver or kidney problems
    - Pauses in breathing during sleep
    - Suicidal potential
    - Alcohol addiction
    - Drug addiction
    - Uncontrolled pain

To help avoid side effects and ensure proper use, talk to your healthcare professional about any health conditions or problems you or your child may have BEFORE taking PRIMIDONE including if you or your child:

- Have ever had a rash or unusual reaction while taking primidone or any other anti-epileptic drug.
- Have kidney or liver problems. Your doctor may need to adjust the dose.
- Drink alcohol. Drinking alcohol with PRIMIDONE may make you less alert and may make any feelings of anger, confusion or sadness worse.
- Are pregnant or planning to become pregnant. You must only take PRIMIDONE during pregnancy if your doctor tells you to.

- If you become pregnant while taking PRIMIDONE, talk to your healthcare provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic medicine during pregnancy. You can enroll in this registry by calling 1-888-233-2334. Information on the registry can also be found at the website http://www.aedpregnancyregistry.org/.

- Are nursing or plan to nurse your baby. Nursing while you are taking PRIMIDONE is not recommended.
- Are taking birth control.
  -PRIMIDONE may make hormonal birth control such as "the pill" less effective.
  -Use other forms of safe and effective birth control when taking PRIMIDONE.
  -You need to use the other forms of birth control until the end of your menstrual cycle after stopping treatment.
- Have any of the following diseases or conditions:
  - Suffer from seizures that spread to the whole brain
  - Heart problems
  - Hypothyroidism (a condition in which your body has low thyroid hormone)
  - Myasthenia Gravis (a chronic disease that causes severe muscle weakness)
  - Central nervous system depression
  - Low blood pressure
  - Severe anemia (low red blood cell count)
  - Hemorrhagic shock (shock due to bleeding)
  - Asthma (wheeze or gasp for air due to spasm of the airway)
  - Diabetes Mellitus
  - Hyperkinesis tendencies (abnormally heightened, sometimes uncontrollable muscle movement)

Other warnings you should know about:

- If you use PRIMIDONE regularly for a long time, it may cause mental and physical dependence.
- Sudden removal of this drug may cause unwanted side effects. Your doctor should discontinue your drug slowly and carefully.
- Ask your doctor about signs and symptoms of life-threatening skin reactions including Stevens-Johnson syndrome (SJS, a skin reaction with rash and blisters) and Toxic Epidermal Necrolysis (TEN, skin rash often with blisters, lesions and lifting skin), that have been reported with the use of PRIMIDONE. Closely monitor for skin reactions. Most often, SJS or TEN happen in the first few weeks of treatment. If symptoms or signs of SJS or TEN are present, PRIMIDONE treatment should be stopped and you should seek urgent medical treatment. The best results in managing SJS and TEN come from early detection and stopping the drug treatment right away (see table of Serious Side Effects and What to do About Them, below).

DURING treatment with PRIMIDONE, tell your doctor if you or your child develops:

- Thoughts of suicide or self-harm
- Abnormal vision (blurry or double vision)

Driving and using machines:

Before doing tasks that require special attention, wait until you know how you respond to PRIMIDONE. Being dizzy or drowsy can occur. Be careful to avoid accidental injury or falls.

Tell your healthcare professional about all the medicines you or your child take, including any

drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with PRIMIDONE:
- Birth control pills
- Other anti-epileptic drugs including phenytoin, valproic acid, carbamazepine
- Oral coumarin anticoagulants
- Antidepressants, MAO Inhibitors (e.g. isocarboxazid, moclobemide, or linezolid etc.)
- Tricyclic antidepressants (e.g. clomipramine, imipramine, or nortriptyline, amitriptyline)
- CNS depressants, including alcohol, benzodiazepines
- Corticosteroids (e.g. beclomethasone, bluticasone furoate etc.)
- Griseofulvin (an antifungal drug)
- Digitoxin
- Doxycycline (an antibiotic)
- Ketamine
- Anesthetics
- To a lesser extent: acetaminophen, estrogens, digitalis, digitoxin, cyclophosphamide, doxycycline, quinidine, and vitamin D.

How to take PRIMIDONE:
- **Do not stop taking PRIMIDONE without talking to your doctor**. Stopping PRIMIDONE suddenly can cause serious problems, including seizures that will not stop. Your doctor will tell you if and when you or your child can stop taking this medicine.

Usual dose:

Week	Adults and Children over 8 years	Children under 8 years
1	250 mg at bedtime	125 mg at bedtime
2	250 mg once in the morning & once in the evening	125 mg once in the morning & once in the evening
3	250 mg three times a day	125 mg three times a day
4	250 mg four times a day	125 mg four times a day

Overdose:

If you think you have taken too much PRIMIDONE, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you or your child misses a dose, take it as soon as you remember. After taking the missed dose allow enough time between taking the missed dose and the next dose to make sure that the recommended daily dose of 2000 mg is not exceeded. The next day, the normal dosing schedule should be resumed.

What are possible side effects from using PRIMIDONE?
These are not all the possible side effects you may feel when taking PRIMIDONE. If you or your child experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

The most common side effects associated with the use of PRIMIDONE are:
- Sleepiness/drowsiness, feeling tired/fatigue
- Headache, dizziness along with the feeling of a spinning movement
- Nausea/ vomiting
- Broken sleep
- Depression
- Diarrhea, constipation
- Unusual or unexpected feeling of joy, happiness, excitement and confusion
- Hypotension (low blood pressure)
- Hyperactivity in children
- "Hangover" confusion especially in the elderly (drowsiness the day after a dose)
- Shakiness

Other possible side effects associated with the use of PRIMIDONE:
- Increase/worsening of pre-existing pain
- Epigastric pain (pain in the upper abdomen)

Serious Side Effects and What to do About Them				
Symptom / effect		**Talk to your Healthcare Professional**		**Get Immediate Medical Help**
		Only if Severe	**In all Cases**	
Common	Low sodium level in blood (symptoms like lack of energy, confusion, muscular twitching or convulsions)		X	
	Nervous system problems (symptoms like dizziness, trouble walking or with coordination, feeling sleepy and tired, trouble concentrating, vision problems etc.)		X	
	Allergies (symptoms like fever, rash and swollen lymph nodes, and may be associated with symptoms involving other organs, e.g., liver)		X	

Serious Side Effects and What to do About Them				
Symptom / effect		**Talk to your Healthcare Professional**		**Get Immediate Medical Help**
		Only if Severe	**In all Cases**	
Uncommon	Liver problems (symptoms like yellowing of your skin or the whites of your eyes, nausea or vomiting, loss of appetite, stomach pain, dark [brownish] urine etc.)		X	
	Thoughts of suicide or self-harm			X
	Respiratory depression (shallow slow, weak breathing)			X
	Thinning of the bone, bone softening, bone disease, or fractures (In situations where healthy people would not normally break a bone you may have sudden pain in any location and especially in the wrist, spine or hip. This may be a fracture.)		X	
	Altered numbers and types of blood cells (symptoms like unexplained tiredness, weakness, shortness of breath, and sometimes, feeling like you are going to pass out and increased bruising, nosebleeds, sore throats, or infections)		X You should tell your doctor who may want to perform a blood test	
Rare	Severe allergic reactions (symptoms like swelling of face, eyes, lips, or tongue, trouble swallowing or breathing, skin rash)			X

Serious Side Effects and What to do About Them				
Symptom / effect		**Talk to your Healthcare Professional**		**Get Immediate Medical Help**
		Only if Severe	**In all Cases**	
	A rare, serious disorder in which your skin reacts severely to a medication (Stevens Johnson Syndrome; SJS). If symptoms or signs of SJS (e.g. skin rash often with blisters or lesions) are present, PRIMIDONE treatment should be stopped right away.			X
	Severe skin reaction where the upper surface of your skin detaches like a patient who has suffered burns (Toxic Epidermal Necrolysis [TEN]). If symptoms or signs of TEN (e.g. skin rash often with blisters or mucosal lesions and lifting skin) are present, PRIMIDONE treatment should be stopped right away.			X

If you or your child have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with daily activities, talk to your healthcare professional.

Reporting Side Effects
You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.
3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to: 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

    Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at controlled room temperature (between 15°C to 30°C).

Keep out of reach and sight of children.

If you want more information about PRIMIDONE:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website (www.aapharma.ca); or, by calling 1-877-998-9097.

This leaflet was prepared by AA Pharma Inc.

Last Revised: June 30, 2015