

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Epilepsy

Epilepsy is the most common neurological condition worldwide. It has no age, racial, geographic or socio-economic boundaries. Epilepsy is a condition characterized by recurrent (two or more) epileptic seizures unprovoked by an immediate identifiable cause. Epileptic seizures are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness and control of bowel or bladder function.

It has been stated by the World Health Organisation that one in twenty people (or 5% of the general population) who live a normal life span can expect to have at least one epileptic seizure at some point in their life. Virtually any injury or abnormality of the brain can cause irritation of vulnerable neurons to produce the extraordinarily wide variety of positive symptoms that constitute epileptic seizures. The nature of these symptoms depends upon the parts of the brain involved in the disturbance.

The prevalence of epilepsy in Europe is 8.2 per 1000 people; thus, in Europe, around 6,000,000 people currently have epilepsy, while 15,000,000 people will have had epilepsy at some time in their lives. Studies of the prevalence of epilepsy show that 1 out of every 20 or 30 persons in parts of the world with poor health conditions have epilepsy; in other parts, such as Europe, the prevalence is about 1 out of every 100 to 150. Thus, a typical family physician in Europe will have 10-20 persons with epilepsy among his or her patients and may therefore not consider epilepsy a priority or keep track of the latest developments in the field of epileptology [**WHO, 2011**].

The prevalence of epilepsy appears to be lower in Africa, while studies from Asia (mainly China and India) have demonstrated rates similar to those in the Western world. Moreover, there can be marked variation in the incidence and prevalence rates between different regions within the same country, although most but not all studies have shown that rates are higher in rural than in urban areas [**Aidan Neligan and J.W. Sander, 2014**].

Peripheral Neuropathy

Peripheral neuropathy is a common neurological disorder characterised by numbness, weakness, tingling and pain, often starting in the hands or feet. Peripheral neuropathy is a term which describes damage to the peripheral nervous system. The damage means that the messages that travel between your central and peripheral nervous system (from the brain to the spinal cord) are disrupted. There are many different conditions that can lead to peripheral neuropathy.

Diabetic peripheral neuropathy (DPN) is the most common type of peripheral neuropathy, which describes a family of nerve disorders that are directly caused by complications from

diabetes. People with diabetes who have trouble controlling their blood glucose (or blood sugar) levels, along with individuals with high cholesterol, high blood pressure, or obesity, are at an elevated risk for developing DPN.

There are about 60 million people with diabetes in the European Region, or about 10.3% of men and 9.6% of women aged 25 years and over.

The prevalence of diabetes is increasing among all ages in the European region, mostly due to increases in the numbers of individuals who are overweight or obese, who maintain unhealthy diets, and who are physically inactive. Worldwide, high blood glucose kills about 3.4 million people annually. Almost 80% of these deaths occur in low- and middle-income countries, and almost half are people aged under 70 years. The World Health Organisation (WHO) has predicted that diabetes deaths will double between 2005 and 2030.

Taking diabetes as a risk factor, about half of people who have had diabetes for 25 years have peripheral neuropathy, which supports the fact that the two are linked [**WHO, 2015**] [**The Neuropathy Action Foundation, 2013**].

Post-herpetic neuralgia (PHN) is the most common complication of herpes zoster (shingles). It produces chronic pain along cutaneous nerves and often some distortion of sensation. The pain can either persist after the acute episode of shingles, or it can recur in an area previously affected by shingles. Herpes zoster is a relatively common condition; the incidence of acute herpes zoster (HZ) in the general population in Europe ranges from about 1.2 to 5.2 per 1000 person-years (annual events per 1000 population). There is a strong correlation between the incidence of HZ and increasing age, with a marked rise in incidence at the age of 50–60 years and older. The lifetime risk of HZ is estimated to be up to 25% in the general population; thus one in four people may experience HZ in their lifetime. This risk rises to 50% in those aged > 85 years [**R. W. Johnson and J. McElhaney, 2009**] [**Gérard Mick et al, 2013**].

It has been stated that the lifetime incidence of herpes zoster (shingles) is around 25%. Studies in the United States and the Netherlands found that 2.6% and 10%, respectively, will develop chronic post-herpetic neuralgia [**International Association for the study of pain, 2014**].

VI.2.2 Summary of treatment benefits

Essential human studies were not conducted for evaluating effective and safe use of Gabapentin, considering this is a generic medicine (i.e., a medicine that is developed to be the same as a reference medicine that has already been authorized). The available medical literature is considered sufficient to evaluate the safety of Gabapentin in the proposed therapeutic indication(s) for Gabapentin Amneal 100 mg, 300 mg and 400 mg hard capsules.

VI.2.3 Unknowns relating to treatment benefits

Insufficient information is available on the use of gabapentin in pregnant women. Studies in animals have shown reproductive toxicity. However, the potential risk for humans is unknown. There is insufficient information on the use of gabapentin in breast-feeding women, as the effects of gabapentin on the breast-fed infants are unknown.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	What is known	Preventability
<p>Allergic Reactions (Hypersensitivity)</p>	<p>Allergic reactions (hypersensitivity) have been associated to the active substance or to any of the excipients of Gabapentin Amneal.</p> <p>Furthermore, the adverse reactions observed during clinical studies conducted in association with allergic reactions (hypersensitivity) consist of: Uncommon adverse reaction (may affect up to 1 in 100 people)</p> <ul style="list-style-type: none"> Allergic reactions, such as urticarial (also known as hives, which are raised, itchy areas of skin that are usually a sign of an allergic reaction) <p>Not known adverse reactions have also been reported which include symptoms such as: Stevens-Johnson syndrome (a serious systemic [body wide] allergic reaction, with a characteristic rash involving the skin) angioedema (swelling that is similar to hives, but the swelling is under skin instead of the on the surface of the skin), erythema multiforme (an allergic reaction</p>	<p>Yes.</p> <p>The patient should not take Gabapentin Amneal if:</p> <ul style="list-style-type: none"> The patient is allergic (hypersensitive) to gabapentin or any of the other ingredients of this medicine <p>A small number of people taking Gabapentin Amneal get an allergic reaction or potentially serious skin reaction, which may develop into more serious problems if they are not treated. The patient needs to know the symptoms to look out for while they are taking Gabapentin Amneal.</p> <p>The patient is advised to contact their doctor immediately if they experience any of the following symptoms after taking this medicine as they can be serious:</p> <ul style="list-style-type: none"> Severe skin reactions that require immediate attention, swelling of the lips and face, skin rash and redness, and/or hair loss (these may be

Risk	What is known	Preventability
	<p>usually triggered by infections, most commonly herpes simplex virus [HSV]), alopecia (hair loss), hypersensitivity syndrome, a systemic reaction with a variable presentation that can include fever, rash, hepatitis, lymphadenopathy (a disease affecting the lymph nodes), eosinophilia (increased number of eosinophils in your blood), occurring in response to some allergens), and sometimes other signs and symptoms</p>	<p>symptoms of a serious allergic reaction)</p> <ul style="list-style-type: none"> • Gabapentin Amneal may cause a serious or life-threatening allergic reaction that may affect your skin or other parts of your body such as your liver or blood cells. The patient may or may not have rash when they get this type of reaction. It may cause the patient to be hospitalized or to stop taking Gabapentin Amneal. <p>The patient should contact their doctor right away if they have any of the following symptoms:</p> <ul style="list-style-type: none"> • skin rash • hives • fever • swelling of your lip and tongue <p>The below list are the possible side effects associated with Gabapentin Amneal:</p> <p>Common (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Facial swelling, bruises, rash, itch, acne • Swelling in the legs and arms, difficulty with walking, weakness, pain, feeling unwell, flu-like symptoms

Risk	What is known	Preventability
		<p>Uncommon (may affect up to 1 in 100 people):</p> <ul style="list-style-type: none"> • Allergic reaction such as hives • Swelling that may involve the face, trunk and limbs
<p>Thoughts or attempts of harming or killing themselves (Suicidal ideation and behaviour)</p>	<p>Thoughts or attempts of harming or killing themselves (suicidal ideation and behaviour) have been reported in patients treated with Gabapentin Amneal.</p> <p>Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients, family members and caregivers of patients should be advised to seek medical advice should signs, thoughts or attempts of harming or killing themselves (suicidal ideation or behaviour) emerge.</p>	<p>Yes.</p> <p>The patient should talk to their doctor or pharmacist before taking Gabapentin Amneal due to the:</p> <p>A small number of people being treated with Gabapentin Amneal have had thoughts of harming or killing themselves. If at any time the patient has these thoughts, they are advised to immediately contact their doctor</p> <p>With regards to possible side effects the below have been reported:</p> <p>Commonly occurring possible side effects: (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Anger towards others, confusion, mood changes, depression, anxiety, nervousness, difficulty with thinking. <p>Additionally in clinical studies in children, aggressive behaviour were reported commonly. After marketing Gabapentin Amneal the following side effects have been reported:</p> <ul style="list-style-type: none"> • Adverse events following the abrupt discontinuation of gabapentin (anxiety,

Risk	What is known	Preventability
		difficulty sleeping, feeling sick, pain, sweating).
<p>Sudden inflammation of the pancreas (Acute Pancreatitis)</p>	<p>If a patient develops acute pancreatitis under treatment with gabapentin, discontinuation of Gabapentin Amneal should be considered.</p> <p>Adverse reactions reported from post-marketing experience found the below adverse reactions under gastrointestinal disorders:</p> <ul style="list-style-type: none"> • Pancreatitis • Under treatment with gabapentin cases of acute pancreatitis were reported. 	<p>Yes.</p> <p>If the patient develops signs such as persistent stomach pain, feeling sick and being sick contact they are advised to contact their doctor immediately as these may be symptoms of acute pancreatitis (an inflamed pancreas).</p>
<p>Fits (Seizures)</p>	<p>Gabapentin Amneal is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization (seizures that are initially limited to certain parts of the brain, whether the seizure spreads to other parts of the brain or not) in adults and children aged 6 years and above.</p> <p>Gabapentin Amneal is indicated as monotherapy (single drug for treatment) in the treatment of partial seizures with and without secondary generalization (seizures that are initially limited to certain parts of the brain, whether the seizure spreads to other parts of the brain or not) in adults and adolescents aged 12 years and above.</p> <p>Although there is no evidence of rebound seizures with gabapentin, abrupt withdrawal of anticonvulsants in epileptic patients may precipitate status epilepticus.</p>	<p>Yes.</p> <p>Gabapentin Amneal is used to treat various forms of epilepsy (seizures that are initially limited to certain parts of the brain, whether the seizure spreads to other parts of the brain or not).</p> <p>The patient's doctor will prescribe Gabapentin Amneal for the patient to help treat their epilepsy when you their current treatment is not fully controlling the condition. The patient should take Gabapentin Amneal in addition to their current treatment unless told otherwise.</p> <p>Gabapentin Amneal can also be used on its own to treat adults and children over 12 years of age.</p> <p>There have been no studies specifically looking at the use of gabapentin in pregnant women, but other medications used to treat seizures have reported an increased risk of harm to the</p>

Risk	What is known	Preventability
	<p>As with other antiepileptic medicinal products, some patients may experience an increase in seizure frequency or the onset of new types of seizures with Gabapentin Amneal.</p> <p>As with other anti-epileptics, attempts to withdraw concomitant anti-epileptics in treatment refractive patients on more than one anti-epileptic, in order to reach Gabapentin Amneal monotherapy have a low success rate.</p> <p>Gabapentin Amneal is not considered effective against primary generalized seizures such as absences and may aggravate these seizures in some patients. Therefore, gabapentin should be used with caution in patients with mixed seizures including absences.</p> <p>With regards to pregnancy and risks related to epilepsy and antiepileptic medicinal products in general: No sudden discontinuation of antiepileptic therapy should be undertaken as this may lead to breakthrough seizures, which could have serious consequences for both mother and child.</p>	<p>developing baby, particularly when more than one seizure medication is taken at the same time. Therefore, whenever possible, the patient should try to take only one seizure medication during pregnancy and only under the advice of their doctor.</p> <p>The patient is advised to contact their doctor immediately if they become pregnant, think they might be pregnant or are planning to become pregnant while taking Gabapentin Amneal.</p> <p>The patient must not suddenly discontinue taking this medicine as this may lead to a breakthrough seizure, which could have serious consequences for the patient and their baby.</p> <p>The patient must not stop taking Gabapentin Amneal unless their doctor tells them to do so. If the treatment is stopped it should be done gradually over a minimum of 1 week.</p> <p>If the patient stops taking Gabapentin Amneal suddenly or before they are told by their doctor, there is an increased risk of seizures.</p>
<p>Drug Rash with Eosinophilia (increased number of eosinophils in the blood) and Systemic Symptoms (fever,</p>	<p>Severe, life-threatening, systemic hypersensitivity reactions such as Drug rash with eosinophilia (increased number of eosinophils) and systemic symptoms (fever, swollen lymph nodes, inflammation of liver) [DRESS]</p>	<p>Yes.</p> <p>The patient is advised to contact their doctor immediately if they experience any of the following symptoms after taking this medicine as they can be serious:</p> <ul style="list-style-type: none"> • Gabapentin Amneal may cause a serious or life-

Risk	What is known	Preventability
<p>swollen lymph nodes, inflammation of liver) [DRESS syndrome]</p>	<p>have been reported in patients taking Gabapentin Amneal.</p> <p>It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy (a disease affecting the lymph nodes), may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Gabapentin Amneal should be discontinued if an alternative etiology for the signs or symptoms cannot be established.</p> <p>Adverse reactions reported from post-marketing experience found the below adverse reactions under immune system disorders and skin and subcutaneous tissue disorders: Hypersensitivity syndrome, a systemic reaction with a variable presentation that can include fever, rash, hepatitis, lymphadenopathy, drug rash with eosinophilia (increased number of eosinophils in the blood), and sometimes other signs and symptoms.</p>	<p>threatening allergic reaction that may affect the skin or other parts of the body such as the liver or blood cells. The patient may or may not have rash when they get this type of reaction. It may cause the patient to be hospitalized or to stop Gabapentin Amneal.</p> <p>The patient is advised to contact their doctor right away if they have any of the following symptoms:</p> <ul style="list-style-type: none"> • skin rash • fever <p>After marketing Gabapentin Amneal the following side effects have been reported: A group of side effects that could include swollen lymph nodes (isolated small raised lumps under the skin), fever, rash, and inflammation of liver occurring.</p>
<p>Use in elderly patients (65 years of age)</p>	<p>Elderly patients may require dosage adjustment because of declining kidney (renal) function with age. Somnolence (drowsiness, sleepiness), peripheral oedema (swelling usually in the lower limbs) and asthenia (loss of strength and energy) may be more frequent in elderly patients.</p> <p>No systematic studies in patients 65 years or older have been conducted with gabapentin. In one</p>	<p>Yes.</p> <p>Patients that are elderly (over 65 years of age), are advised to take the normal dose of Gabapentin Amneal unless the patient has problems with their kidneys.</p> <p>The patient's doctor may prescribe a different dosing schedule and/or dose if the patient has problems with their kidneys.</p> <p>If the patient has the impression that the effect of Gabapentin</p>

Risk	What is known	Preventability
	<p>double blind study in patients with neuropathic pain, somnolence, peripheral oedema and asthenia occurred in a somewhat higher percentage in patients aged 65 years or above, than in younger patients. Apart from these findings, clinical investigations in this age group do not indicate an adverse event profile different from that observed in younger patients.</p> <p>The effects of long-term (greater than 36 weeks) gabapentin therapy on learning, intelligence, and development in children and adolescents have not been adequately studied. The benefits of prolonged therapy must therefore be weighed against the potential risks of such therapy.</p>	<p>Amneal is too strong or too weak, they are advised to contact their doctor or pharmacist as soon as possible.</p>
<p>Infections and Infestations</p>	<p>The adverse reactions observed during clinical studies conducted in epilepsy are as follows:</p> <p>Very common adverse reactions (may affect more than 1 in 10 people)</p> <ul style="list-style-type: none"> • Viral Infection <p>Common adverse reactions (may affect up to 1 in 10 people)</p> <ul style="list-style-type: none"> • Pneumonia (lung infection), respiratory infection (infection of the respiratory tract), urinary tract infection (an infection of the kidney, ureters, bladder or urethra [urinary system]), infection, and otitis media (infection of the middle ear) 	<p>Yes.</p> <p>The patient is advise to contact their doctor right away if they have any of the following symptoms:</p> <ul style="list-style-type: none"> • frequent infections <p>Furthermore, very commonly associated side effect (may affect more than 1 in 10 people) have been reported and include the following:</p> <ul style="list-style-type: none"> • Viral infection <p>Commonly associate side effects have also been reported (may affect up to 1 in 10 people)</p> <ul style="list-style-type: none"> • Pneumonia, respiratory infections, urinary tract infection, inflammation

Risk	What is known	Preventability
	<ul style="list-style-type: none"> Respiratory tract infections, otitis media (infection of the middle ear), convulsions (fits) and bronchitis (infection of the bronchi [large and medium-sized airways of the lungs]) were reported only in clinical studies in children. 	<p>of the ear or other infections</p>
<p>Nervous System Disorders</p>	<p>Gabapentin Amneal may have minor or moderate influence on the ability to drive and use machines. Gabapentin Amneal acts on the central nervous system and may cause drowsiness, dizziness or other related symptoms. Even, if they were only of mild or moderate degree, these undesirable effects could be potentially dangerous in patients driving or operating machinery. This is especially true at the beginning of the treatment and after increase in dose.</p> <p>The adverse reactions observed during clinical studies conducted in epilepsy (adjunctive and monotherapy) and neuropathic pain are as follows:</p> <p>Very common adverse reactions have been reported (may affect more than 1 in 10 people): Somnolence (sleepiness and drowsiness), dizziness, ataxia (loss of full control of bodily movements).</p> <p>Common adverse reactions have also been reported (may affect up to 1 in 10 people): Convulsions (fits), hyperkinesias (abnormally increased</p>	<p>Yes, Gabapentin Amneal may produce dizziness, drowsiness and tiredness.</p> <p>Patient's should not drive, operate complex machinery or take part in other potentially hazardous activities until they know whether this medication affects their ability to perform these activities.</p> <p>Higher than recommended doses may result in an increase in side effects including loss of consciousness, dizziness, double vision, slurred speech, drowsiness and diarrhoea. The patient is advised to contact their doctor or go to the nearest hospital emergency unit immediately if they take more Gabapentin Amneal than the doctor prescribed. The patient is advised to take along any capsules that have not been taken, together with the container and the label so that the hospital can easily tell what medicine the patient has taken.</p> <p>Like all medicines, this medicine can cause side effects, although</p>

Risk	What is known	Preventability
	<p>uncontrolled activity or muscular movements), dysarthria (difficulty speaking), amnesia (a partial or total loss of memory), tremor (involuntary shaking of the body or limbs), insomnia (difficulty sleeping), headache, sensations such as paresthesia (numbness), hypaesthesia (sensitivity towards the skin), coordination abnormal, nystagmus (rapid involuntary movements of the eyes), increased, decreased, or absent reflexes.</p>	<p>no everybody gets them. The below adverse reactions have been reported:</p> <p>Very common (may affect more than 1 in 10 people):</p> <ul style="list-style-type: none"> • Feeling drowsy, dizziness, lack of coordination <p>Common (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Convulsions, jerky movements, difficulty with speaking, loss of memory, tremor, difficulty sleeping, headache, sensitive skin, decreased sensation (numbness), difficulty with coordination, unusual eye movement, increased, decreased or absent reflexes <p>Additionally in clinical studies in children, aggressive behaviour and jerky movements were reported commonly.</p> <p>Uncommon (may affect up to 1 in 100 people):</p> <ul style="list-style-type: none"> • Decreased movement <p>After marketing Gabapentin Amneal the following side effects have been reported:</p> <ul style="list-style-type: none"> • Problems with abnormal movements such as writhing, jerking movements and stiffness.
<p>Eye Disorders</p>	<p>The adverse reactions observed during clinical studies conducted in epilepsy (adjunctive and monotherapy) and neuropathic pain are as follows:</p>	<p>Yes.</p> <p>If a patients take more Gabapentin Amneal than they should:</p> <p>Higher than recommended doses may result in an increase in side</p>

Risk	What is known	Preventability
	<p>Common reported adverse reactions include the following: Visual disturbances such as amblyopia (impaired or dim vision without obvious defect or change in the eyes), diplopia (double vision)</p>	<p>effects including: loss of consciousness, dizziness and double vision. The patient is advised to contact their doctor or go to the nearest hospital emergency unit immediately if they take more Gabapentin Amneal than their doctor prescribed. The patient should take along any capsules that they have not taken, together with the container and the label so that the hospital can easily tell what medicine they have taken.</p> <p>Like all medicines, this medicine can cause side effects, although not everybody gets them. The below adverse reactions have been reported: Common (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Unusual eye movement, increased, decreased or absent reflexes. • Blurred vision, double vision
<p>Diseases of the blood vessels (Vascular Disorders)</p>	<p>The adverse reactions observed during clinical studies conducted in epilepsy (adjunctive and monotherapy) and neuropathic pain are as follows: Common reported adverse reactions (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Hypertension (high blood pressure), flushing or vasodilation (dilation of blood vessels). 	<p>Yes.</p> <p>Like all medicines, this medicine can cause side effects, although not everybody gets them. Common (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • High blood pressure, flushing or dilation of blood vessels.
<p>Disease affecting breathing and</p>	<p>The adverse reactions observed during clinical studies conducted</p>	<p>Yes, Like all medicines, this medicine can cause side</p>

Risk	What is known	Preventability
<p>causing oxygen levels in the blood to abruptly drop lower than normal (Respiratory Disorders)</p>	<p>in epilepsy and neuropathic pain are as follows:</p> <p>Very common adverse reactions (may affect more than 1 in 10 people):</p> <ul style="list-style-type: none"> • Viral Infection <p>Common adverse reactions (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Pneumonia (lung infection), respiratory infection (infection of the respiratory tract), urinary tract infection (an infection of the kidney, ureters, bladder or urethra [urinary system]), infection, and otitis media (infection of the middle ear) <p>In addition the below common adverse reactions have also been reported:</p> <ul style="list-style-type: none"> • Dyspnoea (difficulty breathing), bronchitis (inflammation of the bronchi [large and medium sized airways] of the lungs), pharyngitis (inflammation causing sore throat), cough, rhinitis (inflammation of the mucous membrane of the nose). <p>Respiratory tract infections, otitis media (infection of the middle ear), and bronchitis (infection of the bronchi [large and medium-sized airways of the lungs]) were</p>	<p>effects, although not everybody gets them.</p> <p>Very common (may affect more than 1 in 10 people):</p> <ul style="list-style-type: none"> • Viral infection <p>Common (may affect up to 1 in 10 people):</p> <ul style="list-style-type: none"> • Pneumonia, respiratory infections, urinary tract infection, inflammation of the ear or other infections • Difficulty breathing, bronchitis, sore throat, cough, dry nose

Risk	What is known	Preventability
	reported only in clinical studies in children.	
<p>Patients on haemodialysis (A medical procedure to remove fluid and waste products from the blood –treatment for kidney dialysis)</p>	<p>The adverse reactions observed during clinical studies conducted in epilepsy (adjunctive and monotherapy) and neuropathic pain include: In patients on haemodialysis due to end-stage renal failure, myopathy with elevated creatine kinase levels has been reported.</p> <p>Although Gabapentin Amneal can be removed by haemodialysis, based on prior experience it is not usually required. However, in patients with severe renal (kidney) impairment, haemodialysis may be indicated.</p> <p>Gabapentin Amneal is removed from plasma by haemodialysis. Dosage adjustment in patients with compromised renal function or undergoing haemodialysis is recommended.</p>	<p>Yes.</p> <p>The patient is advised to contact their doctor or pharmacist before taking Gabapentin Amneal:</p> <ul style="list-style-type: none"> • If they are on haemodialysis (to remove waste products because of kidney failure) <p>If a patient has kidney problems or are receiving haemodialysis: The patient’s doctor may prescribe a different dosing schedule and/or dose if they have problems with their kidneys or are undergoing haemodialysis. Like all medicines, this medicine can cause side effects, although not everybody gets them.</p> <ul style="list-style-type: none"> • If the patient is on haemodialysis, they should tell their doctor if they develop muscle pain and/or weakness.

Important potential risks:

Risk	What is known
<p>Discontinuation</p>	<p>If Gabapentin Amneal has to be discontinued it is recommended that this should be carried out gradually over a minimum of 1 week independent of the indication.</p> <p>If a patient develops acute pancreatitis (sudden inflammation of the pancreas) under treatment with Gabapentin Amneal, it has been advised that the discontinuation of Gabapentin Amneal should be considered.</p> <p>In addition, there is no evidence of rebound seizures (fits) with Gabapentin Amneal, abrupt withdrawal of anticonvulsants in epileptic</p>

Risk	What is known
	<p>patients may precipitate status epilepticus (a dangerous condition in which epileptics fits follow one another without recovery of consciousness between them).</p> <p>As with other antiepileptic medicinal products, some patients may experience an increase in seizure frequency or the onset of new types of seizures with Gabapentin Amneal. As with other anti-epileptics, attempts to withdraw concomitant anti-epileptics in treatment refractive patients on more than one anti-epileptic, in order to reach Gabapentin Amneal monotherapy have a low success rate.</p> <p>Severe, life-threatening, systemic hypersensitivity reactions such as Drug rash with eosinophilia (increased number of eosinophils) and systemic symptoms (fever, swollen lymph nodes, inflammation of liver) [DRESS] have been reported in patients taking antiepileptic drugs including Gabapentin Amneal.</p> <p>It is important to note that early manifestations of hypersensitivity (allergic reactions), such as fever or lymphadenopathy (disease affecting the lymph nodes), may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Gabapentin Amneal should be discontinued if an alternative cause for the signs or symptoms cannot be established.</p> <p>Specialist advice should be given to women who are likely to become pregnant or who are of childbearing potential and the need for antiepileptic treatment should be reviewed when a woman is planning to become pregnant. No sudden discontinuation of antiepileptic therapy should be undertaken as this may lead to breakthrough seizures, which could have serious consequences for both mother and child.</p> <p>In terms of undesirable effects, the below general disorders and administration site conditions have been reported:</p> <ul style="list-style-type: none"> • Withdrawal reactions (mostly anxiety, insomnia, nausea, pains, sweating), chest pain. Sudden unexplained deaths have been reported where a causal relationship to treatment with gabapentin has not been established.

Missing information:

Risk	What is known
Pregnancy	<p>The risk of birth defects is increased in the offspring of mothers treated with an antiepileptic medicinal product. Most frequently reported are cleft lip (a split in the upper lip on one or both sides of the centre), cardiovascular (relating to the heart and blood vessels)</p>

Risk	What is known
	<p>malformations and neural tube defects. Multiple antiepileptic drug therapy may be associated with a higher risk of congenital malformations (a disease or abnormally present from birth) than monotherapy, therefore it is important that monotherapy is practised whenever possible. Specialist advice should be given to women who are likely to become pregnant or who are of childbearing potential and the need for antiepileptic treatment should be reviewed when a woman is planning to become pregnant. No sudden discontinuation of antiepileptic therapy should be undertaken as this may lead to breakthrough seizures, which could have serious consequences for both mother and child. Developmental delay in children of mothers with epilepsy has been observed rarely. It is not possible to differentiate if the developmental delay is caused by genetic, social factors, maternal epilepsy or the antiepileptic therapy.</p> <p>Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Gabapentin Amneal should not be used during pregnancy unless the potential benefit to the mother clearly outweighs the potential risk to the foetus. No definite conclusion can be made as to whether gabapentin is associated with an increased risk of congenital malformations when taken during pregnancy, because of epilepsy itself and the presence of concomitant antiepileptic medicinal products during each reported pregnancy.</p> <p>The below adverse reactions have been observed during clinical studies conducted in epilepsy:</p> <p>Commonly occurring adverse reactions (may affect up to 1 in 10 people): Impotence. However the below adverse reactions were reported post-marketing:</p> <p>Breast hypertrophy, gynaecomastia, sexual dysfunction (including changes in libido, ejaculation disorders and anorgasmia): Not Known</p>
<p>Lactation (Breast-feeding)</p>	<p>Gabapentin Amneal is present in the breast milk of breast-feeding women. Because the effect on the breast-fed infant is unknown, caution should be exercised when Gabapentin Amneal is administered to a breastfeeding mother. Gabapentin Amneal should be used in breast-feeding mothers only if the benefits clearly outweigh the risks.</p>

VI.2.5 Summary of additional risk minimization measures by safety concern

The Summary of Product Characteristics (SmPC) of Gabapentin Amneal 100 mg, 300 mg and 400 mg hard capsules provides physicians, pharmacists and other health care professionals with details on how to use the medicine, and the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PIL). All these risk minimization measures are given in the SmPC and PIL of Gabapentin Amneal 100 mg, 300 mg and 400 mg hard capsules.

No additional risk minimization measures have been proposed for this generic medicine.

VI.2.6 Planned post authorisation development plan

No post authorisation study is planned for this product.

VI.2.7 Summary of changes to the Risk Management Plan over time

Version	Date (dd-mm-yyyy)	Safety Concerns	Comment
02	11.01.2016	Safety concern (Discontinuation) has been added to important potential risks as suggested by agency.	As per agency suggestion