STATUTORY INSTRUMENTS

2012 No. 1916

The Human Medicines Regulations 2012

PART 5

Marketing authorisations

Consideration of application

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58.—(1) The licensing authority must take all reasonable steps to ensure that it makes a decision to grant or refuse a UK marketing authorisation before the end of 210 days beginning immediately after the day on which the application for the authorisation is submitted in accordance with regulations 49 to 55.

(2) If the licensing authority requests the applicant to provide any further information or material, the period referred to in paragraph (1) is suspended for the period—

(a) beginning with the date on which the request is made; and

(b) ending with the date on which the information or material is provided.

(3) If the licensing authority requests the applicant to give an oral or written explanation of the application, the period referred to in paragraph (1) is suspended for the period—

(a) beginning with the date on which the request is made; and

(b) ending with the date on which the explanation is provided.

(4) The licensing authority may grant the application only if, having considered the application and the accompanying material, the authority thinks that—

(a) the applicant has established the therapeutic efficacy of the product to which the application relates;

(b) the positive therapeutic effects of the product outweigh the risks to the health of patients or of the public associated with the product;

(c) the application and the accompanying material complies with regulations 49 to 55; and

(d) the product's qualitative and quantitative composition is as described in the application and the accompanying material.

(5) Schedule 11 makes provision about advice and representations in relation to an application for the grant of a UK marketing authorisation.

(6) This regulation does not apply to an application that—

(a) has been submitted to the licensing authority in accordance with Article 28 of the 2001 Directive; or

(b) has been referred to the Committee for Medicinal Products for Human Use established under Regulation (EC) No 726/2004 for the application of the procedure laid down in Articles 32 to 34 of the 2001 Directive.

(7) An application to which paragraph (6) applies is to be determined by the licensing authority in accordance with Chapter 4 of Title III of the 2001 Directive.

Conditions of UK marketing authorisation: general

59.—(1) The licensing authority may—

(a) grant a UK marketing authorisation subject to one or more of the conditions in paragraph (2); or

(b) vary or remove a condition in paragraph (2) to which the UK marketing authorisation is subject.

(2) Those conditions are—

(a) to take certain measures for ensuring the safe use of the medicinal product and include them in the risk management plan;

(b) to conduct post-authorisation safety studies;

(c) to comply with obligations on the recording or reporting of suspected adverse reactions which are stricter than those referred to in Part 11;

(d) any other conditions or restrictions with regard to the safe and effective use of the medicinal product;

(e) the existence of an adequate pharmacovigilance system; and

(f) to conduct post-authorisation efficacy studies where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed.

(3) An obligation to conduct such studies as are referred to in paragraph (2)(f) must be based on the delegated acts adopted pursuant to Article 22b of the 2001 Directive, while taking into account the scientific guidance referred to in Article 108a of the 2001 Directive.

(4) The marketing authorisation must lay down deadlines for the fulfilment of the conditions in paragraph (2) where necessary.

(5) The licensing authority must notify the EMA of any marketing authorisation that it has granted subject to a condition included in accordance with this regulation.

(6) The holder of the authorisation must incorporate any condition included in a marketing authorisation in accordance with this regulation into the risk management system for the product.

(7) Schedule 11 makes provision about advice and representations in relation to proposals to vary or remove a condition to which a UK marketing authorisation is subject.

Conditions of UK marketing authorisation: exceptional circumstances

60.—(1) The licensing authority may—

(a) grant a UK marketing authorisation subject to conditions in accordance with the following paragraphs of this regulation; or

(b) vary or remove such a condition to which the UK marketing authorisation is subject.

(2) The powers in paragraph (1) may be exercised only after consultation with the applicant for the authorisation or (as the case may be) its holder.

(3) The power in paragraph (1)(a) to grant an authorisation subject to conditions may be exercised only—

(a) in exceptional circumstances; and

(b) when the applicant can show that the applicant is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use.

(4) The conditions must relate to a matter addressed by Annex I to the 2001 Directive.

(5) The conditions may, in particular, relate to the safety of the product to which the authorisation relates.

(6) The conditions may, in particular, require that, where there is a serious adverse reaction relating to the use of the product—

(a) the reaction must be reported to the licensing authority; and

(b) such other action as may be specified in the conditions must be taken.

(7) The licensing authority must keep under review—

(a) the conditions under this regulation to which a UK marketing authorisation is subject; and

(b) the holder's compliance with those conditions.

(8) The licensing authority must consider those matters no less frequently than—

(a) at the end of the period of one year beginning with the date on which the authorisation was granted; and

(b) at the end of each subsequent period of one year.

(9) The licensing authority must notify the EMA of any marketing authorisation that it has granted subject to a condition included in accordance with this regulation.

(10) The holder of the authorisation must incorporate any condition included in a marketing authorisation in accordance with this regulation into the risk management system for the product.

(11) Schedule 11 makes provision about advice and representations in relation to proposals to vary or remove a condition to which a UK marketing authorisation is subject.

Conditions of UK marketing authorisation: new obligations post-authorisation

61.—(1) After the granting of a UK marketing authorisation, the licensing authority may impose an obligation on the holder of the authorisation in accordance with either or both of —

(a) paragraph (4), in a case where paragraph (2) applies; or

(b) paragraph (5), in a case where paragraph (3) applies.

(2) This paragraph applies if there are concerns about the risks of a medicinal product that is the subject of a marketing authorisation.

(3) This paragraph applies if the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly.

(4) The obligation in this paragraph is to conduct a post-authorisation safety study.

(5) The obligation in this paragraph is to conduct a post-authorisation efficacy study.

(6) If concerns as described in paragraph (2) apply to more than one medicinal product, the licensing authority shall, following consultation with the Pharmacovigilance Risk Assessment Committee, encourage the marketing authorisation holders concerned to conduct a joint post-authorisation safety study.

(7) The obligation under paragraph (5) shall be based on the delegated acts adopted pursuant to Article 22b of the 2001 Directive while taking account of the scientific guidance referred to in Article 108a of the 2001 Directive.

(8) Where the licensing authority imposes an obligation under paragraph (4) or (5), it must without delay give written notice to the holder of —

(a) the imposition of the obligation;

(b) the justification for the imposition;

(c) the objectives and timeframe for submission and conduct of the study; and

(d) the opportunity to present written observations in accordance with paragraph (9) and the time limit specified for doing so.

(9) Where the holder so requests within the period of thirty days beginning on the day after the receipt by the holder of the notice referred to in paragraph (8), the licensing authority must provide the holder of the authorisation with an opportunity to present written observations in response to the imposition of the obligation within the time limit specified by the licensing authority in the notice.

(10) Where the holder presents written observations under paragraph (9), the licensing authority must withdraw or confirm the imposition of the obligation under paragraph (4) or (5) on the basis of the written observations as soon as is reasonably practicable.

(11) Paragraph (12) applies where the licensing authority—

(a) imposes an obligation under paragraph (4) or (5) and the holder does not present written representations under paragraph (9); or

(b) confirms the imposition of an obligation under paragraph (10).

(12) Where this paragraph applies, the licensing authority must vary the marketing authorisation to include the obligation as a condition of the marketing authorisation as if it were a condition imposed under regulation 59 (conditions of UK marketing authorisations: general).

(13) The licensing authority must notify the EMA that the marketing authorisation is subject to a condition included in accordance with paragraph (12).

(14) The holder of the authorisation must incorporate any condition included in a marketing authorisation in accordance with paragraph (12) into the risk management system for the product.

(15) Schedule 11, which makes provision about advice and representations in relation to proposals to vary or remove a condition to which a UK marketing authorisation is subject, shall apply in relation to the variation or removal of a condition included in a marketing authorisation in accordance with paragraph (12).

Classification of UK marketing authorisation

62.—(1) A UK marketing authorisation must include a term that the product to which the authorisation relates is to be available—

(a) only on prescription;

(b) only from a pharmacy; or

(c) on general sale.

(2) In making a determination under paragraph (1), the licensing authority must have regard to the following in relation to the product—

(a) the maximum single dose;

(b) the maximum daily dose;

(c) the strength of the product;

(d) its pharmaceutical form;

(e) its packaging; and

(f) such other circumstances relating to its use as the licensing authority considers relevant.

(3) A UK marketing authorisation must be granted subject to a condition that the product to which the authorisation relates is to be available only on prescription if the licensing authority considers that the product—

(a) is likely to present a direct or indirect danger to human health, even when used correctly, if used without the supervision of a doctor or dentist;

(b) is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health;

(c) contains substances, or preparations of substances, of which the activity requires, or the side effects require, further investigation; or

(d) is normally prescribed by a doctor or dentist for parenteral administration.

(4) In deciding whether paragraph (3) applies to a product, the licensing authority must take into account whether the product—

(a) contains a substance listed in any of Schedules I, II or IV to the Narcotics Drugs Convention (where the product is not a preparation listed in Schedule III to that Convention);

(b) contains a substance listed in any of Schedules I to IV of the Psychotropic Substances Convention (where the product is not a preparation which may be exempted from measures of control in accordance with paragraphs 2 and 3 of article 3 of that Convention);

(c) is likely, if incorrectly used—

(i) to present a substantial risk of medicinal abuse,

(ii) to lead to addiction, or

(iii) to be used for illegal purposes;

(d) contains a substance that, by reason of its novelty or properties, might fall within paragraph (c), but as to which there is insufficient information available to determine whether it does so fall;

(e) by reason of its pharmaceutical characteristics or novelty, or in the interests of public health, is reserved for treatments that can only be followed in a hospital;

(f) is used in the treatment of conditions that must be diagnosed in a hospital or in an institution with special diagnostic facilities (although administration and subsequent supervision may be carried out elsewhere); or

(g) is intended for outpatients but may produce very serious side effects which would require a prescription drawn up as required by a specialist and special supervision throughout the treatment.

(5) A UK marketing authorisation may include a term that the product to which the authorisation relates is to be available on general sale only if the licensing authority considers that the product can with reasonable safety be sold or supplied otherwise than by, or under the supervision of, a pharmacist.

Frequency of periodic safety update reports

63.—(1) The licensing authority must, if paragraph (2) applies, include in a UK marketing authorisation a term that specifies the frequency, calculated from the date on which the authorisation is granted, with which the holder of the authorisation must submit periodic safety update reports in accordance with regulation 191(8) (obligation on holder to submit periodic safety update reports: general requirements).

(2) This paragraph applies in the case of a medicinal product in relation to which regulation 191(8) applies by virtue of regulation 191(1).

Duties of licensing authority in connection with determination

64.—(1) This regulation applies if the licensing authority grants a UK marketing authorisation.

(2) The licensing authority must inform the holder of the authorisation of the summary of the product characteristics as approved by the authority.

(3) The licensing authority must ensure that the summary of the product characteristics continues to match the version it has approved, subject to any changes it approves.

(4) As soon as is reasonably practicable after granting the marketing authorisation, the licensing authority must make available publicly—

(a) the marketing authorisation;

(b) the package leaflet;

(c) the summary of the product characteristics;

(d) any conditions established in accordance with Articles 21a, 22 and 22a of the 2001 Directive; and

(e) any deadlines for the fulfilment of those conditions.

(5) The licensing authority must draw up an assessment report and make comments on the file as regards—

(a) the results of the pharmaceutical and pre-clinical tests, the clinical trials, the risk management system and the pharmacovigilance system of the product to which the authorisation relates; or

(b) in the case of a national homoeopathic medicinal product within the meaning of Schedule 10, the information submitted under paragraphs 3 to 5 of that Schedule.

(6) The licensing authority must—

(a) revise the assessment report whenever new information becomes available that is of importance for the evaluation of the quality, safety or efficacy of the medicinal product;

(b) make the assessment report publicly available (with the omission of information of a commercially confidential nature) as soon as is reasonably practicable after it has been prepared or revised; and

(c) include in the assessment report a summary, written in a manner that is understandable to the public, that contains, in particular, a section relating to the conditions of use of the medicinal product.

(7) The assessment must be provided separately for each indication that is authorised.