EU regulatory tools for expedited antibacterial development programmes

Expediting antibacterial development: core lessons and key tools for a rocky road, ECCMID 2018, Madrid

Presented by Marco Cavaleri on 22 April 2018

An agency of the European Union

Regulatory tools and initiatives aimed at unmet medical needs

Tools in legislation

Conditional Marketing authorisation

- Based on less comprehensive data and with obligation to generate these data post-authorisation

Marketing authorisation under exceptional circumstances

- When comprehensive data can not be general at all, subject to specific obligations

Accelerated assessment

- Reduced assessment time for products of major public health interest

Compassionate use

- Products made available to patients prior granting of marketing authorisation

Other tools and initiatives

PRIME

- Support scheme with early and enhanced scientific dialogue

Adaptive pathways

- Scientific concept of medicines development and data generation

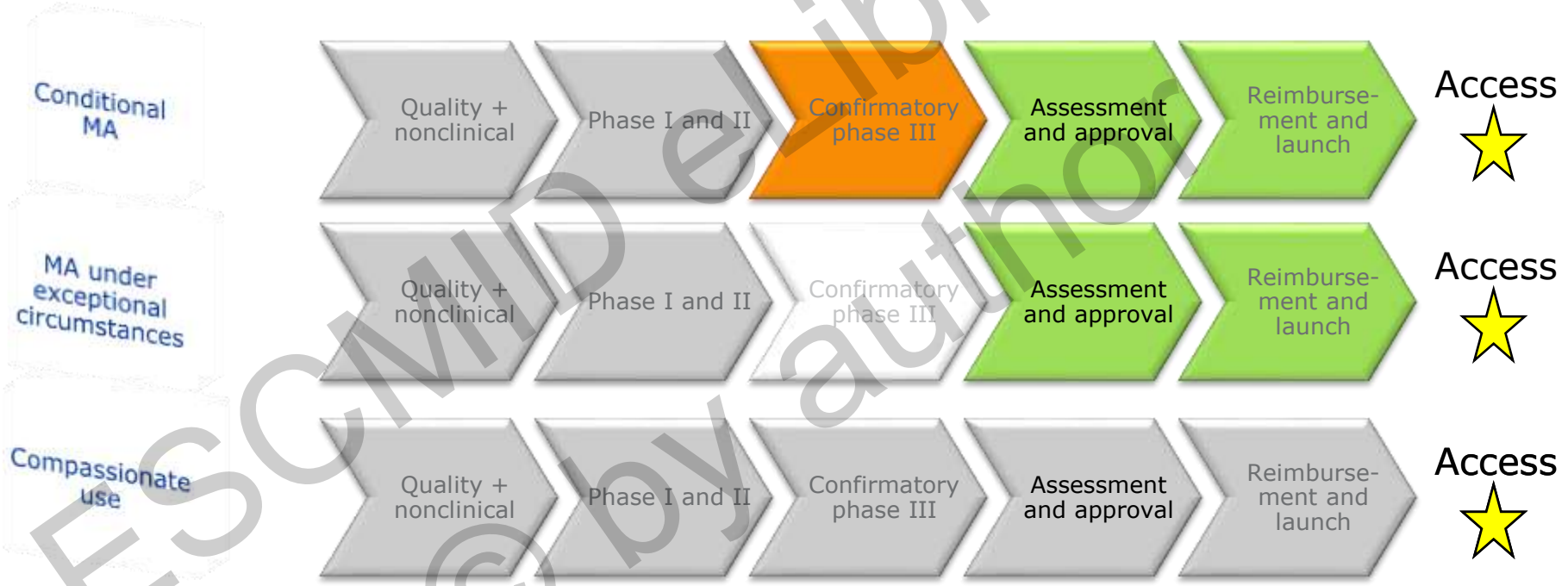
Innovation task force

- Forum for informal early dialogue

Early dialogue with EMA

- Other tools and initiatives

Tools in the Legislation



Conditional Marketing authorisation

Comprehensive data not yet available

Scope (at least 1)

- Seriously debilitating or life-threatening diseases
- Emergency situations
- Orphan products

Criteria (all)

- Positive benefit-risk balance
- Comprehensive data can be provided after authorisation
- Unmet medical needs will be addressed
- Benefits of immediate availability outweigh the risks

'**unmet medical needs**' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected

Commission Regulation (EC) No 507/2006

Marketing Authorisation Under Exceptional Circumstances

Impossible to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, for objective, verifiable reasons

Criteria (at least 1)

the indications are encountered so rarely that it be expected to obtain comprehensive evidence, or

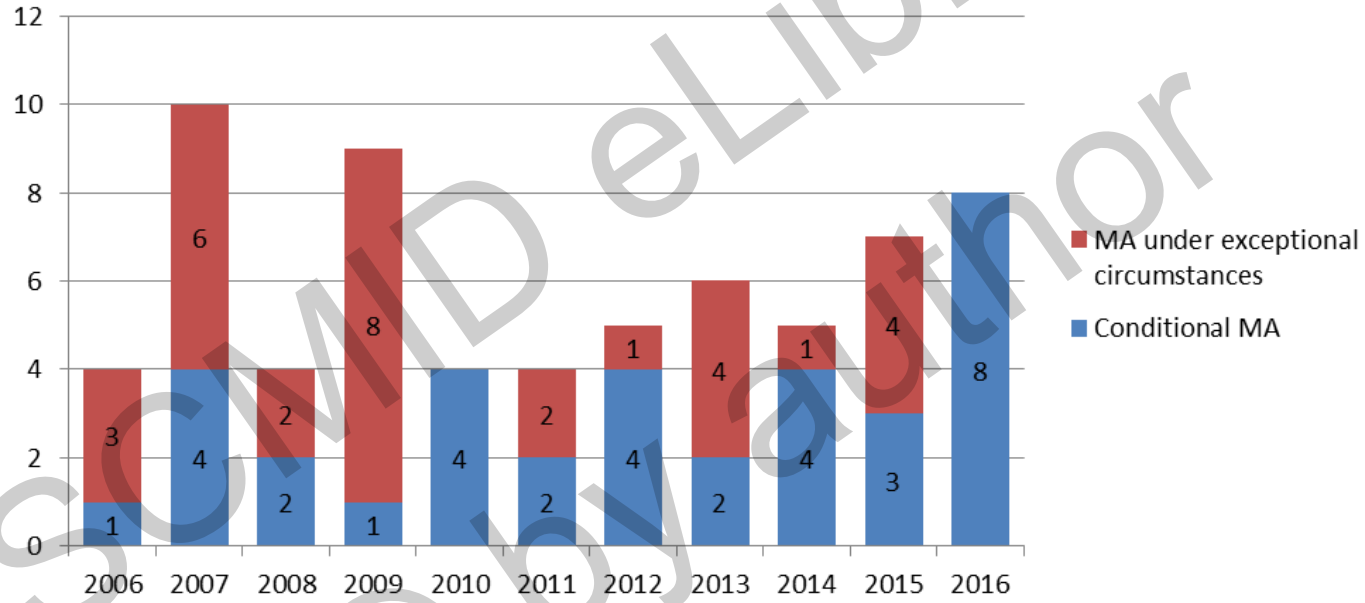
in the present state of scientific knowledge, comprehensive information cannot be provided, or

it would be contrary to generally accepted principles of medical ethics to collect such information

Comparison

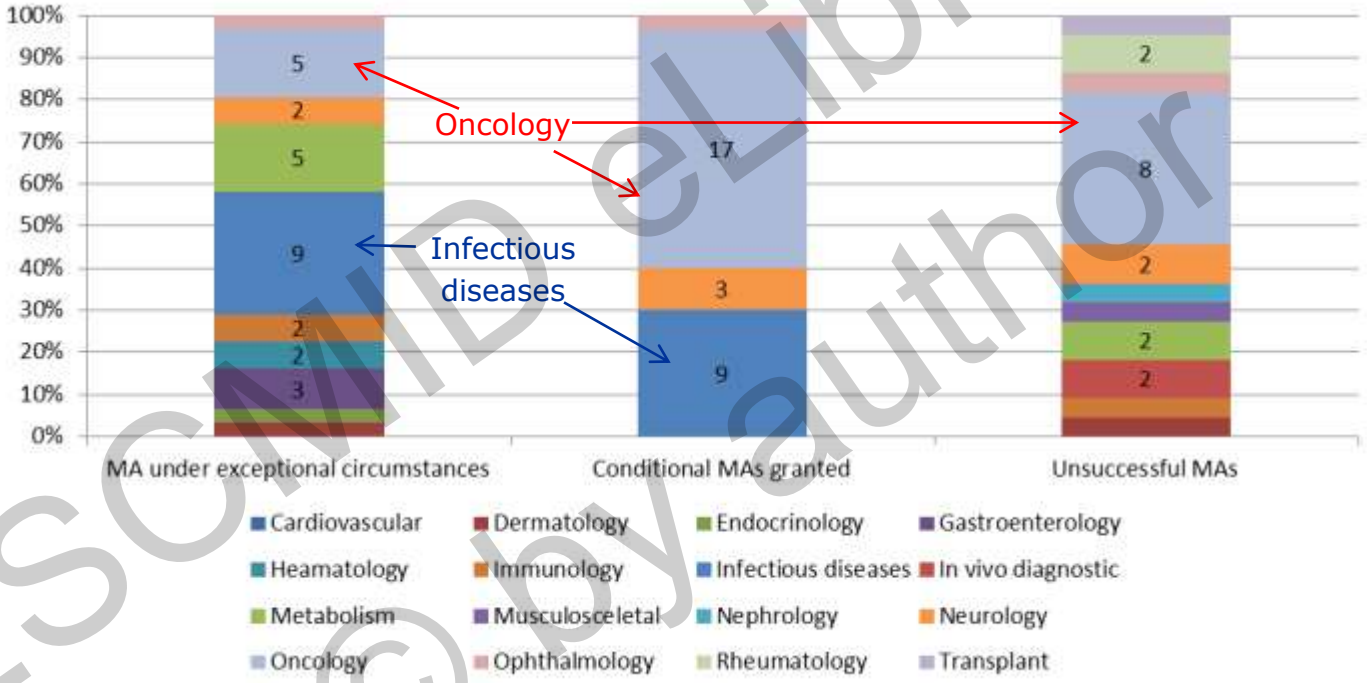
Conditional MA	MA under exceptional circumstances
Comprehensive data **after authorisation**	Comprehensive data **not possible**
To later **switch** to 'standard' MA	To remain such **indefinitely**
Valid for **1 year** only (annual renewals)	Valid for **5 years** (renewable) + annual re-assessment
Possible in centralised procedure only	Possible in all registration procedures
Specific Obligations + may have conditions	**Specific obligations** + may have conditions

Last 10 years in numbers



Data updated with DLP 31 Dec 2016

Therapeutic areas



Accelerated Assessment

- AA reduces the timeframe for review of an application to up to 150 days.
  - The Old AA split the assessment in **120/30** days.
  - The New AA split the assessment in **90/30/30** days.

Scientific Advice

- Scientific advice can be provided on **ANY scientific question** – quality, non-clinical and clinical
- At **any time point of the development** – early advice with subsequent follow-up is recommended
- **Broad advice on eligibility** of the proposed development for Conditional approval/Exceptional circumstances
- **Protocol assistance** for designated orphan medicinal products
- **Qualification of biomarkers** and other novel methodologies
- Possibility of **Parallel Consultation with HTA bodies**
- Possibility of **Parallel Scientific Advice with FDA**

Parallel Consultation with regulators and HTA

Synergy through alignment of evidence generation plans

Starting point: Regulators and HTAs

- answer different questions
- have different requirements in terms of evidence

Aim: decision makers come together early to discuss

- the planned development including populations / comparators / design of trial / endpoints
- the requirements for post-licensing evidence generation

Expectation: Optimised evidence generation plan ➔ Improve access for patients

Across the life cycle; early, late, and qualification (non product related)

EMA/ FDA interactions

- ***EMA/FDA Parallel scientific advice*:**
- **Review in parallel sponsor's scientific questions**
- **Discuss** via teleconference or in writing
- **Provide oral feedback to sponsor** at trilateral meeting
- **Provide individual formal feedback** to sponsor as outcome
- ***EMA/FDA Consultative Advice option*** allows sponsors to request scientific advice from one regulatory agency and concurrently notify the other regulatory agency of the request

Independently from the above options, new development plans are mutually discussed between FDA, PMDA, HC and EMA on a monthly basis

Eligibility to PRIME scheme

Based on Accelerated Assessment criteria

Medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation.

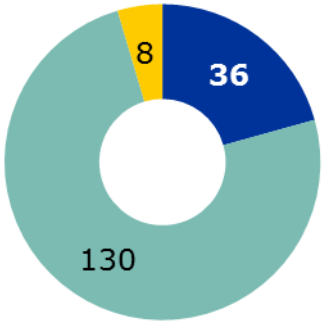
- Potential to address to a significant extent **an unmet medical need**
- Scientific justification, based on data and evidence available from nonclinical and clinical development

No satisfactory method or if method exists, bring a major therapeutic advantage

Introducing new methods or improving existing ones

Meaningful improvement of efficacy (impact on onset, duration, improving morbidity, mortality)

Two years of PRIME



■ Granted ■ Denied ■ Out of scope*

22% success rate

174 eligibility requests

> 50% from SMEs

36 granted*

+

Publication of report and list of products on EMA website

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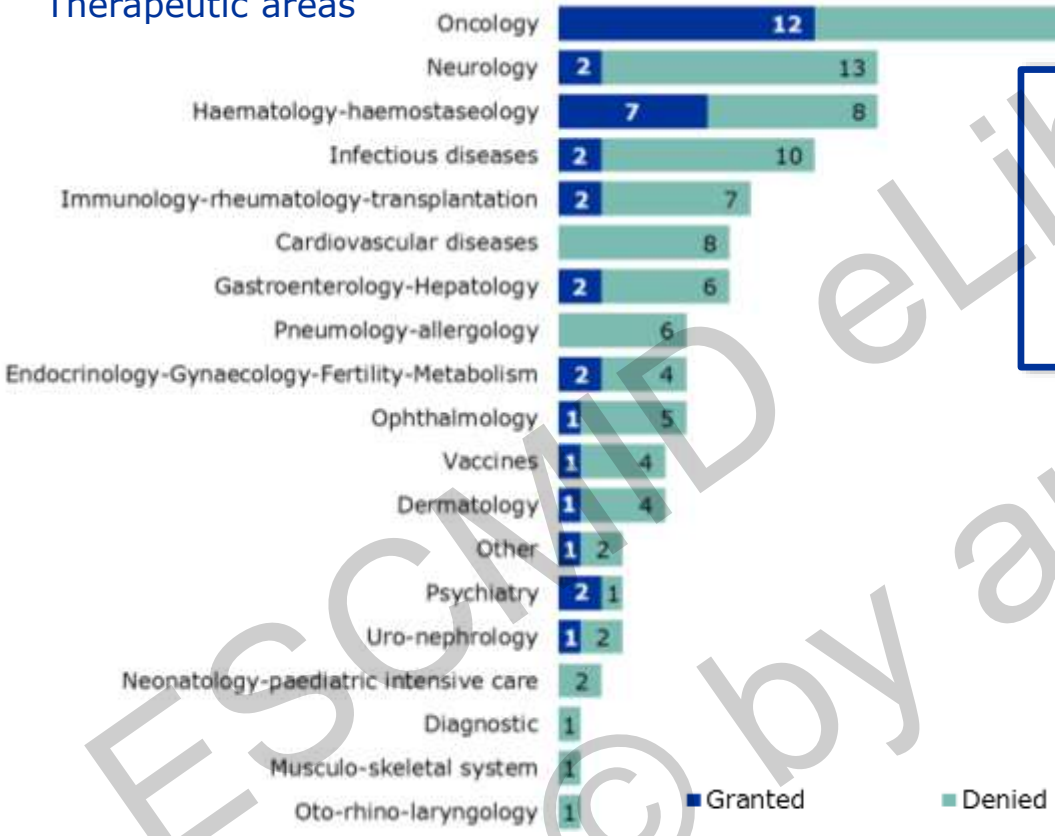
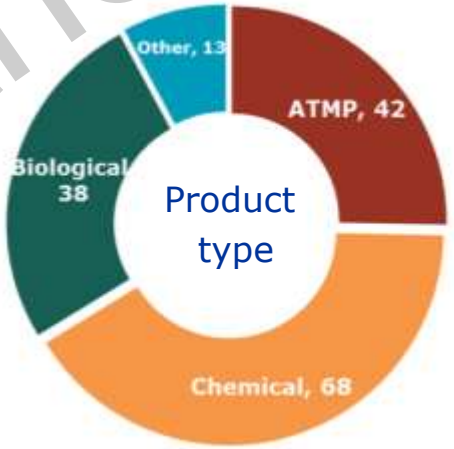
Therapeutic areas



>40 % in oncology/haematology

No antibacterial agent designated so far



Features of the PRIME scheme

Early access tool, supporting patient access to innovative medicines.

- **Written confirmation of PRIME eligibility** and potential for accelerated assessment;
- **Early CHMP Rapporteur appointment** during development;
- **Kick off meeting** with multidisciplinary expertise from EU network;
- **Enhanced scientific advice** at key development milestones/decision points;
- **EMA dedicated contact point**;
- **Fee incentives** for SMEs and academics on Scientific Advice requests.

EMA Guidance to developers of new antibacterial agents

- **CPMP/EWP/559/95 Rev 2 (2011)** Guideline on the evaluation of medicinal products indicated for treatment of bacterial infections
- **EMA/CHMP/351889/2013** Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections

These two guidelines will be merged into a single updated document

Concept Paper to be released soon

- **EMA/CHMP/594085/2015** Guideline on the use of pharmacokinetics and pharmacodynamics in the development of antimicrobial medicinal products
- **EMA/CHMP/187859/2017** Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address paediatric-specific clinical data requirements.
- ***DRAFT just released for consultation***.

Conclusions

- EMA makes various tools available to facilitate the development of new antibacterial agents
- The guidelines to industry in this area have been expanded and continuously updated in light of emergent needs
- Several options for interaction with EMA, from formal to more informal, are available and early dialogue is strongly encouraged
- Dialogue with international regulators and HTAs is increasing
- EMA creates also other opportunities to bring stakeholders together, e.g. dedicated workshops

Any questions?

Further information

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