sanofi aventis

Because health matters

Direct Healthcare Professional Communication (DHPC)

RE: abnormal brain MRI findings and movement disorders in patients treated with Sabril® (vigabatrin)

July 2010

Dear Healthcare Professional,

As part of the ongoing safety monitoring of Sabril®, reports of cases of brain MRI abnormalities and movement disorders have been analysed.

Summary:

- **Cases of abnormal brain MRI findings have been reported, in particular in young infants treated for infantile spasms with high doses of vigabatrin. The clinical significance of these findings is currently unknown.**
- **Movement disorders including dystonia, dyskinesia and hypertonia have been reported in patients treated for infantile spasms. The benefit/risk of vigabatrin should be evaluated on an individual patient basis.**
- **If new movement disorders occur during treatment with vigabatrin, consideration should be given to dose reduction or a gradual discontinuation of treatment.**

The Summary of Product Characteristics (SmPC) will be updated accordingly.

Further information on the safety issue

Sanofi-aventis, in agreement with the CHMP Pharmacovigilance Working Party (PhVWP) and the Irish Medicines Board, would like to inform you about revised prescribing and safety information in the Summary of Product Characteristics (SmPC) for Sabril® 500mg film-coated tablets and 500mg granules for oral solution, indicated in:

- Treatment in combination with other anti-epileptic drugs for patients with resistant partial epilepsy, with or without secondary generalisation, that is where all other appropriate drug combinations have proved inadequate or have not been tolerated;
- Monotherapy in the treatment of infantile spasms (West's syndrome).

Pharmacovigilance data have shown that exposure to high doses of vigabatrin may be associated with MRI abnormalities in the brains of infants with infantile spasms. These abnormalities involve the gray matter in a small subset of patients less than 3 years of age. In general they are transient and resolve when vigabatrin is discontinued. In some cases, it was also observed that brain MRI abnormalities resolved under continued treatment. Case reports suggest that some infants may have transient motor signs, such as dystonia, dyskinesia and/or hypertonia, accompanying the signal changes on MRI. Whether these clinical manifestations are associated with brain MRI abnormalities has not been demonstrated. To date, the mechanism of these imaging abnormalities has not been established, and it is possible that their aetiology may be multifactorial, (e.g. vigabatrin, other coadministered anticonvulsants, ketogenic diet, underlying disease).
As a consequence, to ensure the safe and effective use of vigabatrin with adequate safety monitoring in the appropriate patient populations, the SmPC has been revised to recommend to the prescriber:

- to evaluate the benefit/risk of vigabatrin on an individual patient basis,
- to consider a dose reduction or a gradual discontinuation of treatment if new movement disorders occur during treatment with vigabatrin.

Call for reporting

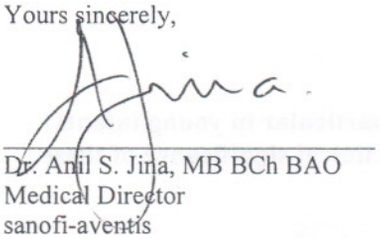
Please report any adverse reactions experienced by your patients to sanofi-aventis Ireland Pharmacovigilance at (01) 403 5600 and further information about adverse reaction reporting can be found at www.imb.ie.

Communication information
Please read carefully the revised enclosed Summary of Product Characteristics and contact sanofi-aventis if you have any additional questions.

Medical Information Department
sanofi-aventis Ireland Ltd.
Citywest Business Campus
Dublin 24
Tel: 01 4035600
Fax: 01 4035687
IEmedinfo@sanofi-aventis.com

We remain at your disposal for any further information you may need.

Yours sincerely,



Dr. Anil S. Jina, MB BCh BAO
Medical Director
sanofi-aventis

Annexes:
Text of the revised SmPC (with changes made visible)