Annex III

Amendments to relevant sections of the Product Information

Note:

These amendments to the relevant sections of the Summary of Product Characteristics and package leaflet are the outcome of the referral procedure.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the Reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

Amendments to the relevant sections of the Product Information

[For all products in Annex I, the existing product information shall be amended (insertion, replacement or deletion of the text, as appropriate) to reflect the agreed wording as provided below.]

SUMMARY OF PRODUCT CHARACTERISTICS

- *Medicinal products containing topiramate monocomponent*

[The following wording should be added preceding section 1, in line with the quality review of documents (QRD) template.]

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

4.2 Posology and method of administration

- *Medicinal products containing topiramate monocomponent*

[This section should include the following wording. Wording within angle brackets is applicable depending on if the medicinal product is indicated in populations below 18 years of age and adults, or if the medicinal product is indicated only for adults.]

<Female children and women> <Women> of childbearing potential

Treatment with topiramate should be initiated and supervised by a physician experienced in the management of epilepsy or migraine.

Alternative therapeutic options should be considered in <female children and> women of childbearing potential. The need for topiramate treatment in these populations should be reassessed at least annually (see sections 4.3, 4.4 and 4.6).

- *Medicinal products containing topiramate/phentermine*

[This section should include the following wording.]

Women of childbearing potential

Treatment with topiramate/phentermine should be initiated and supervised by a physician experienced in weight management.

Alternative therapeutic options should be considered in women of childbearing potential. The need for topiramate/phentermine treatment in this population should be reassessed at least annually (see sections 4.3, 4.4 and 4.6).

4.3 Contraindications

- *Medicinal products containing topiramate monocomponent*

[Any existing information concerning pregnancy and women of childbearing potential in section 4.3 should be replaced by the following.]

Prophylaxis of migraine:

- in pregnancy (see sections 4.4 and 4.6).
- in women of childbearing potential not using highly effective contraception (see sections 4.4, 4.5 and 4.6).

Epilepsy:

- in pregnancy, unless there is no suitable alternative treatment (see sections 4.4 and 4.6).
- in women of childbearing potential not using highly effective contraception. The only exception is a woman for whom there is no suitable alternative but who plans a pregnancy and who is fully informed about the risks of taking topiramate during pregnancy (see sections 4.4, 4.5 and 4.6).

- *Medicinal products containing topiramate/phentermine*

[Any existing information concerning pregnancy and women of childbearing potential in section 4.3 should be replaced by the following.]

<Invented name> is contraindicated:

- in pregnancy (see sections 4.4 and 4.6).
- in women of childbearing potential not using highly effective contraception (see sections 4.4, 4.5 and 4.6).

4.4 Special warnings and precautions for use

- *Medicinal products containing topiramate monocomponent*

[Any existing information concerning women of childbearing potential in section 4.4 should be replaced by the following text. Note that any existing study results regarding pregnancy should be removed.]

Pregnancy prevention programme

Topiramate can cause major congenital malformations and foetal growth restriction when administered to a pregnant woman.

Some data suggest an increased risk of neurodevelopmental disorders in children exposed to topiramate in utero, while other data do not suggest such an increased risk (see section 4.6).

Women of childbearing potential

Pregnancy testing should be performed before initiating treatment with topiramate in a woman of childbearing potential.

The patient must be fully informed and understand the risks related to the use of topiramate during pregnancy (see sections 4.3 and 4.6). This includes the need for specialist consultation if the woman is planning a pregnancy to discuss switching to alternative treatments prior to discontinuation of

contraception, and for prompt contact with a specialist if she becomes pregnant or thinks she may be pregnant.

[Text below within angle brackets should be added only for medicinal products with indications in populations below 18 years of age.]

<Female children

Prescribers must ensure that parent(s)/caregiver(s) of female children using topiramate understand the need to contact a specialist once the child experiences menarche. At that time, the patient and parent(s)/caregiver(s) should be provided with comprehensive information about the risks due to topiramate exposure in utero, and the need for using highly effective contraception as soon as relevant. The need for continued topiramate therapy should be reassessed and alternative treatment options should also be considered.>

Educational materials regarding these measures are available for healthcare professionals and patients (or parents/caregivers). The patient guide must be provided to all women of childbearing potential using topiramate and to parents / caregivers of female children. A patient card is provided with the package of <Invented name>.

- *Medicinal products containing topiramate/phentermine*

[Any existing information concerning women of childbearing potential in section 4.4 should be replaced by the following text.]

Pregnancy prevention programme

Topiramate can cause major congenital malformations and foetal growth restriction when administered to a pregnant woman.

Some data suggest an increased risk of neurodevelopmental disorders in children exposed to topiramate in utero, while other data do not suggest such an increased risk (see section 4.6).

Women of childbearing potential

Pregnancy testing should be performed before initiating treatment with topiramate/phentermine in a woman of childbearing potential.

The patient must be fully informed and understand the risks related to the use of topiramate/phentermine during pregnancy (see sections 4.3 and 4.6). This includes the need for specialist consultation if the woman is planning pregnancy to discontinue treatment with topiramate/phentermine and to discuss whether alternative treatment is needed prior to discontinuation of contraception, and for prompt contact with a specialist if she becomes pregnant or thinks she may be pregnant.

Educational materials regarding these measures are available for healthcare professionals and patients. The patient guide must be provided to all women of childbearing potential using topiramate/phentermine. A patient card is provided with the package of <Invented name>.

4.5 Interactions with other medicinal products and other forms of interaction

- *Medicinal products containing topiramate monocomponent*

[Any existing text in section 4.5 regarding contraceptives should be revised to include the following wording. Note that the subheading should read "Systemic hormonal contraceptives" (if the current subheading states "Oral contraceptives" it should be revised).]

Systemic hormonal contraceptives

[…] The clinical significance of the changes observed is not known. The possibility of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking systemic hormonal contraceptive products with <Invented name>. Patients should be asked to report any change in their bleeding patterns. Contraceptive efficacy can be decreased even in the absence of breakthrough bleeding. Women using systemic hormonal contraceptives should be advised to also use a barrier method.

- *Medicinal products containing topiramate/phentermine*

[Any existing text in section 4.5 regarding contraceptives should be replaced by the following wording. Note that the subheading should read "Systemic hormonal contraceptives" (if the current subheading states "Oral contraceptives" it should be revised).]

Systemic hormonal contraceptives

Co-administration of multiple dose of <Invented name> 15 mg/92 mg once daily with a single dose of oral contraceptive containing 35 µg ethinylestradiol (oestrogen component) and 1 mg norethisterone (progestin component), in obese otherwise healthy volunteers, decreased the exposure of ethinylestradiol by 16% and increased the exposure of norethisterone by 22%. The possibility of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking systemic hormonal contraceptive products with <Invented name>. Patients should be asked to report any change in their bleeding patterns. Contraceptive efficacy can be decreased even in the absence of breakthrough bleeding. Women using systemic hormonal contraceptives should be advised to also use a barrier method.

4.6 Fertility, pregnancy and lactation

- *Medicinal products containing topiramate monocomponent*

[Any existing information concerning pregnancy and women of childbearing potential in section 4.6 should be replaced by the following.]

<u>Pregnancy</u>

Risk related to epilepsy and anti-epileptic drugs (AEDs) in general

Specialist advice regarding the potential risks to a foetus caused by both seizures and antiepileptic treatment should be given to women of childbearing potential, and especially to women planning for pregnancy and women who are pregnant. The need for treatment with AEDs should be reviewed when a woman is planning to become pregnant. In women being treated for epilepsy, sudden discontinuation of AED therapy should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the foetus. Monotherapy should be preferred whenever possible because therapy with multiple AEDs could be associated with a higher risk of congenital malformations than monotherapy, depending on the associated antiepileptics.

Risk related to topiramate

Topiramate is teratogenic in mice, rats and rabbits (see section 5.3). In rats, topiramate crosses the placental barrier.

In humans, topiramate crosses the placenta and similar concentrations have been reported in the umbilical cord and maternal blood.

Clinical data from pregnancy registries indicate that infants exposed in utero to topiramate monotherapy have:

Major congenital malformation and foetal growth restriction

- An increased risk of congenital malformations (particularly cleft lip/palate, hypospadias, and anomalies involving various body systems) following exposure during the first trimester. The North American Antiepileptic Drug pregnancy registry data for topiramate monotherapy showed an approximate 3-fold higher prevalence of major congenital malformations (4.3%), compared with a reference group not taking AEDs (1.4%). Data from an observational population-based registry study from the Nordic countries showed a 2 to 3-fold higher prevalence of major congenital malformations (up to 9.5 %), compared with a reference group not taking AEDs (3.0%). In addition, data from other studies indicate that, compared with monotherapy, there is an increased risk of teratogenic effects associated with the use of AEDs in combination therapy. The risk has been reported to be dose dependent; effects were observed in all doses. In women treated with topiramate who have had a child with a congenital malformation, there appears to be an increased risk of malformations in subsequent pregnancies when exposed to topiramate.
- A higher prevalence of low birth weight (<2500 grams) compared with a reference group.
- An increased prevalence of being small for gestational age (SGA; defined as birth weight below the 10th percentile corrected for their gestational age, stratified by sex). In the North American Antiepileptic Drug Pregnancy Registry, the risk of SGA in children of women receiving topiramate was 18 % compared with 5 % in children of women without epilepsy not receiving an AED. The long-term consequences of the SGA findings could not be determined.

Neurodevelopmental disorders

- Data from two observational population-based registry studies undertaken in largely the same dataset from the Nordic countries suggest that there may be a 2 to 3-fold higher prevalence of autism spectrum disorders, intellectual disability or attention deficit hyperactivity disorder (ADHD) in almost 300 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED. A third observational cohort study from the U.S.A did not suggest an increased cumulative incidence of these outcomes by 8 years of age in approximately 1000 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED.

Indication epilepsy

- Topiramate is contraindicated in pregnancy, unless there is no suitable alternative treatment (see sections 4.3 and 4.4).

- The woman must be fully informed of and understand the risks of using topiramate during pregnancy. This includes discussion about the risks of uncontrolled epilepsy to the pregnancy.
- If a woman is planning to become pregnant, efforts should be made to switch to an appropriate alternative treatment before contraception is discontinued.
- If a woman becomes pregnant while taking topiramate, she should promptly be referred to a specialist to reassess topiramate treatment and consider alternative treatment options.
- If topiramate is used during pregnancy, the patient should be referred to a specialist for evaluation and counselling regarding the exposed pregnancy. Careful prenatal monitoring should be performed.

Indication migraine prophylaxis

Topiramate is contraindicated in pregnancy (see sections 4.3 and 4.4).

Women of childbearing potential (all indications)

Topiramate is contraindicated in women of childbearing potential not using highly effective contraception. The only exception is a woman with epilepsy for whom there is no suitable alternative but who plans a pregnancy and who is fully informed about the risks of taking topiramate during pregnancy (see sections 4.4, 4.5 and 4.6).

At least one highly effective method of contraception (such as an intrauterine device) or two complementary forms of contraception including a barrier method should be used (see sections 4.3, 4.4 and 4.5) during treatment and for at least 4 weeks after stopping treatment with <Invented name>.

Alternative therapeutic options should be considered in women of childbearing potential.

Pregnancy testing should be performed before initiating treatment with topiramate in a woman of childbearing potential.

The patient must be fully informed and understand the risks related to the use of topiramate during pregnancy. This includes the need for specialist consultation if the woman is planning for pregnancy, and for prompt contact with a specialist if she becomes pregnant or thinks she may be pregnant and is taking topiramate.

For women with epilepsy, the risks of uncontrolled epilepsy to the pregnancy should also be taken into account (see sections 4.3 and 4.4).

[Text below within angle brackets should be added only for medicinal products with indications in populations below 18 years of age.]

<For female children (see section 4.4).>

- *Medicinal products containing topiramate/phentermine*

[Any existing information concerning pregnancy and women of childbearing potential in section 4.6 should be replaced by the following.]

<u>Pregnancy</u>

<substances / Invented name> is contraindicated in pregnancy (see sections 4.3 and 4.4).

Topiramate is known to be teratogenic in animals (see section 5.3) and humans. In humans, topiramate crosses the placenta and similar concentrations have been reported in the umbilical cord and maternal blood.

Clinical data from pregnancy registries indicate that infants exposed in utero to topiramate monotherapy have:

Major congenital malformation and foetal growth restriction

- An increased risk of congenital malformations (particularly cleft lip/palate, hypospadias, and anomalies involving various body systems) following exposure during the first trimester. The North American Antiepileptic Drug pregnancy registry data for topiramate monotherapy showed an approximate 3-fold higher prevalence of major congenital malformations (4.3%), compared with a reference group not taking AEDs (1.4%). Data from an observational population-based registry study from the Nordic countries showed a 2 to 3-fold higher prevalence of major congenital malformations (up to 9.5 %), compared with a reference group not taking AEDs (3.0%). In women treated with topiramate who have had a child with a congenital malformation, there appears to be an increased risk of malformations in subsequent pregnancies when exposed to topiramate.
- A higher prevalence of low birth weight (<2500 grams) compared with a reference group.
- An increased prevalence of being small for gestational age (SGA; defined as birth weight below the 10th percentile corrected for their gestational age, stratified by sex). In the North American Antiepileptic Drug Pregnancy Registry, the risk of SGA in children of women receiving topiramate was 18 %, compared with 5 % in children of women without epilepsy not receiving an AED. The long-term consequences of the SGA findings could not be determined.

Neurodevelopmental disorders

- Data from two observational population-based registry studies undertaken in largely the same dataset from the Nordic countries suggest that there may be a 2 to 3-fold higher prevalence of autism spectrum disorders, intellectual disability or attention deficit hyperactivity disorder (ADHD) in almost 300 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED. A third observational cohort study from the U.S.A did not suggest an increased cumulative incidence of these outcomes by 8 years of age in approximately 1000 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED.

<u>Women of childbearing potential</u>

Topiramate/phentermine is contraindicated in women of childbearing potential not using highly effective contraception. At least one highly effective method of contraception (such as an intrauterine device) or two complementary forms of contraception including a barrier method should be used (see sections 4.3, 4.4 and 4.5) during treatment and for at least 4 weeks after stopping treatment with <Invented name>.

Alternative therapeutic options should be considered in women of childbearing potential.

Pregnancy testing should be performed before initiating treatment with topiramate/phentermine in a woman of childbearing potential.

The patient must be fully informed and understand the risks related to the use of topiramate/phentermine during pregnancy. This includes the need for specialist consultation if the woman is planning pregnancy, and for prompt contact with a specialist if she becomes pregnant or thinks she may be pregnant and is taking topiramate/phentermine.

LABELLING

[The following wording for labelling is applicable for all medicinal products.]

Outer packaging

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

7. OTHER SPECIAL WARNING(S), IF NECESSARY

[This section should include the following wording.]

Warning for women who are able to become pregnant:

This medicine can seriously harm an unborn child. Always use highly effective contraception during your treatment.

If you become pregnant, talk to your doctor straight away.

[*Text below to be included only for medicinal products with indication epilepsy.]*

<If you have epilepsy, do not stop taking this medicine unless your doctor tells you to.>

Patient card

[The proposed new text should be included at the very end of the labelling text document, on a new page. The patient card should be placed inside or affixed to one side of the outer packaging without covering any information.]

Patient card for <Invented name> – For women and girls who are able to become pregnant

Contraception and Pregnancy Prevention

What you must know

- <Invented name> is a medicine for {add relevant indication}.
- <Invented name>can seriously harm an unborn child if taken during pregnancy.

What you must do

- Read the package leaflet and Patient guide carefully before use.

- Use highly effective contraception during your treatment with topiramate and for at least 4 weeks after the last topiramate dose. Your doctor will advise you on the most suitable method for you.
- Visit your doctor to review your treatment at least once a year.
- If you think you have become pregnant, talk to your doctor straight away.
- If you are thinking about having a child, do not stop using contraception before you have talked to your doctor.

[Text below within angle brackets to be included only for medicinal products with indication epilepsy.]

- <If you have epilepsy, do not stop using topiramate unless your doctor tells you to, as your condition may become worse.>

[Inclusion of a Quick Response (QR)-code is to be decided nationally (see text below within angle brackets).]

Ask your doctor to give you the Patient Guide<.><or scan this QR-code for it.

{QR code to be included + URL}>

Keep this card.

PACKAGE LEAFLET

- *Medicinal products containing topiramate monocomponent*

[The following wording should be added in the beginning of PL in line with the QRD template, directly following the text "(Invented) name strength pharmaceutical form, active substance(s)".]

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

2. What you need to know before you take <Invented name>

- *Medicinal products containing topiramate monocomponent*

Do not take <Invented name>

[Any existing information concerning pregnancy and women of childbearing potential in the section "Do not take <Invented name>" should be replaced by the following.]

Migraine prevention

- You must not use <Invented name> if you are pregnant.

- If you are a woman who is able to become pregnant, you must not take <Invented name>, unless you use highly effective contraception (birth control) during your treatment. See below under "Pregnancy, breast-feeding and fertility – Important advice for women".

Treatment of epilepsy

- You must not use <Invented name> if you are pregnant, unless no other treatment gives sufficient seizure control for you.
- If you are a woman who is able to become pregnant, you must not take <Invented name> unless you use highly effective contraception (birth control) during your treatment. The only exception is if <Invented name> is the only treatment giving you sufficient seizure control and you are planning to become pregnant. You must speak to your doctor to make sure you have received information about the risks of taking <Invented name> during pregnancy and the risks of seizures during pregnancy. See below under "Pregnancy, breast-feeding and fertility – Important advice for women".

[Inclusion of a QR-code is to be decided nationally (see text below within angle brackets).]

Make sure you read the patient guide that you will receive from your doctor<.><or scan the QR-code for it (see section 6 'Other sources of information')>.

A patient card is provided with the <Invented name> package to remind you of the risks in pregnancy.

[…]

Warnings and precautions

Talk to your doctor before taking <Invented name> if you:

[Any existing information concerning pregnancy and women of childbearing potential in the section "Warnings and precautions" should be replaced by the following text. Any existing information similar to the last two sentences below ("If you are not sure…" and "If you have epilepsy…") should also be revised.]

- are a woman who is able to become pregnant. <Invented name> can harm an unborn child when taken during pregnancy. Highly effective contraception (birth control) must be used during your treatment and for at least 4 weeks after the last <Invented name> dose. See section 'pregnancy and breastfeeding' for further information.
- are pregnant. <Invented name> can harm an unborn child when taken during pregnancy.

If you are not sure if any of the above apply to you, talk to your doctor before using <Invented name>.

If you have epilepsy, it is important that you do not stop taking your medicine without first consulting your doctor.

Other medicines and <Invented name>

Especially, tell your doctor or pharmacist if you are taking:

[Any existing text in the section "Other medicines and <Invented name>" regarding contraceptives (e.g. birth control pills) should be replaced by the following text.]

- hormonal contraceptives. <Invented name> may make hormonal contraceptives less effective. An additional barrier method of contraception such as a condom or pessary/diaphragm should be used. You should talk to your doctor about the best kind of contraception to use while you are taking <Invented name>.

Tell your doctor if your menstrual bleeding changes while you are taking hormonal contraceptives and <Invented name>. Irregular bleeding may occur. In this case, continue taking the hormonal contraceptives and inform your doctor.

Pregnancy <,><and> breast-feeding <and fertility>

[Any existing information concerning pregnancy and women of childbearing potential in the section "Pregnancy, breast-feeding <and fertility>" should be replaced by the following.]

Important advice for women who are able to become pregnant

<Invented name> can harm an unborn child. If you are a woman who is able to become pregnant, talk to your doctor about other possible treatments. Visit your doctor to review your treatment and discuss the risks at least once a year.

Migraine prevention

- For migraine, you must not use <Invented name> if you are pregnant.
- For migraine, you must not use <Invented name> if you are a woman who is able to become pregnant unless you are using highly effective contraception.
- Before the start of treatment with <Invented name> a pregnancy test should be performed in a woman who is able to become pregnant.

Treatment of epilepsy

- For epilepsy, you must not use <Invented name> if you are pregnant, unless no other treatment gives sufficient seizure control for you.
- For epilepsy, you must not use <Invented name> if you are a woman who is able to become pregnant unless you are using highly effective contraception. The only exception is if <invented name> is the only treatment giving you sufficient seizure control, and you are planning to become pregnant. You must speak to your doctor to make sure you have received information about the risks of taking <Invented name> during pregnancy and about the risks of seizures during pregnancy, which may put you or your unborn child at risk.
- Before the start of treatment with <Invented name> a pregnancy test should be performed in a woman who is able to become pregnant.

The risks of topiramate when taken during pregnancy (irrespective of the disease for which topiramate is used):

There is a risk of harm to the unborn child if <Invented name> is used during pregnancy.

- If you take <Invented name> during pregnancy, your child has a higher risk for birth defects. In women who take topiramate, around 4 - 9 children in every 100 will have birth defects. This

compares to 1-3 children in every 100 born to women who do not have epilepsy and do not take an antiepileptic treatment. Particularly, cleft lip (split in the top lip) and cleft palate (split in the roof of the mouth) have been observed. Newborn boys may also have a malformation of the penis (hypospadia). These defects can develop early in pregnancy, even before you know you are pregnant.

- If you take <Invented name> during pregnancy, your child may have a 2- to 3-fold higher risk for autism spectrum disorders, intellectual disabilities, or attention deficit hyperactivity disorder (ADHD) compared with children born to women with epilepsy not taking antiepileptic medication.
- If you take <Invented name> during pregnancy, your child may be smaller and weigh less than expected at birth. In one study, 18 % of children of mothers taking topiramate during pregnancy were smaller and weighed less than expected at birth, while 5 % of children born to women without epilepsy and not taking antiepileptic medication were smaller and weighted less than expected at birth.
- Talk to your doctor if you have questions about this risk during pregnancy.
- There may be other medicines to treat your condition that have a lower risk of birth defects.

Need for contraception in women who are able to become pregnant:

- If you are a woman who is able to become pregnant, talk to your doctor about other possible treatments instead of <Invented name>. If the decision is made to use <Invented name>, you must use highly effective contraception during your treatment and for at least 4 weeks after the last <Invented name> dose.
- One highly effective contraception (such as an intrauterine device) or two complementary contraceptives such as birth control pill together with a barrier method of birth control (such as a condom or pessary/diaphragm) must be used. Talk to your doctor about what contraception is most appropriate for you.
- If you are taking hormonal contraceptives, there is the possibility of reduced effectiveness of the hormonal contraceptive due to topiramate. Therefore, an additional barrier contraceptive method (such as a condom or pessary/diaphragm) should be used.
- Tell your doctor if you experience irregular menstrual bleeding.

[Text below within angle brackets should be added only for medicinal products with indications in populations below 18 years of age.]

<Use of <Invented name> in girls:

If you are a parent or a caregiver of a girl treated with <Invented name>, you must contact her doctor immediately once your child experiences her first period (menarche). The doctor will inform you about the risks to an unborn child due to topiramate exposure during pregnancy, and the need for using highly effective contraception.>

If you wish to become pregnant while taking <Invented name>:

- Schedule an appointment with your doctor.

- Do not stop using your contraception until you have discussed this with your doctor.
- If you take <Invented name> for epilepsy, do not stop taking it until you have discussed this with your doctor because your illness may become worse.
- Your doctor will reassess your treatment and evaluate alternative treatment options. The doctor will counsel you about the risks of <Invented name> during pregnancy. He/she may also refer you to another specialist.

If you have become pregnant or think you may be pregnant while taking <Invented name>:

- Schedule an urgent appointment with your doctor.
- If you are taking <Invented name> to prevent migraine, stop taking the medicine straight away, and contact your doctor to evaluate if you need alternative treatment.
- If you are taking <Invented name> for epilepsy, do not stop taking this medicine until you have discussed this with your doctor, as this may worsen your illness. Worsening of your epilepsy may put you or your unborn child at risk.
- Your doctor will reassess your treatment and evaluate alternative treatment options. The doctor will counsel you about the risks of <Invented name> during pregnancy. He/she may also refer you to another specialist.
- If <Invented name> is used during pregnancy, you will be monitored closely to check how your unborn child is developing.

[Inclusion of a QR-code is to be decided nationally (see text below within angle brackets).]

Make sure you read the patient guide that you will receive from your doctor. <The patient guide is also available by scanning a QR code, see section 6 'Other sources of information'.> A patient card is provided with the <Invented name> package to remind you of topiramate risks in pregnancy.

- *Medicinal products containing topiramate/phentermine*

Do not take <Invented name> if you are:

[Any existing information concerning pregnancy and women of childbearing potential in the section "Do not take <Invented name>" should be replaced by the following.]

- pregnant, or a woman who is able to become pregnant unless you are using highly effective contraception (see section 'Pregnancy and breastfeeding' for further information). You should talk to your doctor about the best kind of contraception to use while you are taking <Invented name>.

[Inclusion of a QR-code is to be decided nationally (see text below within angle brackets).]

Make sure you read the patient guide that you will receive from your doctor<.><or scan the QR-code for it (see section 6 'Other sources of information').>

A patient card is provided with the <Invented name> package to remind you of the risks in pregnancy.

Warnings and precautions

Talk to your doctor before or during taking <Invented name> if you are:

[Any existing information concerning pregnancy and women of childbearing potential in the section "Warnings and precautions" should be replaced by the following text.]

- a woman who is able to become pregnant. <Invented name> can harm an unborn child when taken during pregnancy. Highly effective contraception (birth control) must be used during your treatment and for at least 4 weeks after the last <Invented name> dose. See section 'pregnancy and breastfeeding' for further information.
- pregnant: <Invented name> can harm an unborn child when taken during pregnancy.

Other medicines and <Invented name>

Please also tell your doctor or pharmacist if you are taking:

[Any existing text in the section "Other medicines and <Invented name>" regarding contraceptives (e.g. birth control pills) should be replaced by the following text.]

- hormonal contraceptives. The possibility of decreased contraceptive efficacy and irregular bleeding may occur when additionally taking <Invented name> with hormonal contraceptives. Contraceptive efficacy can be reduced even in the absence of bleeding. An additional barrier method of contraception such as a condom or a pessary/diaphragm should be used. You should talk to your doctor about the best kind of contraception to use while you are taking <Invented name>.

Irregular bleeding may occur. In this case, continue taking the hormonal contraceptives and inform your doctor.

Pregnancy<,><and> breast-feeding <and fertility>

[Any existing information concerning pregnancy and women of childbearing potential in the section "Pregnancy, breast-feeding <and fertility>" should be replaced by the following.]

<u>Important advice for women who are able to become pregnant</u>

If you are a woman who is able to become pregnant, talk to your doctor about other possible treatments. Visit your doctor to review your treatment and discuss the risks at least once a year.

Do not take this medicine if you are pregnant.

You must not use this medicine if you are a woman who is able to become pregnant unless you are using highly effective contraception.

Pregnancy testing should be performed before starting treatment with <Invented name> in a woman who is able to become pregnant.

The risks of topiramate (one of the active substances of <Invented name>, also used to treat epilepsy) when taken during pregnancy:

- Topiramate can harm and reduce growth of the foetus when taken during pregnancy. Your child has a higher risk for birth defects. In women who take topiramate, around 4 - 9 children in every 100 will have birth defects. This compares to 1-3 children in every 100 born to women who do not have epilepsy and do not take an antiepileptic treatment. Particularly, cleft lip (split in the top lip) and cleft palate (split in the roof of the mouth) have been observed. Newborn

boys may also have a malformation of the penis (hypospadia). These defects can develop early in pregnancy, even before you know you are pregnant.

- If you take <Invented name> during pregnancy, your child may have a 2- to 3-fold higher risk for autism spectrum disorders, intellectual disabilities, or developing attention deficit hyperactivity disorder (ADHD) compared with children born to women with epilepsy not taking antiepileptic medication.
- If you take <Invented name> during pregnancy, your child may be smaller and weigh less than expected at birth. In one study, 18 % of children of mothers taking topiramate during pregnancy were smaller and weighed less than expected at birth, while 5 % of children born to women without epilepsy and not taking antiepileptic medication were smaller and weighted less than expected at birth.

Need for contraception in women who are able to become pregnant:

- If you are a woman who is able to become pregnant, you should talk to your doctor about other possible treatments instead of <Invented name>. If the decision is made to use <Invented name>, you must use highly effective contraception during your treatment and for at least 4 weeks after the last <Invented name> dose.
- One highly effective contraception (such as an intrauterine device) or two complementary contraceptives such as birth control pill together with a barrier method of birth control (such as a condom or pessary/diaphragm) must be used. Talk to your doctor about what contraception that is most appropriate for you.
- If you are taking hormonal contraceptives, there is the possibility of reduced effectiveness of the hormonal contraceptive due to topiramate. Therefore, an additional barrier contraceptive method should be used. Tell your doctor if you experience irregular bleeding.
- Stop taking <Invented name> immediately and tell your doctor if you miss a menstrual period or suspect you are pregnant.

If you wish to become pregnant while taking <Invented name>:

- Schedule an appointment with your doctor.
- Do not stop using your contraception until you have discussed this with your doctor.

If you have become pregnant or think you may be pregnant while taking <Invented name>:

- Schedule an urgent appointment with your doctor.
- Stop taking <Invented name> immediately and tell your doctor.
- The doctor will counsel you about the risks of <Invented name> during pregnancy.

[Inclusion of a QR-code is to be decided nationally (see text below within angle brackets).]

Make sure you read the patient guide that you will receive from your doctor. <The patient guide is also available by scanning a QR code, see section 6 'Other sources of information'.>

A patient card is provided with the <Invented name> package to remind you of topiramate risks in pregnancy.

3. How to take <Invented name>

- *Medicinal products containing topiramate monocomponent*

[The following wording should be added to section 3 directly following "Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.". Wording within angle brackets is applicable depending on if the medicinal product is indicated in populations below 18 years of age and adults, or if the medicinal product is indicated only for adults.]

<Girls and women><Women> who are able to become pregnant:

<Invented name> treatment should be started and supervised by a doctor experienced in the treatment of epilepsy or migraine. Visit your doctor to review your treatment at least once a year.

- *Medicinal products containing topiramate/phentermine*

[The following wording should be added to section 3 directly following "Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.".]

<Invented name> treatment should be started and supervised by a doctor experienced in the treatment of weight management. Women who are able to become pregnant should visit their doctor to review their treatment at least once a year.

6. Contents of the pack and other information

[The following wording is applicable for all medicinal products.]

Other sources of information

[Inclusion of a QR-code is to be decided nationally (see text below within angle brackets).]

<Latest approved information {add type of information, e.g. product information, educational material} on this medicine is available by scanning the following QR code with a smartphone. The same information is also available on the following website (URL):

{URL to be included}>