EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Class waiver list review

Background, approach and outcome
Consequences for regulatory submissions

EMA Industry stakeholder platform on Paediatric medicines

Presented by Ralf Herold on 11 May 2015
Paediatric Medicines Office - Product Development Scientific Support Department

Background

- Class waiver list has been reviewed in the past
- New paediatric data and knowledge to be considered
- Data on new medicines becoming available
- Ongoing review communicated in PDCO monthly reports
- Protect and promote child health

Regulation (EC) No. 1901/2006, Article 14

1. The Agency shall maintain a list of all waivers. The list shall be regularly updated (at least every year) and made available to the public.
2. The Paediatric Committee may, at any time, adopt an opinion advocating the review of a granted waiver. In the case of a change affecting a product-specific waiver, the procedure laid down in Article 25 shall apply. In the case of a change affecting a class waiver, paragraphs 6 and 7 of Article 25 shall apply.
3. If a particular product-specific or class waiver is revoked, the requirement set out in Articles 7 and 8 shall not apply for 36 months from the date of the removal from the list of waivers.

Agency's List of all waivers (product-specific waivers and class waivers):
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000415.jsp&mid=WC0b01ac05801177cc

Increased paediatric knowledge and data

- About 500 publications per year on paediatric trials are published in core clinical journals indexed in Medline, across all therapeutic areas
- Increasing number of systematic non-clinical studies for screening disease models and medicinal product activity
- Information on orphan conditions and their evolution
- Assessment of paediatric studies by competent authorities (in particular under Article 45 and 46 of paediatric regulation)

Recently authorised, new medicines

- Significant advances for patients
- Having completely novel pharmacological properties and heterogeneous characteristics
- Addressing a range of conditions for which the respective medical plausibility could not be anticipated by scientific committees
- Example: 26 newly authorised anti-cancer medicines (2012-2014) = a surge in diversity and number of medicines (previous 26: 2007-2011)
- Agency seeks to respond to patients' needs

Approach of class waiver review by PDCO

- Need to integrate evolution of science and of regulatory experience
- Scientific evaluation of paediatric data on medicines related to current class waivers
- Where relevant, update class waiver
  - Integrate into class waiver characteristics of a medicinal product(s) or a class of medicinal products
  - Granting class waiver for group of conditions when justified by available data, characteristics of diseases and of medicinal product or class of medicinal products
- Where appropriate, revoke class waiver
- Confirm remaining class waivers

Overview outcome of class waiver list review (anticipated)

- Confirmation of waivers
  - for 1 class of medicinal products for treatment of 1 condition (diabetes)
  - for all classes of medicinal products for treatment of 8 conditions (e.g., metabolism, neurology, pulmonology, oncology)
- Revocation of 8 waivers (areas of neurology, metabolism, oncology)
- Update of waivers for 17 classes of medicinal products for treatment of 14 conditions or groups of conditions (mainly oncology, metabolism)
- Draft of PDCO Opinion with details on classes of medicinal products and condition has been shared with industry stakeholders

Outcome example: revised class waiver

Current class waiver: For all “medicinal products intended to treat lung carcinoma (small cell and non-small cell carcinoma)”

“The revised waivers are: [...]

the class of thymidylate synthase inhibitor medicinal products

for treatment of intestinal malignant neoplasms and lung malignant neoplasms;”

Examples: Pemetrexed, Raltitrexed

Conditions or groups of conditions

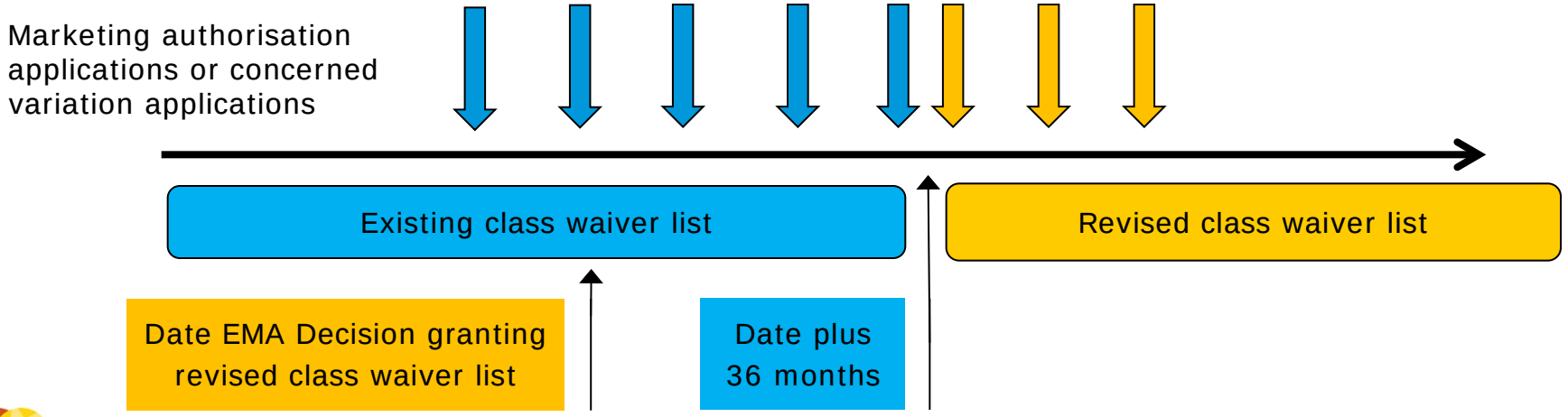
Warwick et al. Phase 2 Trial of Pemetrexed in Children and Adolescents [...] Pediatr Blood Cancer 2013, 60: 237
Malempati et al. Phase I trial and pharmacokinetic study of pemetrexed in children [...] J Clin Oncol 2007, 25: 1505
Horton et al. Phase I trial and pharmacokinetic study of raltitrexed in children [...] Clin Cancer Res 2005, 11: 1884

Outcome example: revoked class waiver

- Waiver of all medicinal products for treatment of coronary atherosclerosis, of peripheral atherosclerosis and of vascular dementia and vascular cognitive disorder / impairment
- Signs and symptoms of atherosclerosis occur and can be measured in children, such as increased intima-media thickness, arterial stiffness, endothelial dysfunction
- Over time, plaques and vessel function worsen, increasing the risk for strokes
- Atherosclerosis occurs in children and represents unmet needs of the paediatric population in terms of prevention as well as treatment
- PDCO recommends revocation

Transition period of 3 years

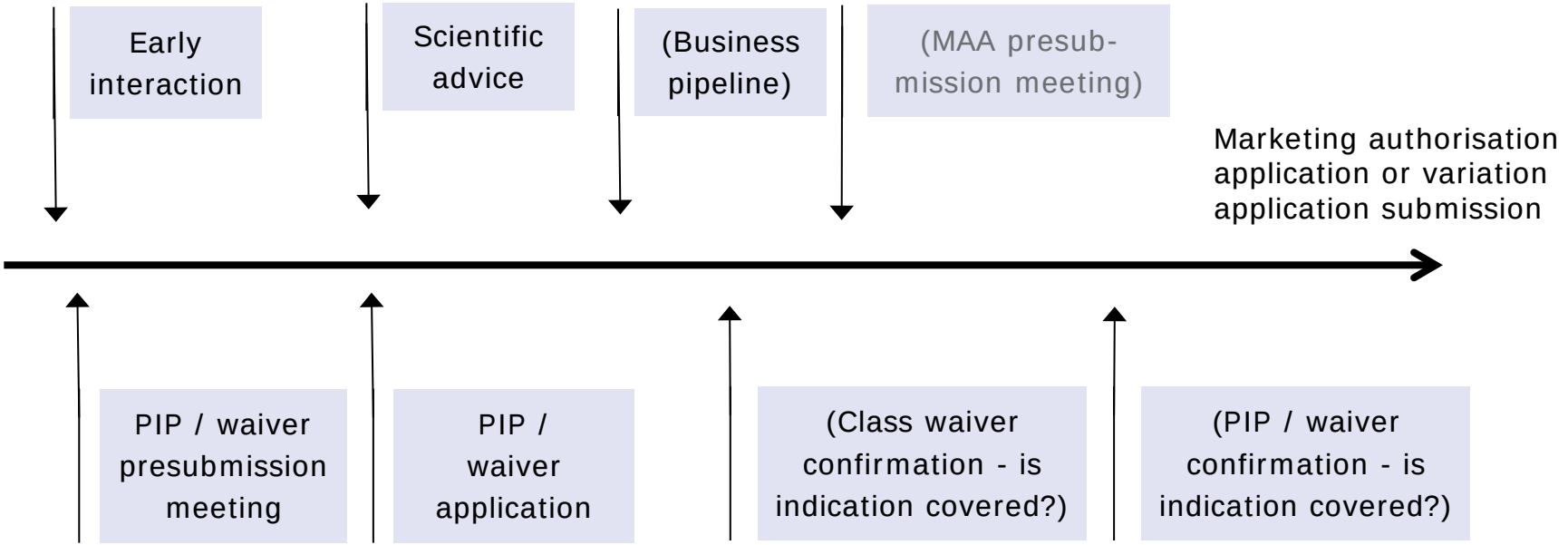
- EMA Decision on PDCO Opinion revising class waivers is anticipated to include that Articles 7 and 8 of Regulation (EC) 1901/2006 shall not apply to applications falling under current class waivers for 36 months from the publication of this Decision



Applications not falling under current or revised class waiver

- “Diagnosis of …” = Use of medicinal product to establish a condition
- “Prevention of …” = Use for primary prevention
- It has been a repeat question, in which way the treatment of symptoms is “covered” by a class waiver for the treatment of an underlying condition: This question requires scientific evaluation by the PDCO, for example of the studied populations and endpoints. Option: seek confirmation of applicability of class waiver

Possibilities for addressing paediatric aspects



Further consequences

For PDCO: Increased systematic opportunities for scientific review: *"In its work, the Paediatric Committee should consider the potential significant therapeutic benefits for the paediatric patients involved in the studies or the paediatric population at large including the need to avoid unnecessary studies."* (Recital 8 paediatric regulation)

For applicants:

- Possibility to request a product-specific waiver
- Early and more interactions as well as better engagement with the PDCO, in particular on characteristics of the medicinal product
- Opportunities for business development, for obtaining a reward and for benefitting from incentives for paediatric research and development

Summary

- Review of PDCO class waiver list took due account of new information on diseases affecting the paediatric population and of the related medicinal products or classes of medicinal products
- Review is anticipated to lead to update the majority of class waivers, and to revoke some class waivers, across all therapeutic areas
- Transitional period for coming into effect for applications is 3 years
- Supportive measures for applicants available to assist and provide useful guidance
- EMA and PDCO inviting industry stakeholders to discuss and comment

Next steps – class waiver list review

- Discussion and your comments
- Continuation and finalisation of PDCO discussion, leading to
- PDCO adoption of Opinion currently planned for 22 May 2015
- EMA issuing Decision within 10 days after receipt of PDCO Opinion

Discussion with industry stakeholders

- PDCO and EMA have seen many opportunities for developing medicines for children
- Several companies have explained to EMA their new approaches to develop medicines for children
- There is a call for action from paediatricians

- *How do you envisage addressing the needs?*
- *In which way is this an opportunity to link closer with paediatric researchers?*

Thank you for your attention

Further information

Paediatric Medicines • paediatrics@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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