Ordinance on the placing on the market of unauthorised medicinal products for compassionate use

(Ordinance on Medicinal Products for Compassionate Use – *AMHV*)

14th July 2010

On the basis of Section 80, sentence 1, number 3a, in conjunction with sentences 3 and 4 and in conjunction with Section 83 of the Law on Medicinal Products, Section 83 of which was last amended by Article 1, number 70 of the Act of 17th July 2009 (Federal Law Gazette I, p. 1990), the Federal Ministry of Health hereby enacts as follows:

Section 1

Scope

(1) The present ordinance regulates the procedure for the placing on the market of unauthorised medicinal products for compassionate use under the conditions contained in Section 21, sub-section 2, number 6 of the Law on Medicinal Products in conjunction with Article 83 of Regulation (EC) No. 726/2004 of the European Parliament and the Council of 31st March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJL L 136, 30/4/2004, p. 1). The Ordinance shall apply to finished medicinal products intended for use in or on human beings and which are not authorised, either within the territorial scope of the Law on Medicinal Products, in another Member State of the European Union or in another State Party to the Agreement on the European Economic Area, but are subject to the obligation to obtain an authorisation pursuant to Article 3 (1) and (2) of Regulation (EC) No. 726/2004 or the obligation to obtain a marketing authorisation pursuant to Section 21, sub-section 1 of the Law on Medicinal Products.

(2) The present Ordinance shall not be utilised for the individual use of an unauthorised medicinal product by a single patient or by a patient under the direct supervision of a doctor.

Section 2

Definition of terms

(1) A compassionate use programme is a programme according to Regulation (EC) No. 726/2004. Within the framework of a compassionate use programme, unauthorised medicinal products may be placed at the disposal of a specific patient group if sufficient indications of the efficacy and safety of the medicinal product exist and if a clinical trial is being conducted on it or an application for a marketing authorisation has been submitted to the European Medicines Agency, the competent higher federal authority or an authority responsible for granting the marketing authorisation in a Member State.

(2) A case for compassionate use, within the meaning of the present Ordinance is said to exist when a group of patients who are suffering from a disease, which would lead to serious disability or is life-threatening cannot be satisfactorily treated with a medicinal product which is authorised for placing on the market within the territorial scope of the Law on Medicinal Products.

Section 3

Notification of the compassionate use programme

(1) A person who assumes responsibility for the commissioning, organisation and financing of a compassionate use programme (responsible person) shall be responsible for notifying the competent higher federal authority of the compassionate use programme. If the responsible person does not have his/her registered place of business in a Member State of the European Union, or in another State Party to the Agreement of the European Economic Area, he/she shall name a representative registered in the European Union or in another State Party to the Agreement of the European Economic Area.

(2) For notification purposes, the following information and documents shall be required:

1. name or firm and address of the responsible person and, where available, that of the representative registered in the European Union or in another State Party to the Agreement of the European Economic Area,

2. the name or code of the medicinal product, the name of the active substances by type and quantity, other constituents by nature, pharmaceutical form, method of administration, dosage and treatment plan,

3. description of the disease that leads to a serious disability, or is life-threatening, from which the patient is suffering and for the treatment of which the medicinal product is intended,

4. criteria for the selection of patients and notification of the anticipated number of patients,

5. grounds explaining why these patients cannot be satisfactorily treated with a medicinal product authorised for placing on the market within the territorial scope of the Law on Medicinal Products,

6. grounds explaining why the patients cannot be included in an ongoing clinical trial,

7. evidence to support the fact that the medicinal product is of the appropriate quality in keeping with recognised pharmaceutical regulations, as well as confirmation by the qualified person pursuant to Section 14 of the Law on Medicinal Products that the medicinal product has been manufactured according to the principles and guidelines of good manufacturing practice for medicinal products,

8. evidence and grounds for the assumption that the medicinal product is safe and effective for the envisaged use, as a rule through submission of the results of confirming clinical trials,

9. criteria for the suspension or premature discontinuation of the compassionate use programme,

10. further details regarding:

    a) the authorised clinical trial of the medicinal product in the envisaged area of application, giving the EudraCT-number, or

    b) the clinical trial of the medicinal product in the envisaged area of application in a third state and evidence that this is being conducted according to the internationally harmonised Standards of Good Clinical Practice, or

c) the application for authorisation or marketing authorisation, which has been submitted for the medicinal product in the envisaged area of application, to the European Medicines Agency, the competent higher federal authority or to an authority responsible for marketing authorisation in a Member State,

11. in the case of medicinal products which consist of or contain a genetically modified organism or a combination of genetically modified organisms, documents pursuant to Annexes II and III of Directive 2001/18/EC of the European Parliament and the Council of 12th March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC (OJL L 106 of 17/4/2001, p. 1),

12. grounds for a treatment with a medicinal product the application for marketing authorisation of which has been rejected, withdrawn, revoked or suspended or the authorisation of a clinical trial refused, withdrawn, revoked or suspended, giving the reasons for the decision,

13. the current investigator's brochure placed at the disposal of the investigator in the clinical trial or the envisaged draft of a summary of the medicinal product's product characteristics contained in the application for authorisation or marketing authorisation,

14. information and documents which are given to patients, in German, as well as a description of the procedure for informed consent after instruction by a participating physician,

15. requirements on the medical facilities and the qualifications of the participating doctors,

16. description of the envisaged measures to guarantee the safe storage, use and whereabouts of the medicinal products made available,

17. information, where appropriate, on ongoing compassionate use programmes in Member States of the European Union or other States Party to the Agreement of the European Economic Area and, where available, expert opinions of the Committee for Medicinal Products for Human Use pursuant to Article 83 (4) of Regulation (EC) No. 726/2004,

18. declaration of consent regarding the publication of information on the main features of the notified compassionate use programme.

(3) The notification and the required documents pursuant to sub-section 2 shall be made in writing and electronically. The documents may be submitted in German or in English; this excludes documents pursuant to sub-section 2, number 14.

(4) The competent higher federal authority shall publish instructions for submitting the information and documents to its website.

Section 4

Commencement of the compassionate use programme, objection

(1) The competent higher federal authority shall confirm to the responsible person, within a two-week period, giving the date of receipt, that the notification received is in accordance with the regulations (confirmed notification). If documents necessary for the notification are missing, or if the notification is not in accordance with regulations for other

reasons, the competent higher federal authority shall similarly call upon the responsible person to remedy these formal defects within a period of two weeks. The competent higher federal authority shall confirm to the responsible person that the notification is in accordance with regulations within a two-week period, following the receipt of subsequently submitted documents (confirmed notification), in so far as the notification is now complete and in accordance with regulations.

(2) The compassionate use programme can be commenced as soon as the confirmed notification has been received and the competent higher federal authority has raised no objections.

(3) The competent higher federal authority may raise objections if the prerequisites for the implementation of the compassionate use programme are not fulfilled or there are indications that the information submitted is incorrect or that the safe use of the medicinal product is not guaranteed. The competent higher federal authority can also raise objections *a posteriori* if the reasons given in sentence 1 occur after the commencement of the compassionate use programme. If the competent higher federal authority has raised objections, the compassionate use programme may neither be commenced nor continued.

(4) If the notification refers to an advanced therapy medicinal product, which has not yet been evaluated by the competent higher federal authority in an authorisation procedure for any clinical trial, an appropriate deadline shall apply, by way of derogation from sub-section 1, which shall not exceed 60 days.

(5) In the case of medicinal products which consist of or contain genetically modified organisms or a combination of genetically modified organisms, the authorisation of the clinical trial by the competent higher federal authority shall also include the release of these genetically modified organisms within the framework of the compassionate use programme. This shall apply only in so far as no changes are made to the authorised clinical trial which are capable of modifying the assessment of the risk it poses to the health of third parties and the environment. In the case of changes capable of modifying the assessment of the risk to the health of third parties and the environment, the competent higher federal authority shall take a decision within an appropriate period of time, in consultation with the Federal Agency for Consumer Protection and Food Safety. By way of derogation from sub-sections 2 and 4, a compassionate use programme, with medicinal products for which a risk assessment pursuant to sentence 2 is necessary, may only be commenced upon receipt of the authorisation required for this purpose.

Section 5

Duration of the compassionate use programme, re-notification

(1) The compassionate use programme shall end, without prejudice to Section 4, sub-section 3, with the early termination by the responsible person or with the normal availability of the medicinal product on the market, however, at the latest one year after the receipt of the confirmed notification or the authorisation required pursuant to Section 4, sub-section 5.

(2) A re-notification is permissible. In the process, reference may be made to documents already submitted, in so far as no changes have taken place with respect to them.

Section 6

Obligation of the responsible person to disclose information

(1) The responsible person is obliged, pursuant to Section 3, sub-section 1:

1. to document every suspected case of a serious side-effects reported to him/her by participating doctors or brought to his/her knowledge in another way, and to inform the competent higher federal authority immediately, electronically, at the latest, however, within a period of 15 days,

2. to inform the competent higher federal authority immediately of every change in the information pursuant to Section 3 and to include the corresponding documents,

3. to inform the competent higher federal authority immediately of the early termination of the compassionate use programme, giving reasons,

4. to submit a safety report to the competent higher federal authority after completion of the compassionate use programme containing and evaluating, in particular, all of the serious side-effects and all of the non-serious unexpected side-effects,

5. to immediately submit to or inform the competent higher federal authority of new expert opinions pursuant to Article 83 (4) of Regulation (EC) No. 726/2004 and findings from other compassionate use programmes which are being conducted in another Member State of the European Union or in another State Party to the Agreement of the European Economic Area.

(2) Changes relating to the therapeutic indication, the strength or the pharmaceutical form of the medicinal product within the framework of the compassionate use programme, as well as changes which are capable of having an effect on the safety of the patients, may only be carried out after receipt of a new confirmed notification pursuant to Section 4.

(3) The responsible person shall ensure that medicinal product risks are reported to the competent higher federal authority immediately. He/she shall take the necessary risk-prevention measures without delay.

Section 7

Area of responsibility of the responsible person

The responsible person pursuant to Section 3, sub-section 1, shall ensure that:

1. the compassionate use programme is properly conducted,

2. all conditions and restrictions with respect to the safe and effective use of the medicinal product are observed and that the persons involved receive the information necessary to this end,

3. the medicinal product only enters the market if the containers and, if used, the outer packaging, bear at least the following information:

   a) name or code of the medicinal product,

   b) name and address of the responsible person,

   c) batch identification,

d) method of administration,

e) name of the active substance,

f) expiry date,

g) where necessary, retention and storage instructions,

h) indication that the medicinal product is made available within the framework of a compassionate use programme without an authorisation or marketing authorisation,

4. the manufacture, import and release take place according to the regulations for investigational medicinal products provided for in the Ordinance on the Manufacture of Medicinal Products and Active Substances,

5. the essential documents pertaining to the compassionate use programme are retained for at least ten years subsequent to its completion or early termination; this shall be without prejudice to other regulations governing the retention of medical documents.

Section 8

Information obligations of the competent higher federal authority

(1) In the case of medicinal products which are comprised of or contain a genetically modified organism or a combination of genetically modified organisms, the competent higher federal authority shall inform the Federal Agency for Consumer Protection and Food Safety about the receipt of the notification.

(2) The competent higher federal authority shall inform the European Medicines Agency of the compassionate use programmes of which it has been notified.

(3) The competent higher federal authority shall make sure that every suspected serious side-effect is recorded and the European Medicines Agency informed thereof immediately, however, at the latest within 15 days of receipt of the information.

(4) The competent higher federal authority shall make information on the compassionate use programmes, of which it has been notified, accessible to the public.

Section 9

Transitional provisions

Compassionate use programmes, which are being conducted at the time when the present ordinance enters into force, may be continued independently of the provisions contained herein.

Section 10

Entry into force

The present ordinance shall enter into force on the day following its publication.

Bonn, 14th July 2010

The Federal Minister of Health

Dr. Philipp Rösler