Ordinance 1/2010 of the Pharmig Board regarding Non-Interventional Studies (VO-NIS 1/2010)

Based on Art. 8.7 in conj. w. Art. 14 of the Pharmig Code of Conduct, the following provisions are enacted with regard to Art. 8.3 VHC (Non-Interventional Studies, NIS):

Article 1

Scope of Application

1.1 In addition to the provisions of the Austrian Medicinal Products Act (AMG) and its implementing ordinances as well as the Code of Conduct, the provisions of the present Ordinance shall apply to NIS in accordance with Sec. 2a (3) AMG.

1.2 The term NIS includes, in particular, post-marketing surveillances, case control studies, cross-sectional studies, correlation studies with aggregated data, analyses of registers and spontaneous reporting systems.

1.3 The provisions of the present Ordinance shall apply to pharmaceutical companies, which directly design, review, approve and/or finance an NIS or on whose behalf an NIS is designed and/or reviewed.

Article 2

Definitions

2.1 For the purposes of the present Ordinance, the following definitions shall apply:

a) “Design”, in particular the planning of NIS, the development of the study plan, the drafting of the necessary agreements, the selection of suitable survey instruments (such as questionnaires, blood count, peak flow, X-ray, ECG), implementation (such as selecting and approaching physicians/hospitals /pharmacies), the preparation of adequate documentation, the realisation and support throughout the run time, the analysis of study results, the drafting of the final report;

b) “Review”, in particular any and all quality assurance measures in order to secure the completeness and validity of data and remedying shortcomings;

c) “Approval”, in particular the internal approval process.

Article 3

Purpose of NIS

3.1 NIS are used to obtain, further develop and expand knowledge in the use of a medicinal product as well as its effectiveness and tolerance after marketing authorisation according to the daily use practice. In particular, the above shall include the following:

a) Gaining knowledge in the consideration of the summaries of product characteristics and patient information leaflets, acceptance and compliance, practicability, consideration of marketing authorisation requirements;

b) Gaining knowledge of hitherto unknown, particularly rare adverse drug reactions to the medicinal product and interactions;

c) Gaining knowledge of special populations within the approved indications;

d) Further developing knowledge of adverse drug reactions in daily use practice(e.g. assessment of severity, incidence and interactions);

e) Expanding knowledge of approved indications under conditions of daily use practice.

3.2 NIS are not suitable as evidence of efficacy in the sense of phase II to IV in a clinical trial.

3.3 NIS may not be misused for the purpose of influencing therapy or procurement decisions or for pure marketing purposes. Any decision on the prescription of a medicinal product shall be made independently from the decision of including a patient in an NIS.

Article 4

Distinction from Clinical Studies

4.1 The distinction between NIS and clinical studies lies in the observance of non-intervention. Non-intervention in the context of NIS means:

a) the attending physician shall not be given any instructions on whether there should be any treatment at all or which medicinal product should be administered and under what circumstances a therapy should be discontinued or modified and

b) treatment with medicinal products complies with the information regarding their use specified in their marketing authorisation (this also includes all marketing authorisation information regarding contraindications, dosage and dosage schedules, concomitant medication, patient populations, combination therapies, etc.) and

c) the physician performs the treatment, including diagnosis and monitoring, in accordance with customary local medical therapeutic practice and

d) no additional diagnostic and/or therapeutic measures will be made necessary for the patient or no additional burdens will result for the patient.

Article 5

Designing an NIS

5.1 An NIS shall be designed under the direction of the pharmaceutical company's medical department or, in its absence, under the direction of a person with relevant medical qualifications who does not belong to the marketing/sales division. If staff from other divisions are involved in preparing an NIS, they shall be trained accordingly and such training shall be documented.

5.2 The selection of an adequate survey instrument shall be determined in accordance with the scientific objective of the NIS. The selected survey instrument must be methodologically adequate, conclusive, and efficient (with regard to the number of patients, for instance) so as to attain the scientific objective.

5.3 Study plan

5.3.1 The study plan shall be based on daily use practice/treatment; to this end, requirements set forth in the study plan should allow for systematic observation and should support the objective of consistency in the observations.

5.3.2 Study plans shall include at least the following information:

a) Formulating one (or several) detailed question(s), including a justification to explain why the NIS is an adequate instrument for answering them;

b) Determining the characteristics to be surveyed, a description of their relevance as well as their significance for answering the questions (target variable, influencing variable, confounding variable);

c) Observation schedule (procedure and survey periods);

d) Description of the survey instruments required for observation, including a justification that the data collected in this manner are suitable for answering the formulated question;

e) Description of the approach used in selecting suitable physicians/hospitals/pharmacies;

f) Description of type and scope of documentation for physicians/hospitals/pharmacies;

g) Justification of the number of patients to be included;

h) Reporting regulation for adverse drug reactions to the medicinal product;

i) Description of quality assurance measures;

j) Description of statistic analysis; data analysis shall use biostatistical methods that do justice to the problem issues at hand and the planned approach shall be determined in advance in the study plan;

k) Definition of responsibilities (sponsor, project manager, responsible biostatistician, for instance); the person responsible for pharmacovigilance must always be

involved so as to ensure compliance with the applicable reporting provisions of the Pharmacovigilance Ordinance;

l) Regulations regarding the reporting modalities - including biostatistical and medical assessment - and planned publication;

m) Justification, whether there is additional need for information in view of the handling of patient data; as the case may be, description of how patient consent is obtained.

5.3.3 In addition, study plans shall include the following information if applicable:

a) Description of patient selection. With a view to the question(s), measures shall be taken to guarantee the best possible representativeness of the patients included in the NIS (if possible, by including all suitable patients for each physician, by using a log for available patients);

b) Description of measures to achieve representativeness (for physicians/hospitals/pharmacies and/or patients);

c) Discussion of possible confounding variables and description of measures to control these;

d) Documentation samples and patient consent form samples.

5.4 Final report

5.4.1 The final report shall include at least the following information:

a) All information in accordance with Art. 5.3.2 and, if applicable, in accordance with Art. 5.3.3 of the study plan;

b) A biostatistical analysis of the collected data;

c) If applicable, an assessment of effectiveness from a medical point of view, particularly of adverse reactions;

d) All adverse reactions reported as part of the NIS, which need to be reported to comply with Sec. 75b (1) AMG;

e) A list of all involved physicians/hospitals/pharmacies.

5.4.2 The final report shall be completed 12 months after completion of the NIS at the latest (after final observation of the last NIS patient) and shall be archived for no less than 15 years.

5.5 The NIS results shall be presented in a suitable manner in the periodic safety update reports. If necessary, the risk-benefit profile of the medicinal product shall be updated and, if available, the risk management plan shall be revised.

Article 6

Reviewing an NIS

6.1 An NIS shall be reviewed under the direction of the pharmaceutical company's medical department or, in its absence, under the direction of a person with relevant medical qualifications who does not belong to the marketing/sales division. If staff from other divisions are involved in reviewing an NIS, they shall be trained accordingly and such training shall be documented.

6.2 Quality assurance systems shall be used that ensure the validity and representativeness of the collected data. For example, greater attention must be paid to checking the data sets for plausibility and completeness when no data control is ensured on site, as customarily is the case.

6.3 Data validation, data coordination and data analysis shall be performed by involving an adequately qualified person.

Article 7

Approving an NIS

7.1 An NIS shall be approved under the direction of the pharmaceutical company's medical department or, in its absence, under the direction of a person with relevant medical qualifications who does not belong to the marketing/sales division. If staff from other divisions are involved in approving an NIS, they shall be trained accordingly and such training shall be documented.

Article 8

Commencement and Transitional Provisions

8.1 The present Ordinance shall enter into force on 01 March 2010.

8.2 NIS, in which the first patient is documented after 30 June 2010, must be in compliance with the provisions of this Ordinance.