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Inspections, Human Medicines Pharmacovigilance & Committees Division

Highlights from the 11th EMA Industry Platform meeting on the operation of EU pharmacovigilance legislation – 2 June 2017

The following records announcements and action points from the 11th Pharmacovigilance Industry Platform meeting held on 2 June 2017.

Welcome and matters arising

- The Regulators updated on the matters arising including the EMA Management Board announcement on achievement of full functionality of EudraVigilance and its improvements.
- The regulators followed up with the PRAC work plan for 2017, highlighting an increased collaboration with Scientific Advice Working Party (which now meets in parallel with the PRAC), PRAC involvement in the PRIME's assessments, and a cross-committee Brexit task force. The GVP on paediatric pharmacovigilance has been agreed and a public hearing for the referral on valproate will be held in September 2017. SCOPE update was provided, including its guidance and outputs (accessible via the SCOPE website), which provide a helpful e-learning opportunity for EU network and the MAHs. The utility of the SCOPE infographics has been further reaffirmed during a recent workshop between East African regulators and EMA.
- The regulators updated on the PRAC Impact Strategy. This included the December 2016 workshop, the recommendations for review of the framework, the importance for systematic data collection, robust methodologies, an engagement with patients/HCP organisations and a process for identifying public health outcomes of regulatory decisions. The reflection paper on criteria for impact research is being revised currently. A tender has been recently published for impact studies after Art 31 referrals (diclofenac-CV risk and hydroxyzine). EMA industry stakeholder group on pharmacovigilance impact strategy was presented as the platform for sharing data and collaboration on methods. AESGP, Europa BIO, EFPIA and Medicines for Europe expressed interests in volunteering in this group.



- The CMDh updates included specific safety topics from recent PSUSAs for finasteride and budesonide¹. For the PSUSA on finasteride, the CMDh considered that the changes recommended for finasteride 1 mg tablets, introduced as an outcome of a parallel work-sharing variation, should additionally be part of the single assessment outcome of this PSUR procedure. During the assessment of the PSUSA of budesonide a class effect of corticosteroids was identified. The CMDh requested all concerned MAHs to implement the outcome via the appropriate regulatory procedure.

Action: In similar scenarios, the CMDh to consider listing specific safety issues at a higher (class) level in their outputs (Agenda and Minutes) to facilitate the monitoring by all concerned MAHs.

- Finally, the regulators pointed out several documents on the UK withdrawal from the EU including a [notice](#) to the MAHs of CAPs to remind pharmaceutical companies of their legal obligations further to the UK notification of its intention to withdraw on 29 March 2017 from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless the withdrawal agreement establishes another date or the period is extended by the European Council in accordance with Article 50(3) of the Treaty on European Union, all Union primary and secondary law cease to apply to the UK from 30 March 2019. The UK will then become a 'third country'. In this regard, MAHs of centrally authorised medicinal products for human and veterinary use are reminded of certain legal repercussions, which need to be considered in relation for instance to obligation for MAHs establishment and certain activities (e.g. PhV, batch release etc...) in the EEA to ensure a continuous validity and exploitation of manufacturing, supply and Marketing Authorisations status.
- On the 31 May 2017, a 1st set of Q&A guidance related to the UK withdrawal from the EU with regard to medicinal products for human and veterinary use for centrally authorised medicinal products was published. The Q&A document concerns information related to the location of establishment of a company in the context of centralised procedures and certain activities, including the location of orphan designation holders, QPPVs and companies' manufacturing and batch release sites i.e. 9 questions – Q4 QPPV obligations and Q5 PhV System Master File.
- The CMDh has also published information for MAHs of nationally authorised products for human use, for specific guidance the concerned MAHs are referred to the Heads of Medicines Agencies (HMA) website².
- Further guidance documents will be published on EMA's website in due course. The industry is advised to regularly check EMA's dedicated webpage. For any questions, the MAHs are advised to liaise either with the EMA contact point (product or procedure specific) or send a question via "Ask EMA".

Good pharmacovigilance practices for the EU

- The regulators presented GVPs' status update. A dedicated guideline for paediatric pharmacovigilance developed by the former PhVWP (available on the EMA website) will be incorporated and updated as a new GVP considerations chapter for the paediatric population, with the public consultation expected to start mid-2017. Industry comments on their experience with paediatric pharmacovigilance are welcomed by the regulators.
- The regulators followed up with the update on the implementation on the GVP V and, outside GVP the new RMP template Rev. 2, including transitional arrangements, the Q&A on scientific aspects

¹ <http://www.hma.eu/457.html>

and the content of the RMP, as well as lessons learnt to improve RMPs quality. AR template and EPARs processed will also be updated and will include public summary of the RMP (to be prepared by the applicant). All RMP summaries (initial and post-authorisation RMPs) will be published when they are assessed in the new template. Trainings are planned for assessors and for the industry. MAHs should pay attention to the timelines of the submission of the RMPs in the new template. Related questions on the process should be sent via "Ask EMA".

Action: EMA to consider sharing the EU-NTC RMP assessor training materials with the MAHs.

- Finally, the assessments of RMPs for nationally authorised products/MRP/DCP procedures were discussed. All new medicinal products are requested to have RMP since July 2012, whereas older medicinal product can be requested to have one throughout their life cycle. A few topics highlighted included data availability for older generic products; differences in the list of safety concerns across the MAHs and MSs, lack of regulatory tool for generic MAHs in case the originator's updates RMP; the scenarios for submission and updates of a generic RMP. The CMDh & Industry Ad Hoc Group to discuss RMP Initiatives will discuss a draft proposal for Work sharing assessments of RMPs prepared by Medicines for Europe/EFPIA and AESGP on how to address the above mentioned issues including the possibilities to come to a common core document acceptable to all MSs. It has been suggested that a future workshop with relevant stakeholders may be organised to facilitate the discussions.

Signal Management process

- The industry presented their consolidated positions regarding the signal management process, specifically the timelines, expected workload, periodicity and methodology of data monitoring in EudraVigilance at the substance level taking into account company established processes and highlighted the importance of preventing effort duplication, disparate conclusions, or multiple company notifications to regulators. A repository of 'listedness' for non-CAPs and publishing of confirmed and non-confirmed signals were suggested as tools to facilitate signal detection by the industry. The industry considers how to best approach SmPCs' harmonisation issues across non-CAPs, signal detection for biosimilar products, the expectation at the validation stage, the MAH traditional focus on product-specific (defect, break in cold chain transport etc.) rather than substance related issues. The work-sharing among MAHs for signal management was not supported at this stage due to several legal/audit constrains, and uncertain quality assurance.
- The regulators detailed the plans for the MAHs access to EudraVigilance following the announcement of its full functionality by the EMA Management Board, the tools to be provided which incorporate PROTECT findings, the level of the access, the registration to the system, the access rights of the MAHs EVDAS users, and related training tools.
- Several EV monitoring aspects were highlighted, such as a risk-proportionate frequency of screening (more intensive for new substances), and up to 6 months interval for established products, transparency for MAH validated signals, timelines for ESI notifications, the documentation of signal detection and validation by the MAHs. A phased implementation of the

requirement for MAHs to monitor EudraVigilance is being considered, starting with a subset of EU authorised substances. Transitional arrangements for the industry are under consideration.

Next meetings/topics:

- 21 Sep 2017 (the annual stakeholder meeting),
- 24 November 2017 (12th industry platform),
- Brexit preparations report and MLM experience prioritized for discussion this year (at 12th industry platform).