SCHEDULES

[F1SCHEDULE 12A

Further provision as to the performance of pharmacovigilance activities

Textual Amendments

F1 Sch. 12A inserted (31.12.2020) by The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 (S.I. 2019/775), reg. 1, **Sch. 6** (as amended by S.I. 2019/1385, reg. 1, **Sch. 1 para. 9** and S.I. 2020/1488, reg. 1, **Sch. 2 para. 192**); 2020 c. 1, **Sch. 5 para. 1(1)**

PART 8

Periodic safety update reports

Content of periodic safety update reports

26.—(1) The periodic safety update report ("PSUR") must—

(a) be based on all available data; and

(b) focus on new information which has emerged since the data lock point of the last PSUR.

(2) The PSUR must provide an accurate estimate of the population exposed to the medicinal product, including all data relating to the volume of sales and volume of prescriptions.

(3) The estimate of exposure referred to in sub-paragraph (2) must be accompanied by a qualitative and quantitative analysis of actual use, which must indicate, where appropriate, how actual use differs from the indicated use based on all data available to the holder, including the results of observational or drug utilisation studies.

(4) The PSUR must contain the results of assessments of the effectiveness of risk minimisation activities relevant to the risk–benefit assessment.

(5) Where any conditions are imposed under regulation 59(4A) (conditions in relation to UK marketing authorisations to which paediatric specific provisions apply) or 59(4D) (conditions in relation to UK marketing authorisations for advanced therapy medicinal products), the PSUR must also include an assessment of the effectiveness of any risk management system, and the results of any studies performed, in order to comply with those conditions.

(6) Subject to sub-paragraph (7), holders are not required to include systematically detailed listings of individual cases, including case narratives, in the PSUR.

(7) Holders must provide case narratives in the relevant risk evaluation section of the PSUR where integral to the scientific analysis of a signal or safety concern in the relevant risk evaluation section.

(8) Based on the evaluation of the cumulative safety data and the risk-benefit analysis, the holder must draw conclusions in the PSUR as to the need for changes or actions, including implications for the approved summary of product characteristics for each product for which the PSUR is submitted.

(9) Unless otherwise agreed with the licensing authority, a single PSUR must be prepared for all medicinal products which—

(a) contain the same active substance; and

(b) are authorised for the same holder,

and sub-paragraph (10) applies to that single PSUR.

(10) Where this sub-paragraph applies—

(a) the PSUR must cover all indications, routes of administration, dosage forms and dosing regimens, irrespective of whether authorised under different names and through separate procedures; and

(b) where relevant, data relating to a particular indication, dosage form, route of administration or dosing regimen must be presented in a separate section of the PSUR, with any safety concerns addressed accordingly.

(11) Unless otherwise agreed with the licensing authority, if the substance that is the subject of the PSUR is also authorised as a component of a fixed combination medicinal product, the holder must either—

(a) submit a separate PSUR for the combination of active substances authorised for the same holder, with cross-references to each relevant single-substance PSUR; or

(b) provide the combination data within one of the single-substance PSURs.

Format of periodic safety update reports

27.—(1) Electronic PSURs must be submitted in the following format—

(a) Part I: title page including signature;

(b) Part II: executive summary; and

(c) Part III: table of contents which contains—

(i) introduction,

(ii) worldwide marketing authorisation status,

(iii) actions taken in the reporting interval for safety reasons,

(iv) changes to reference safety information,

(v) estimated exposure and use patterns—

(aa) cumulative subject exposure in clinical trials,

(bb) cumulative and interval patient exposure from marketing experience,

(vi) data in summary tabulations—

(aa) reference information,

(bb) cumulative summary tabulations of serious adverse events in clinical trials,

(cc) cumulative and interval summary tabulations from post-marketing data sources,

(vii) summaries of significant findings from clinical trials during the reporting interval—

(aa) completed clinical trials,

(bb) ongoing clinical trials,

(cc) long-term follow-up,

(dd) other therapeutic use of medicinal product,

(ee) new safety data related to fixed combination therapies,

(viii) findings from non-interventional studies,

(ix) information from other clinical trials and sources,

(x) non-clinical data,

(xi) literature,

(xii) other periodic reports,

(xiii) lack of efficacy in controlled clinical trials,

(xiv) late-breaking information,

(xv) overview on signals: new, ongoing or closed,

(xvi) signal and risk evaluation—

(aa) summaries of safety concerns,

(bb) signal evaluation,

(cc) evaluation of risks and new information,

(dd) characterisation of risks, and

(ee) effectiveness of risk minimisation (if applicable),

(xvii) benefit evaluation—

(aa) important baseline efficacy and effectiveness information,

(bb) newly identified information on efficacy and effectiveness, and

(cc) characterisation of benefits,

(xviii) integrated benefit-risk analysis for authorised indications—

(aa) benefit-risk context: medical need and important alternatives, and

(bb) benefit-risk analysis evaluation,

(xix) conclusions and actions, and

(xx) appendices to the PSUR.

(2) In this paragraph, "signal evaluation" means the process of further evaluating a validated signal taking into account all available evidence, to determine whether there are new risks causally associated with the active substance or medicinal product, or whether known risks have changed, and that process—

(a) may include non-clinical and clinical data; and

(b) must be as comprehensive as possible regarding the sources of information used for that process.**]**

Changes to legislation:
There are currently no known outstanding effects for the The Human Medicines Regulations 2012, PART 8.