ANNEX III

AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS AND THE PACKAGE LEAFLET

These amendments to the SPC and package leaflet are valid at the time of the Commission Decision.

After the Commission Decision the Member State Competent Authorities will update the product information as required

SUMMARY OF PRODUCT CHARACTERISITICS

AMENDMENTS TO BE INCLUDED IN SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS FOR VALPROIC ACID/VALPROATE CONTAINING MEDICINAL PRODUCTS, AS RELEVANT

4.1 Therapeutic indications

[…]

Treatment of manic episode in bipolar disorder when lithium is contraindicated or not tolerated. The continuation of treatment after manic episode could be considered in patients who have responded to <valproate> for acute mania.

[…]

4.2 Posology and method of administration

[…]

Manic episodes in bipolar disorder:

In adults:
The daily dosage should be established and controlled individually by the treating physician.
The initial recommended daily dose is 750 mg. In addition, in clinical trials a starting dose of 20 mg <valproate>/kg body weight has also shown an acceptable safety profile. Prolonged-release formulations can be given once or twice daily. The dose should be increased as rapidly as possible to achieve the lowest therapeutic dose which produces the desired clinical effect. The daily dose should be adapted to the clinical response to establish the lowest effective dose for the individual patient.
The mean daily dose usually ranges between 1000 and 2000 mg <valproate>. Patients receiving daily doses higher than 45mg/kg/day body weight should be carefully monitored.
Continuation of treatment of manic episodes in bipolar disorder should be adapted individually using the lowest effective dose.

In children and adolescents:
The safety and efficacy of {invented name} for the treatment of manic episodes in bipolar disorder have not been evaluated in patients aged less than 18 years.

[…]

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 antiepileptic 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 <active substance>. 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.

[…]

4.6 Pregnancy and lactation

This medicine should not be used during pregnancy and in women of child-bearing potential unless clearly necessary (i.e. in situations where other treatments are ineffective or not tolerated). Women of child-bearing potential have to use effective contraception during treatment.

4.8 Undesirable effects

[…]

Nausea, sedation, extrapyramidal disorders.

[…]

PACKAGE LEAFLET

AMENDMENTS TO BE INCLUDED IN SECTIONS OF THE PACKAGE LEAFLET FOR VALPROIC ACID /VALPROATE CONTAINING PRODUCTS, AS RELEVANT

1. WHAT {INVENTED NAME} IS AND WHAT IT IS USED FOR

{Invented name} is a medicine for the treatment of (…) and mania.

{Invented name} is used in the treatment of

[…]

- Mania, where you may feel very excited, elated, agitated, enthusiastic or hyperactive. Mania occurs in an illness called "bipolar disorder". {Invented name} can be used when lithium can not be used.

2. BEFORE YOU TAKE {INVENTED NAME}

[…]

Take special care with {INVENTED NAME}

A small number of people being treated with anti-epileptics such as <active substance> have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

Children and adolescents

Children and adolescents under 18 years of age:
{Invented name} should not be used in children and adolescents under 18 years of age for the treatment of mania.

Pregnancy and breast-feeding

You should not take this medicine if you are pregnant or a women of child-bearing age unless explicitly advised by your doctor. If you are a woman of child-bearing age, you have to use effective contraception during treatment.

[…]

3. HOW TO TAKE {INVENTED NAME}

[…]

Mania

The daily dosage should be established and controlled individually by your doctor.

Initial dose
The recommended initial daily dose is 750 mg.

Mean daily dose
The recommended daily doses usually range between 1000 mg and 2000 mg.

[…]

4. POSSIBLE SIDE EFFECTS

[…]
Nausea, sedation, extrapyramidal disorders.
[…]