MINISTRY OF HEALTH

ORDER

on approval of Statements for use in the wording of package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing in Romania

Taking into account provisions of Government Ordinance No. 152/1999 on medicinal products for human use, approved with changes and completions through Law No. 336/2002, with further changes and completions and of Government Ordinance No. 125/1998 1998 related to the set up, organisation and functioning of the National Medicines Agency, approved with changes and completions through Law No. 594/2002, with further changes and completions,

on seeing The Approval Report of the General Pharmaceutical and Medical Devices Directorate No. E.N. 9.276/2006,

based on Government Decision No. 168/2005 on organisation and functioning of the Ministry of Health, with further changes and completions,

the minister of health hereby issues the following order:

Article 1. – Approval of Statements for use in the wording package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing in Romania, according to Annexes I–IV which are integral part of this order.

Article 2. – Provisions of this order apply to applications for marketing authorisation submitted to the National Medicines Agency following this order entry into force.

Article 3. – The National Medicines Agency shall carry out provisions of the present order.

Article 4. – The present order is to be published in the Official Gazette of Romania, Part I.

Minister of health,
Gheorghe Eugen Nicolăescu

Bucharest, 12 April 2006.
No. 400.

ANNEX I

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

[1] <{Active substance} <causes> <is suspected to cause> serious birth defects when administered during pregnancy.
{Trade name} is contraindicated (see 4.3) in pregnancy *[only in case of a strict contraindication]*.>
[and if necessary] < Women of childbearing potential have to use effective contraception during (and up to {number} weeks after) treatment.>>

[2] <{Active substance} has harmful pharmacological effects on pregnancy and/or the foetus/new–born child.>
<{Trade name} should not be used during pregnancy unless clearly necessary > *[These circumstances should be specified]*

[3] < There are no adequate data from the use of {Active substance} in pregnant women.>
< Studies in animals have shown reproductive toxicity (see 5.3). The potential risk for humans is unknown.>
[or]
< Animal studies are insufficient with respect to effects on pregnancy /and–or/ embryonal/foetal development/and–or/parturition/and–or/postnatal development (see 5.3). The potential risk for humans is unknown.>

<{Trade name} should not be used during pregnancy unless clearly necessary > *[These circumstances should be specified where possible]*.>

[4] < For {Active substance} no clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy**,** embryonal/foetal development, parturition or postnatal development (see 5.3).
Caution should be exercised when prescribing to pregnant women.>
[5] < Data on a limited number {number} of exposed pregnancies indicate no adverse effects of {Active substance} on pregnancy or on the health of the foetus/new–born child. To date, no other relevant epidemiological data are available. Animal studies have shown reproductive toxicity (see 5.3). The potential risk for humans is unknown.>
[or]
< Animal studies are insufficient with respect to effects on pregnancy/and–or/embryonal/foetal development/and–or/parturition/and–or/postnatal development (see 5.3). The potential risk for humans is unknown.
Caution should be exercised when prescribing to pregnant women.>

[6] < Data on a limited number {number} of exposed pregnancies indicate no adverse effects of {Active substance} on pregnancy or on the health of the foetus/new–born child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see 5.3).
Caution should be exercised when prescribing to pregnant women.>

[7] < The use of {Active substance} within a high {number} of tasks indicates no adverse effects of {Active substance} on pregnancy or on the health of the foetus/new-born child. To date, no other relevant epidemiological data are available.
Caution should be exercised when prescribing to pregnant women.>

[8] < Well–conducted epidemiological studies indicate no adverse effects of {Active substance} on pregnancy or on the health of the foetus/new–born child.
{Trade name} can be used during pregnancy.>

[The subsequent two statements to be included as appropriate.]
[9] [In case of interaction with oral contraceptives information should also be given 4.5]
<<{Active substance} adversely interacts with oral contraceptives. Therefore, an alternative, effective and safe method of contraception should be used during (and up to x weeks after) treatment.
[or]
< The concomitant medication {Active substance} adversely interacts with oral contraceptives. Therefore an alternative, effective and safe method of contraception should be used during (and up to {number} weeks after) treatment.>>
[10] [In case of male–mediated effects on pregnancy outcome information should also be given in 4.4]
< Both sexually active men and women should use effective methods of contraception during (and up to {number} weeks after) treatment.

ANNEX II

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

	[MedDRA frequency convention]
001	<Very common (≥1/10)>
002	<Common (≥1/100 to <1/10)>
003	<Uncommon (≥1/1,000 to <1/100)>
004	<Rare (≥1/10,000 to <1/1,000)>
005	<Very rare (<1/10,000), not known (cannot be estimated from the available data)>
	[MedDRA– system organ class database]
006	Investigations
007	Cardiac disorders
008	Congenital, familial and genetic disorders
009	Blood and lymphatic system disorders
010	Nervous system disorders
011	Eye disorders
012	Ear and labyrinth disorders
013	Respiratory, thoracic and mediastinal disorders
014	Gastrointestinal disorders
015	Renal and urinary disorders
016	Skin and subcutaneous tissue disorders
017	Musculoskeletal and connective tissue disorders
018	Endocrine disorders
019	Metabolism and nutrition disorders
020	Infections and infestations
021	Injury, poisoning and procedural complications
022	Neoplasms benign, malignant and unspecified (incl cysts and polyps)
023	Surgical and medical procedures
024	Vascular disorders
025	General disorders and administration site conditions
026	Pregnancy, puerperium and perinatal conditions
027	Social circumstances
028	Immune system disorders
029	Hepatobiliary disorders
030	Reproductive system and breast disorders
031	Psychiatric disorders

ANNEX III

Statements for use under:
6.4 Special precautions for storage, of the Summary of Product Characteristics (SPC),
9. Special storage conditions, of Labelling,
5. How to store *X*, *of* the Package Leaflet

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>>
<Store in a refrigerator (2°C – 8°C)>
<Store and transport refrigerated (2°C – 8°C)>*
<Store in a freezer {temperature range}>
<Store and transport frozen {temperature range}>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <package>>
<Keep the {container} *** tightly closed>
<Keep the {container} *** in the outer carton>
<This medicinal product does not require any special storage conditions>

<in order to protect from <light> <moisture>>

LABELLING

9. SPECIAL STORAGE CONDITIONS

<Do not store above <25°C> <30°C>> or
<Store below <25°C> <30°C>>
<Store in a refrigerator>
<Store and transport refrigerated>*
<Store in a freezer>
<Store and transport frozen>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <package>>
<Keep the {container} *** tightly closed>
<Keep the {container} *** in the outer carton>

<in order to protect from <light> <moisture>>

PACKAGE LEAFLET

5. How to store *X*

Keep out of the reach and sight of children.

<Do not store above <25°C> <30°C>> or
<Store below <25°C> <30°C>>
<Store in a refrigerator (2°C – 8°C)
<Store and transport refrigerated (2°C – 8°C)>*
<Store in a freezer {temperature range}>
<Store and transport frozen {temperature range}>**
<Do not <refrigerate> <or> <freeze>>
<Store in the original <package>>
<Keep the {container} *** in the outer carton>
<Keep the {container} *** tightly closed>
<This medicinal product does not require any special storage conditions>

<in order to protect from <light> <moisture>>

Do not use X after the expiry date which is stated on the <label> <carton> <bottle> <...>

<Do not use X if you notice {description of the visible signs of deterioration}.>

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* 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.

** The statement should be used only when critical.
*** The actual name of the container should be used (e.g. bottle, blister etc.)

ANNEX IV

Terms for batch number & expiry date to be used on outer and/or inner labelling

Full terms batch number	**Batch** **Lot**
Full terms on expiry date	**Expiry date** **EXP**