Federal Institute
for Drugs
and Medical Devices

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The Liver Forum:
Regulatory update from Europe

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The views expressed in this presentation are primarily those of the author and do not necessarily express those of the BfArM, nor of the EMA

Regulatory update from Europe:

- **Content:**
- The Concept paper on the need for the development of a reflection paper on regulatory requirements for the development of medicinal products for chronic non-infectious liver diseases (PBC, PSC, NASH) (EMA/CHMP/197320/2017)
  - Explanation of background and intent; contents summary
  - Display of its reception
    - Stakeholder involvement
    - Proposals made
  - Further steps
    - Timelines
    - Further stakeholder interaction

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- EMA involvement into Liver Forum (and now PSC Forum) without a clear mandate
- The regulatory involvement into Liver Forum (and PSC Forum) nevertheless provides substantial background and basis for regulatory decisions
- One main focus was therefore to find acknowledgement of main elements discussed in the Liver Forum (and PSC Forum) by CHMP
- However, regulatory interaction for all disease fields limited
    - Usually a full guideline should also reflect experiences with marketing authorisations
    - Therefore only a „Reflection Paper“ intended (may subsequently be replaced by a full guideline).

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- Concept paper main contents:
- Characterisation of the 3 disease entities:
    - Similarities: Unmet medical need, slow progression of diseases, need for long-term observation, potential need for post-approval data, symptoms usually unspecific, feasibility issues with hard clinical endpoints
    - Differences: PBC and PSC are orphan; special features of small populations may need consideration.
- Reflection paper intended to focus on:
    - Identification of adequate endpoints, including validation of surrogate endpoints/biomarkers
    - Identification of suitable study populations
    - Identification of adequate trial designs.
    - Similarities and differences of the 3 disease entities and their impact on regulatory requirements
    - Special needs for paediatric development.

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- Stakeholder involvement/comments received:
  - Organisations directly mentioned/sent: (EASL, AASLD; ESPGHAN, NASPGHAN, IPSCSG, PBCSG, Liver Forum)
  - Reactions: Total number of comments received: 16
    - Which is an extraordinary high number for a concept paper.
  - Different stakeholders:
    - 6 Pharmaceutical companies
    - 5 Patient‘s Organisations
    - 3 Learned Societies/Academic Groups
    - 2 Multi-stakeholder Organisations

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- Proposals/comments received:
  - 14 of the comments expressed general acknowledgement/welcome of the guidance
  - Comments on scope: 3 comments to restrict (e.g. separate NASH from PSC and PBC), and 4 comments to extend the scope (extend by rPSC, ALD, and AIH)
  - Proposals to focus on the following:
    - 6 Non-invasive biomarkers
    - 6 Children
    - 2 each for Endpoints and Populations
    - 1 each for: duration of observation, ehtical problems, study conduct/recruitment, histology evaluation, combination products, choice of control group.

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- Proposals/comments provided:
  - Further Proposals:
    - 4 comments with a wish to include more closely patient‘s organisations
    - Include other stakeholders such as payers/HTAs and research consortia such as IMI LITMUS and NIH NIMBLE
    - Many proposals for amendment of wording
      - However, no revised/refined version of the document planned
        A „Concept paper“ makes only an announcement
      - Thanks for the comments/input!
      - Next step: First version of the Reflection Paper

Regulatory update from Europe: The Concept paper on PBC, PSC, and NASH

- Planned timelines:
  - Publication of the Concept paper: May 2017
  - Public consultation phase June 2017-August 2017
  - „Usual“ proceedings include stakeholder meeting(s):
    - Originally planned to be held in 4th Quarter 2017
  - Original timeline for publication of 1st version of the Reflection paper:
    - 2nd Quarter of 2018
  - Followed by a public consultation phase (usually 6 months)

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- Revision of timelines necessary:

EMA prepares for Brexit **Press release**

Business continuity plan aims to preserve Agency's ability to protect public and animal health

- The business continuity plan is a tool that will help EMA take the difficult decision to reallocate the available resources as needed to maintain its priority activities over the next years. It categorises and prioritises tasks and activities according to their impact on public health and the Agency's ability to function. (Among others) (…) EMA reduced the number of audits as well as some corporate governance and support activities. Participation of EMA staff in external meetings or conferences has been reduced, as has the organisation of EMA meetings and workshops.
- Stakeholder meeting postponed
- First draft of Reflection Paper envisaged 3rd Quarter 2018
- Potential stakeholder meeting during or at end of public consultation phase – would then be 1st Quarter 2019
- Depending on EMA relocation (time and place)

Thank you for your attention!

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