DECISION

No. 21/27.11.2009

on approval of the change of the wording of the package leaflet, summary of product characteristics and labelling information for medicinal products authorised for marketing in Romania, approved by Scientific Council Decision No. 3/27.01.2006

The Scientific Council of the National Medicines Agency, set up based on Order of the Minister of Health No. 1027/22.05.2008, reunited on summons of the National Medicines Agency President in the ordinary meeting of 27.11.2009, in accordance with Article 10 of Government Ordinance No. 125/1998 related to the set up, organisation and operation of the National Medicines Agency, approved as amended through Law No. 594/2002, as amended, agrees on the following

DECISION

Art. 1. – The change of the wording of the package leaflet, summary of product characteristics and labelling information for medicinal products authorised for marketing in Romania is approved, authorised in accordance with Annexes 1-3, which are integral part of this Decision.

Art. 2. – This Decision is approved through Order of the Minister of Health and is to be published in the Official Gazette of Romania, Part I.

Art. 3. – On the date of this Decision coming into force, Annexes 1-3 to NMA Scientific Council Decision No. 3/27.01.2006, approved through Order of the Minister of Public Health No. 400/2006, are amended and replaced with Annexes 1-3 which are integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Medicines Agency,

Acad. Prof. Dr. Victor Voicu

ANNEX 1
(Annex I to Order No. 400/2006)

Statements for use under 4.6 Pregnancy and lactation, of the Summary of Product Characterisitcs (SPC)

Related to "Pregnancy"

[1] <Based on experience in humans *[please specify]*, {active substance} determines <congenital malformations *[please specify]* in case of administration during pregnancy.> *[or]* <harming pharmacological effects during pregnancy and in fetus/newborn.>

{Invented name} is contraindicated <during><the first quarter of pregnancy> *[this case represents a strict contraindication]* (see section 4.3).

<Women of childbearing potential should use efficient contraceptive measures <during <and up to {number of} weeks following> the treatment.>>

[2] <According to the studies conducted on humans *[please state]*, <the {active substance} may be suspected for determining congenital malformations *[please state]* in case of administration during pregnancy.>

A. <Studies on animals have placed the emphasis on the toxic effects upon the reproductive function (see section 5.3).>

[or]

B. <Studies on animals are insufficient in view of emphasizing the toxic effects upon the reproductive function (see section 5.3).>

{Invented name} should not be used <during pregnancy> <<{quarter of} pregnancy>, except for the case in which the clinical condition of the respective woman imposes a treatment based on {active substance}.

<Women of childbearing potential should use efficient contraceptive measures <during <and up to {number of} weeks following> the treatment.>>

[3] <According to studies conducted on humans *[please state]*, <the {active substance} may be suspected for determining congenital malformations *[please state]* in case of administration during pregnancy.>

Studies on animals have not revealed harmful direct or indirect toxic effects upon the reproductive fiunction (see section 5.3).

{Invented name} should not be used <during pregnancy> <<{quarter of} pregnancy>, except for the case in which the clinical condition of the respective woman imposes a treatment based on {active substance}.

<Women of childbearing potential should use efficient contraceptive measures <during <and up to {number of} weeks following> the treatment.>>

[4] <Data issued from the use of {active substance} in pregnant women are inexistent or limited.

A. <Studies on animals have revealed toxic effects upon the reproductive

function (see section 5.3).>

[or]

B. <Studies on animals are insufficient for highlighting the toxic effects upon the reproductive function (see section 5.3).>

{Invented name} is not recommended for use <during pregnancy><<during the {quarter} of pregnancy> in women of childbearing potential who do not use contraceptive measures.>

[5] <Data issued from the use of {active substance} in pregnant women are inexistent or limited (less than 300 results obtained from pregnancies).

Studies in animals have not highlighted the direct/indirect harmful toxic effects upon the reproductive function (see section 5.3).

As a precautionary measure, it is best to avoid the use of {Invented name} <during pregnancy><during the {quarter} of pregnancy>.>

[6] <In accordance with a moderate amount of data (namely between 300 and 1.000 results pooled from pregnancies) concerning pregnant women, concerning pregnant women, no adverse or toxic effects of {active substance} have been indicated on the health of the foetus/newborn children.

A <Studies on animals have revealed toxic effects upon the reproductive function (see section 5.3).>

[or]

B. <Studies on animals are insufficient for highlighting the toxic effects upon the reproductive function (see section 5.3).>

As a precautionary measure, it is best to avoid the use of {Invented name} <during pregnancy><during the {quarter} of pregnancy>.>

[7] <In accordance with a moderate amount of data (namely between 300 and 1.000 results pooled from pregnancies) concerning pregnant women, no adverse or toxic effects of {active substance} have been indicated on the health of the foetus/newborn children.

<Studies on animals have revealed toxic effects upon the reproductive function (see section 5.3).>

The use of {Invented name} <during pregnancy><during the {quarter} of pregnancy> may be considered, if deemed necessary.

[8] <In accordance with the elevated amount of data concerning pregnant women (more than 1000 results per pregnancy), no harmful/toxic effects of {active substance} with respect to embryonal/foetal development have been detected.

{Invented name} may be used <during pregnancy><during the {quarter} of pregnancy>, if clinically relevant.

[9] < The occurrence of adverse reactions during pregnancy is not foreseen, since the systemic exposure to {active substance} is negligible.>

{Invented name} may be used during pregnancy. *[E.g. medicinal products proven to display a negligible systemic exposure/pharmacodynamic systemic action throughout clinical trials.]*

Concerning „Breastfeeding”

[1] <{Active substance}/its metabolites are secreted into human blood indicated effects on newborn children/sucklings breastfed by the women undergoing treatment.>

[or]

<{Active substance}/its metabolites has/have been identificated in newborn children/sucklings breastfed by the women undergoing treatment. <The effect of {active substance} upon newborn children/sucklings is unknown.> *[or]* <There is insufficient information about the effects of {active substance} upon newborn children/sucklings.>>

[or]

<{Active substance}/its metabolites are secreted into human blood in such amount that the occurrence of undesirable effects on newborn children/breastfed children is likely to occurr.>

<{Invented name} <is contra-indicated during breastfeeding (see section 4.3)> *[or]* <should not be used during breastfeeding>.>

[or]

<Breastfeeding should be discontinued during treatment with {Invented name}.>

[or]

<The decision of breastfeeding discontinuation should be taken, or the decision to discontinuate/abstain from the treatment with {Invented name}, considering the benefit of breastfeeding for the child and the benefit of the treatment for the respective woman.>

[2] <It is unknown whether {active substance}/its metabolites are secreted into human blood.>

[or]

<There is insufficient information concerning the secretion of {active substance}/its metabolites in human milk.>

[or]

<There is insufficient information concerning the secretion of {active substance}/its metabolites in animal milk.>

[or]

<Pharmacodynamic/toxicological data in animals have highlighted the secretion of {active substance}/its metabolites in milk (for further details, see section 5.3).>

[or]

<Physico-chemical data suggest the secretion of {active substance}/its metabolites in human milk.>

A risk for newborn children/sucklings cannot be disregarded.

<{Invented name} <is contraindicated during breastfeeding (see section 4.3)> *[or]* <should not be used during breastfeeding>.>

[or]

<Breastfeeding should be discontinued during treatment with {Invented name}.>

[or]

<The decision of breastfeeding discontinuation should be taken, or the decision to discontinuate/abstain from the treatment with {Invented name}, considering the benefit of breastfeeding for the child and the benefit of the treatment for the respective woman.>

[3] No undesirbale effects of {active substance} on newborn children/sucklings breastfed by women undergoing treatment have been signaled.

[or]

<The occurrence of undesirable effects in breastfed newborn children/sucklings is not foreseen, since the systemic exposure to {active substance} of breastfeeding women is negligible.>

[or]

<{Active substance}/metabolites has/have not been identified in the plasma of newborn children/sucklings breastfed by women undergoing treatment.>

[or]<{Active substance}/its metabolites are not secreted in human milk.>*[or]*<{Active substance}/its metabolites are secreted in human milk, but the occurrence of undesirable effects in breastfed newborn children/sucklings is not foreseen for therapeutic doses of {Invented name}.>

{Invented name} may be used during breastfeeding.

ANNEX 2
(Annex II to Order No. 400/2006)

MedDRA terminology to be used under Section 4.8 Undesirable effects, of the Summary of Product Characteristics (SPC)

ANNEX 3
(Annex III to Order No. 400/2006)

Terms to be used under section 6.4 – Special precautions for storage from the Summary of Product Characteristics (SmPC), 9 – Special storage conditions from the Information on labelling and 5 – How to store X from the leaflet

The Summary of Product Characteristics

6.4 **Special precautions for storage**

<Do not store above <25°C> <30°C>> or
<Store below <25°C> <30°C>>
<Refrigerate (2°C – 8°C)>
<Store in the fridge and refrigerate during shipping (2°C – 8°C)>*
<Freeze {temperature range}>
<Store and transport refrigerated {temperature range}>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <packaging> >>****
<Store the {primary packaging} *** thoroughly sealed>****
<Store the {primary packaging} *** in a box>****
<This medicinal product does not require special storage conditions.>
<This medicinal product does not require special storage temperatures.>*****

<to be protected from <light> <humidity>>

A. **Labelling**

9. Special storage conditions

<Do not store above <25°C> <30°C>> or
<Store below <25°C> <30°C>>
<Refrigerate>
<Store and transport refrigerated>*
<Store in the freezer>
<Store in the freezer and freeze during shipping>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <packaging> >>****
<Store the {primary packaging}*** thoroughly sealed>****
<Store the {primary packaging}*** in a box>****

<to be protected from <light> <humidity>>

B. **Leaflet**

5. **How to store X**

Keep out of the reach and sight of children.

<Do not store at temperatures over <25°C> <30°C>> or
<Store at temperatures below <25°C> <30°C>>
<Refrigerate (2°C – 8°C)
<Store and transport refrigerated (2°C – 8°C)>*
<Freeze{temperature range}>
<Store and transport frozen {temperature range}>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <packaging> >>****
<Store the {primary packaging}*** in a box>****
<Keep the {primary packaging} *** tightly sealed>****
<This medicinal product does not require any special storage conditions.>*****
<in order to protect from <light> <humidity>>
Do not use after the expiry date imprinted on the <packaging> <box> <vial> <...>
<Do not use X if you notice {description of visible signs of deterioration}.>

---

* The stability data generated at 25°C/60%RH (acc) should be taken into account when deciding whether or not transport under refrigeration is necessary. The statement should only be used in exceptional cases.

** This specification should be used only when absolutely necessary.

*** Only the name of the primary packaging should be used (e.g. vial, blister etc.)

**** Please specify whether the medicinal product is sensitive to light and/or humidity

***** Depending on the pharmaceutical form and on the properties of the medicinal product, there is a deterioration risk due to physical modifications, in case the medicinal products is submitted to low temperatures. Moreover, low temperatures may have an impact on the packaging, in certain cases. An additional specification may be necessary in order to consider this possibility.