CBG MEB

PUBLIC ASSESSMENT REPORT of the Medicines Evaluation Board in the Netherlands

Gabapentine Sandoz capsules hard, 100, 300 and 400 mg Sandoz B.V., the Netherlands

gabapentin

This assessment report is published by the MEB pursuant Article 21 (3) and (4) of Directive 2001/83/EC. The report comments on the registration dossier that was submitted to the MEB and its fellow –organisations in all concerned EU member states.
It reflects the scientific conclusion reached by the MEB and all concerned member states at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation.
This report is intended for all those involved with the safe and proper use of the medicinal product, i.e. healthcare professionals, patients and their family and carers. Some knowledge of medicines and diseases is expected of the latter category as the language in this report may be difficult for laymen to understand.

This assessment report shall be updated by a following addendum whenever new information becomes available.

General information on the Public Assessment Reports can be found on the website of the MEB.

To the best of the MEB's knowledge, this report does not contain any information that should not have been made available to the public. The MAH has checked this report for the absence of any confidential information.

EU-procedure number: NL/H/0764/001-003/DC
Registration number in the Netherlands: RVG 33683-33685

Date of first publication: 8 april 2009
Last revision: 12 April 2011

Pharmacotherapeutic group:	antiepileptics
ATC code:	N03AX12
Route of administration:	oral
Therapeutic indication:	Epilepsy: as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 6 years and above; as monotherapy in the treatment of partial seizures with and without secondary generalization in adults and adolescents aged 12 years and above. Treatment of peripheral neuropathic pain: treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.
Prescription status:	prescription only
Date of authorisation in NL:	7 August 2007
Concerned Member States:	Decentralised procedure with AT, DE, IT, LU, DK (withdrawn on 29 June 2010), ES, FI (withdrawn on 24 October 2008)
Application type/legal basis:	Directive 2001/83/EC, Article 10(1)

For product information for healthcare professionals and users, including information on pack sizes and presentations, see Summary of Product Characteristics (SPC), package leaflet and labelling.

I INTRODUCTION

Based on the review of the quality, safety and efficacy data, the member states have granted a marketing authorisation for Gabapentine Sandoz capsules 100, 300 and 400 mg, from Sandoz B.V. The date of authorisation was on 7 August 2007 in the Netherlands.

For epilepsy, Gabapentine Sandoz is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults and children aged 6 years and above. Gabapentin is indicated as monotherapy in the treatment of partial seizures with and without secondary generalization in adults and adolescents aged 12 years and above.
Gabapentine Sandoz is also indicated for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.

A comprehensive description of the indications and posology is given in the SPC.

The precise mechanism of action of gabapentin is not known. Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid) but its mechanism of action is different from that of several other active substances that interact with GABA synapses including valproate, barbiturates, benzodiazepines, GABA transaminase inhibitors, GABA uptake inhibitors, GABA agonists, and GABA prodrugs. In vitro studies with radiolabeled gabapentin have characterized a novel peptide binding site in rat brain tissues including neocortex and hippocampus that may relate to anticonvulsant and analgesic activity of gabapentin and its structural derivatives. The binding site for gabapentin has been identified as the alpha2-delta subunit of voltage-gated calcium channels.

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Neurontin 300 mg capsules (NL RVG 22482). The innovator product has been registered in the Netherlands by Pfizer B.V. since 10 November 1999. In addition, reference is made to Neurontin 100, 300, and 400 mg authorisations in the individual member states (reference product).

The marketing authorisation is granted based on article 10(1) of Directive 2001/83/EC.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. This information is not fully available in the public domain. Authorisations for generic products are therefore linked to the 'original' authorised medicinal product, which is legally allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. To this end the MAH has submitted a bioequivalence study in which the pharmacokinetic profile of the product is compared with the pharmacokinetic profile of the reference product Neurontin 400 mg capsules registered in Austria. A bioequivalence study is the widely accepted means of demonstrating that difference of use of different excipients and different methods of manufacture have no influence on efficacy and safety. This generic product can be used instead of its reference product.

No new pre-clinical and clinical studies were conducted, which is acceptable for this abridged application.

No scientific advice has been given to the MAH with respect to these products and no paediatric development programme has been submitted.

II SCIENTIFIC OVERVIEW AND DISCUSSION

II.1 Quality aspects

Compliance with Good Manufacturing Practice
The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place. For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates or satisfactory inspection summary reports, "close-out letters" or "exchange information" issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

Active substance
The active substance is gabapentin, an established active substance described in the USP* Pharmaceutical Forum volume 27(5). The drug substance is a white crystalline powder, and is soluble in water and sparingly soluble in methanol. Gabapentin exists in three polymorphic forms.

The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Manufacture
Gabapentin is prepared via a two-step synthesis. The drug substance has been adequately characterized.

Specification
The drug substance specification is generally in line with the Pharmacopeial Forum. Batch analytical data demonstrating compliance with this specification have been provided for 6 batches.

Stability
Stability data on the active substance have been provided for 8 batches (of which 5 were full-scale) at 25ºC/60%RH and 40ºC/75% RH in accordance with applicable European guidelines demonstrating the stability of the active substance over 48 months. Based on the data submitted, a retest period could be granted of 4 years without specific storage conditions in the commercial packaging

** USP is an official handbook (pharmacopoeia) in which methods of analysis with specifications for substances are laid down by the authorities of the USA.*

Medicinal Product

Composition
Gabapentine Sandoz capsules 100, 300, and 400 mg respectively contain as active substance 100, 300, and 400 mg of gabapentin, and are hard gelatin with white opaque (100 mg capsules), yellow opaque (300 mg capsules), or brown (400 mg capsules) opaque body and cap. Each strength has is own capsule size; capsule size 3 for 100 mg capsules, capsule size 1 for 300 mg capsules, and capsule size 0 for 400 mg capsules. The capsules with different active substance are fully dose proportional except the colouring agents of the capsule wall.

The capsules are packed in PVC/PE/PVDC-aluminium blister packs and in HDPE-containers with a child resistant PP closure.

The excipients are:
Capsule content: Pregelatinised maize starch, maize starch, talc, and colloidal anhydrous silica
Capsule shell: Gelatin and sodium laurel sulphate.

In addition in 100 mg capsules, *hard*: Titanium dioxide (E171)
In addition in 300 mg capsules, *hard*: Titanium dioxide (E 171) and iron oxide yellow (E 172)
In addition in 400 mg capsules, hard: Titanium dioxide (E 171), iron oxide yellow (E 172), and iron oxide red (E 172).

It is declared that the pregelatinised starch, maize starch, talc and silica colloidal anhydrous comply with the current version of the EP. The empty capsules are controlled with an in-house specification. The specification includes requirements for appearance, dimensions, identification for gelatine and titanium dioxide, average mass, disintegration time and loss on drying.

Pharmaceutical development
The aim of the pharmaceutical development of the gabapentin 100 mg, 300 mg and 400 mg capsules was to develop a dose proportional, stable product essentially similar to the brand leader. The brand leader product is marketed as 100, 300 and 400 mg capsule under brand name Neurontin throughout the EU.
Three polymorphic forms of gabapentin exist, i.e Form I, Form II and Form III. In general polymorphic forms of active substances may influence the bioavailability of the medicinal product by virtue of their varying solubility characteristics. However, the diffractograms of all the lots match with respect to same positions, indicating that all the lots belong to the same polymorph. Thus it can be assured that the polymorphic form of Gabapentin supplied is consistent.
The development of the product is satisfactory performed and explained. The excipients used are common in the manufacture of capsules. The packaging materials are usual and suitable for the product at issue.

Manufacturing process and quality control of the medicinal product
The manufacturing process has been validated according to relevant European/ICH guidelines. The drug product is prepared by sieving, mixing and capsule filling. The manufacturing process has been adequately described. Also, the process parameters, and the in-process controls have been sufficiently described. And adequate process validation was performed. Process validation data on the product have been presented for 3 batches of the 100 mg strength, 2 batches of the 300 mg strength and 3 batches of the 400 mg strength.

Product specification
The finished product specifications are adequate to control the relevant parameters for the dosage form. The specifications are in accordance with USP forum volume 28(2) for gabapentin capsules, and includes tests for appearance, identification, uniformity of dosage units, colour identification test for titaniumdioxide, dissolution, assay, related substances, and microbiological purity.

Limits in the specification have been justified and are considered appropriate for adequate quality control of the product.

Satisfactory validation data for the analytical methods have been provided.

Batch analyses data has been provided for 3 batches of the 100 mg strength, 2 batches of the 300 mg strength and 3 batches of the 400 mg strength demonstrating compliance with the release requirements.

Stability tests on the finished product
Stability data on the product have been provided for 3 batches of each strength at 25ºC/60%RH, 30ºC/65%RH and 40%/75% RH in accordance with applicable European guidelines. For none of the batches and pack types and sizes tested, a significant change is observed. The gabapentinlactam content increases during storage at all conditions but remains within the proposed end of shelf-life specifications. On basis of the data submitted, a shelf life was granted of 3 years. No specific storage conditions need to

be included in the SPC or on the label. The shelf life has been changed by a type-IB variation into 3 years (NL/H/764/001-003/IB/002). See also the table 'Steps taken after finalisation of the initial procedure on Page 10.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
It is stated that gelatine is the only excipient of animal origin used in the drug product. Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via medicinal products has been satisfactorily demonstrated.

II.2 Non-clinical aspects

This product is a generic formulation of Neurontin, which is available on the European market. No new preclinical data have been submitted, and therefore the application has not undergone preclinical assessment. This is acceptable for this type of application.

The non-clinical overview on the non-clinical pharmacology, pharmacokinetics and toxicology was adequate.

II.3 Clinical aspects

Gabapentin is a well-known active substance with established efficacy and tolerability.

For this generic application, the MAH has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Gabapentine Sandoz capsules 400 mg is compared with the pharmacokinetic profile of the reference product Neurontin 400 mg capsules.

The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution results and compositions of reference products in different member states.

The formula and preparation of the bioequivalence batch is identical to the formula proposed for marketing.

A single-dose, randomised, two-period, two-treatment, two-sequence, open label crossover bioequivalence study was carried out under fasted conditions in 32 healthy male subjects, aged 19-37 years. Each subject received a single dose (400 mg) of one of the test and reference gabapentin formulations. The capsule was orally administered in solid form with 240 ml water after an overnight fast of at least 10 h. Fasting was continued for 4 hrs after dosing. There were 2 dosing periods, separated by a washout period of 7 days. Blood samples were collected pre-dose and at 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 12, 16, 20, 24, 28 and 36 hours after administration of the products. Samples were collected in vacutainers containing EDTA via an indwelling canullae or by direct venipucture. Samples were immediately centrifuged under refrigeration and afterwards stored below -50ºC.
One subject witdrew his consent in period II of the study. 31 subjects completed the study entirely and were eligible for pharmacokinetic analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of gabapentin under fasted conditions.

Treatment N=31	AUC_{0-t} µg.h/ml	$AUC_{0-\infty}$ µg.h/ml	C_{max} µg/ml	t_{max} h	$t_{1/2}$ h
Test	32.55 ± 8.47	33.45 ± 8.68	3.15 ± 0.89	3.19 ± 1.54	6.6 ± 0.6
Reference	33.79 ± 10.66	34.66 ± 10.78	3.29 ± 0.99	3.18 ± 1.69	6.5 ± 0.8
***Ratio (90% CI)**	0.97 (0.91-1.04)	0.97 (0.91-1.04)	0.96 (0.90-1.02)	---	---
CV (%)	14.6	14.6	14.9	---	---

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum concentration
$t_{1/2}$ half-life

**ln-transformed values*

Gabapentin can be given with or without food. From the literature it is known that food does not interact with the absorption of gabapentin. Therefore, a food interaction study is not deemed necessary. The bioequivalence study under fasting conditions is in accordance with CPMP/EWP/QWP/1401/98 Note for Guidance on the investigation of bioavailability and bioequivalence.

The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are in agreement with those calculated by the MAH and are within the bioequivalence acceptance range of 0.80-1.25. Based on the pharmacokinetic parameters of gabapentin under fasted conditions, it can be concluded that Gabapentine Sandoz 400 mg capsules and the Neurontin 400 mg capsules are bioequivalent with respect to rate and extent of absorption, and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

The 100 and the 300 mg capsules are dose-proportional with the 400 mg capsule. Dissolution profiles obtained for the 100, 300 and 400 mg capsules are comparable (> 90% within 10 min.). In addition, gabapentin shows linear pharmacokinetics up to the 400 mg dose. The results of the bioequivalence study performed with the 400 mg capsules therefore apply to the other strengths.

The MEB has been assured that the bioequivalence study has been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

Risk management plan

Gabapentin was first approved in 1993, and there is now more than 10 years post-authorisation experience with the active substance. The safety profile of gabapentin can be considered to be well established and no product specific pharmacovigilance issues were identified pre- or postauthorisation which are not adequately covered by the current SPC. Additional risk minimisation activities have not been identified for the reference medicinal product. The MAH has a pharmacovigilance system at their disposal, which is based on the current European legislation. Routine pharmacovigilance activities are sufficient to identify actual or potential risks and a detailed European Risk Management Plan is not necessary for this product.
With respect to the risk management plan, the MAH was advised to especially monitor the risk of suicide, as both in the US and EU reports on suicide in patients treated with antiepileptic medicinal products had been received.

Product information

SPC
The SPC was brought in line with the published opinion regarding the article 30 referral for the innovator product Neurontin (EMEA/H/A-30/616).

Readability test
The MAH has not performed a readability test on the PIL. The MAH has brought the PIL in line with the published opinion regarding the article 30 referral for the innovator product Neurontin (EMEA/H/A-30/616). This is deemed acceptable.

III OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

Gabapentine Sandoz 100, 300, and 400 mg capsules have a proven chemical-pharmaceutical quality and are generic forms of Neurontin 100, 300, and 400 mg capsules respectively. Neurontin 100, 300, and 400 mg capsules are a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The SPC was brought in line with the published opinion regarding the article 30 referral for the innovator product Neurontin (EMEA/H/A-30/616). The SPC, package leaflet and labelling are in the agreed templates.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Gabapentine Sandoz 100, 300 and 400 mg capsules with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finished on 10 April 2007. Gabapentine Sandoz 100, 300, and 400 mg were authorised in the Netherlands on 7 August 2007.

The PSUR submission cyclus is 3 years. The first PSUR will cover the period from April 2007 till April 2012.

The date for the first renewal will be: 10 April 2012.

There were no post-approval commitments made during the procedure.

List of abbreviations

ASMF	Active Substance Master File
ATC	Anatomical Therapeutic Chemical classification
AUC	Area Under the Curve
BP	British Pharmacopoeia
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence Interval
C_{max}	Maximum plasma concentration
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CV	Coefficient of Variation
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EU	European Union
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
MEB	Medicines Evaluation Board in the Netherlands
OTC	Over The Counter (to be supplied without prescription)
PAR	Public Assessment Report
Ph.Eur.	European Pharmacopoeia
PIL	Package Leaflet
PSUR	Periodic Safety Update Report
SD	Standard Deviation
SPC	Summary of Product Characteristics
$t_{½}$	Half-life
t_{max}	Time for maximum concentration
TSE	Transmissible Spongiform Encephalopathy
USP	Pharmacopoeia in the United States
XRD	X-ray diffraction

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Scope	Procedure number	Type of modification	Date of start of the procedure	Date of end of the procedure	Approval/ non approval	Assessment report attached
Change in the name of the medicinal product. Change in the name of the medicinal product in Spain from Gabapentina Salutas 300 (400) mg cápsulas EFG into Gabapentina Acebex 300 (400) mg cápsulas EFG.	NL/H/0764/ 002-003/IB/ 001	IB	17-8-2007	16-9-2007	Approval	N
Change in the shelf-life of the finished product as packaged for sale.	NL/H/0764/ 001-003/IB/ 002	IB	17-12-2007	16-1-2008	Approval	N
Change in the name of the medicinal product. As a result of the transfer of the Marketing Authorisation, the product name in Germany changes from Gabapentin Registratiebeheer ... mg – Hartkapseln to GabaHexal ... mg - Hartkapseln.	NL/H/0764/ 001-003/IB/ 003	IB	29-1-2008	28-2-2008	Approval	N
Change in the name of the medicinal product. As a result of the transfer of the Marketing Authorisation, the product name in Austria changes from Gabathing ... mg – Hartkapseln to Gabapentin Hexal ... mg - Hartkapseln.	NL/H/0764/ 001-003/IB/ 004	IB	29-1-2008	28-2-2008	Approval	N
Change in the name of the medicinal product. s a result of the transfer of the Marketing Authorisation, the product name in The Netherlands changes from Gabapentine ... mg, capsules to Gabapentine Sandoz capsules ... mg.	NL/H/0764/ 001-003/IB/ 005	IB	29-1-2008	28-2-2008	Approval	N
Change in the name and/or adress of the marketing authorization holder. Change in the address of the MA holder Stichting Registratiebeheer The Netherlands from Almere to Amsterdam.	NL/H/0764/ 001-003/IA/ 006	IA	9-7-2008	23-7-2008	Approval	N
Change to batch release arrangements and quality control testing of the finished product. Addition of a batch release site including batch control.	NL/H/0764/ 001-003/IA/ 007	IA	9-7-2008	23-7-2008	Approval	N
Change to batch release arrangements and quality control testing of the finished product. Replacement or addition of a manufacturer responsible for batch release, not including batch control/testing.	NL/H/0764/ 001-003/IA/ 008	IA	9-7-2008	23-7-2008	Approval	N
Type II safety warnings on suicidal thoughts in antiepileptics; adaptation of section 4.4 of the SPC and section 2 of the PIL to the PhVWP recommendations.	NL/H/0764/ 001-003/II/ 009	II	29-1-2009	30-1-2009	Approval	Y, annex I
Change in the name of the medicinal product in Spain.	NL/H/0764/ 002-003/IB/ 010	IB	23-1-2009	23-2-2009	Approval	N
Change in the name of the medicinal product in Italy.	NL/H/0764/ 001-003/IB/ 011	IB	14-5-2009	13-6-2009	Approval	N
Change in test procedure of the finished product. Minor change to	NL/H/0764/ 001-003/IA/	IA	22-7-2009	5-8-2009	Approval	N

an approved test procedure.	012					
Change in the name of the medicinal product in Germany.	NL/H/0764/ 001-003/IB/ 012	IB	22-7-2009	26-8-2009	Approval	N
DMF update.	NL/H/0764/ 001-003/II/ 013	II	17-7-2009	15-9-2009	Approval	N
Extension of shelf life to 36 months.	NL/H/0764/ 001-003/IB/ 014	IB	27-7-2009	4-9-2009	Approval	N
Change in batch size of the finished product; up to 10-fold compared to the original batch size approved at the grant of the MA.	NL/H/0764/ 001/IA/015	IA	22-7-2009	5-8-2009	Approval	N
Change in batch size of the finished product; up to 10-fold compared to the original batch size approved at the grant of the MA.	NL/H/0764/ 002/IA/016	IA	22-7-2009	5-8-2009	Approval	N
Change in batch size of the finished product; up to 10-fold compared to the original batch size approved at the grant of the MA.	NL/H/0764/ 003/IA/017	IA	22-7-2009	5-8-2009	Approval	N
Change in the name of the medicinal product in Germany.	NL/H/0764/ 001-003/IB/ 018	IB	27-7-2009	26-8-2009	Approval	N
Chang in the address of the MAH.	NL/H/0764/ 001-003/IA/ 019	IA	1-9-2009	15-9-2009	Approval	N
Grouped IA variations.	NL/H/0764/ 001-003/IA/ 020/G	IA	5-11-2010	2-12-2010	Approval	N
Grouped II variations.	NL/H/0764/ 001-003/II/ 022/G	II	24-9-2010	23-11-2010	Approval	N
Grouped IB variations.	NL/H/0764/ 001-003/IB/ 023/G	IB	17-1-2011	16-2-2011	Approval	N

Annex I to the PAR

Type II variation – Antiepileptics and suicidal behaviour

Inclusion of safety warnings. Adaptation of section 4.4 of the SPC and section 2 of the PIL to the PhVWP recommendations (agreed on by July 2008).

Summary of Product Characteristics

"Section 4.4 Special Warnings and Precautions for Use
Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomised placebo controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for Gabapentine.

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 behaviour emerge."

Package Leaflet
"Section 2 Before you take X
Take special care with
A small number of people being treated with anti-epileptics such as Gabapentine have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor."