Regulatory tools for early access: Conditional marketing authorisations (CMA)

STAMP 2nd meeting
6 May 2015

Olga Solomon, Deputy Head of Unit D5
Medicinal Products – Authorisations, European Medicines Agency
Directorate General for Health and Food Safety

Health and Food Safety

European Commission

Conditional marketing authorisation

Scope:

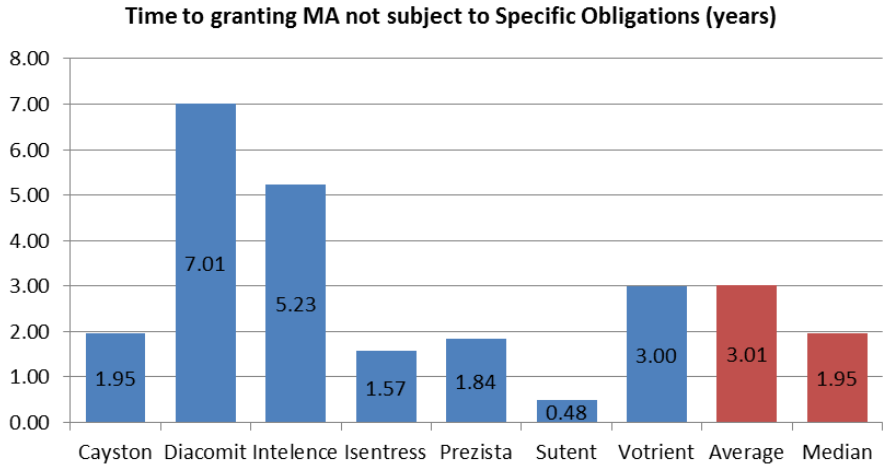
- for **seriously debilitating diseases or life-threatening diseases**; or
- to be used **in emergency situations**; or
- **orphan** medicinal products.

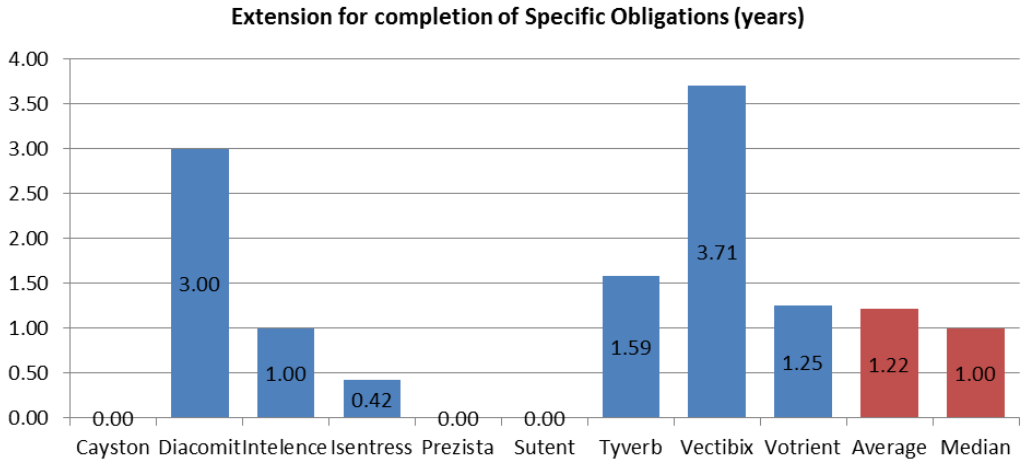
Criteria:

- the **risk-benefit balance is positive**; and
- it is likely that the applicant **will be in a position to provide comprehensive clinical data;** and
- **unmet medical needs** will be fulfilled; and
- the **benefit** to public health **from the immediate availability** on the market of the medicinal product concerned **outweighs the risk** inherent in the fact that additional data are still required.

Time to 'switch' to full MA

- For 7 products that currently have MA not subject to specific obligations, **full MA was granted on average in 3 years**
- Approximately **half of the products** had **changes to the scope and/or deadline** of at least one of the specific obligations
- For 9 products with specific obligations completed, **on average the due date for completion of last specific obligation was extended by 1.22** years





Slide courtesy of the European Medicines Agency

CMA aims to allow medicines **to reach patients with unmet medical needs earlier** than might otherwise be the case, and to ensure that **additional data** on a product are **generated**, **submitted**, **assessed** and **acted upon**

Observations/discussion at the 1st meeting of STAMP:

- ✓ 'Full' authorisation preferred over **CMA-negative perception**
- ✓ Perceived as **burdensome** by industry; specific obligations, annual renewal, no possibility to grant CMA for a new indication of an already authorised medicine with 'full' MA
- ✓ Perception that **compliance with specific obligations** is not optimal-regulatory actions
- ✓ **Lack of prospective planning** applying for CMA -perceived as '**rescue option'** towards the end of the MA evaluation procedure;
- ✓ Sometimes **difficulties with** health technology assessment (**HTA**) and **reimbursement bodies** at national level perception of 'incompleteness' (despite unmet medical need)

Reflection:

Can the use of CMA within the current legal framework **be optimised** by:

- clarifying and rationalising further the application of the legal requirements and procedural aspects of CMA
- improving the confidence in and perception of CMA by all stakeholders?

Ultimately, the CMA has the potential to offer early access to treatment for the benefit of the patients with unmet medical needs.

Process:

CHMP:

- ✓ Reflections on Conditional MA
- ✓ Revision of CHMP Guideline
- ✓ Recommendations for topics to be discussed at STAMP

STAMP:

- ✓ Discussion of regulatory and policy aspects related to the criteria and application of CMA within the legal framework

Discussion

Health and
Food Safety

European Commission

1. SCOPE OF CONDITIONAL MARKETING AUTHORISATION: SERIOUSLY DEBILITATING OR LIFE-THREATENING DISEASES

- **CHMP guideline**: *…..serious debilitation, or fatal outcome should be a prominent feature of the target disease and therapeutic indication*
- CHMP is now considering suitability of CMA also in conditions for which serious debilitation and life-threatening outcomes are expected **only in the long-term**

Discussion:

- **Do Member States have particular proposals on when/what conditions should be considered 'seriously debilitating' or 'life-threatening' diseases for the purposes of granting CMA within the legal context of Commission Regulation (EC) No 507/2006?**

European Commission

2. REQUIREMENTS FOR GRANTING CMAS: UNMET MEDICAL NEED

- '**unmet medical needs**': 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 *(Regulation (EC) 507/2006).*

- **CHMP guideline:** major therapeutic advantage would normally be based on meaningful improvement of efficacy or clinical safety.

- CHMP is now considering whether major improvements in patient care would be major therapeutic advantage.

European Commission

REQUIREMENTS FOR GRANTING CMAs: UNMET MEDICAL NEED

- **orphan designation requirement**: the applicant shall establish that there exists no satisfactory treatment authorised in the EU or if such method exists, that the medicinal product will be of significant benefit (*Regulation (EC) 141/2000*).

- '**significant benefit**' means a "clinically relevant advantage" or a "major contribution to patient care"(COM Reg. (EC) 847/2000). Further guidance about significant benefit in COM communication (2003/C 178/02).

- **'significant benefit' vs 'major therapeutic advantage'**: Level of evidence for major therapeutic advantage as regards CMA, not always enough to demonstrate significant benefit and to confirm orphan criteria at the time of MA.

European Commission

REQUIREMENTS FOR GRANTING CMAs: UNMET MEDICAL NEED

Discussion:

a. Are there **therapeutic areas** for which CMA could be appropriate and further explored for the benefit of patients in terms of unmet medical need?

b. Should potential **CMAs be encouraged** in therapeutic areas with limited experience with this type of authorisation (e.g. by promoting **early dialogue** between regulators and companies)?

c. What an **'unmet medical need'** means for the purposes of granting CMA (e.g. to address long term needs for the society such as antimicrobial resistance)? How should the term 'no satisfactory method' be understood within the legal definition of unmet medical need and from a health policy perspective?

d. What constitutes **major therapeutic advantage** for a product when existing therapeutic options exist in terms of fulfilling unmet medical need and for the purposes of granting CMA?

e. Should more **consistency** be ensured between the **'major therapeutic advantage'** and the **'significant benefit'** for orphan medicinal products eligible for the CMA ?

European Commission

3. CMA FOR A NEW INDICATION OF AN ALREADY APPROVED PRODUCT

COM REGULATION (EC) No 507/2006

- request/proposal for a CMA can be made 'in application submitted in accordance with Article 6 of Regulation (EC) No 726/2004'

Result

- CHMP not able to propose CMA for new indication(s) of an existing MA (e.g. by variation); a new application for the new (conditional) indication is required,
- two separate MAs may lead to delays in patient access to new indication, and is considered burdensome by industry (e.g. parallel post-authorisation maintenance)

Discussion

- **What is the experience of Member States as regards the need for two separate marketing authorisations for "conditional" and "non-conditional" indications for the "same" medicinal product?**
- **Can this delay patient access and increase burden for industry?**
- **Are there any proposals on what can be improved?**

European Commission

4. SCOPE AND STREAMLINING OF ANNUAL RENEWAL

- Application for renewal at least six months before expiry of the CMA. PSUR at least every six months following the granting or renewal of a CMA
- CHMP shall assess the renewal, on the basis that the **r/b balance is to be confirmed**, taking into account the **specific obligations** and give opinion whether the specific obligations or their timeframes need to be retained or modified,
- **CHMP guidelines**: Actual PSUR data required to 'where the due date coincides with the renewal application'. A clinical expert statement addressing the b/r on the basis of *inter alia*, recent PSUR data.
- Data lock points (DLP) and review period for 'PSUR data' in annual renewals are different from those of the actual PSURs.
- New PhV legislation: the scope of the **PSUR assessment** has changed. It **includes a b/r assessment** and if necessary **regulatory measures** can be taken directly.

4. SCOPE AND STREAMLINING OF ANNUAL RENEWAL

Discussion:

a. Do you agree that efforts undertaken under a **PSUR assessment** and the **annual reassessment may overlap**?

b. During **annual renewal** procedural of CMA, **could the benefit-risk reassessment be focused on data generated by SOs**, taking into **account the outcomes of recent PSUR assessments**, rather than requiring (re) submission of PSUR data?

c. Would such an approach be in principle compatible with the legal framework and, if yes, could STAMP accept that this is **a scientific question that needs to be addressed only by the CHMP**?

European Commission

5. NEGATIVE PERCEPTION OF CMA

CMA is also being perceived as a 'rescue' solution during assessment rather than a prospectively planned application. HTA bodies and pricing and reimbursement authorities seem often to also have difficulties with products conditionally authorised.

Discussion:

a. What is the **experience of national regulatory and pricing and reimbursement authorities with CMA**? Member States representatives could use examples of specific CMA products to demonstrate positive and negative aspects.

b. What are the **aspects that would allow reimbursement of CMA products (for unmet medical needs)** when the benefit risk balance has been demonstrated on the basis of less comprehensive data?

c. Could **prospective planning and early dialogue** with relevant stakeholders (including companies, regulatory agencies, HTA bodies, payers, patients, and healthcare professionals) **improve the design and feasibility of SOs**?

European Commission

5. NEGATIVE PERCEPTION OF CMA

- **Discussion (cont):**

d) Could such **prospective planning and early dialogue facilitate HTA and pricing and reimbursement decisions**?

e) How **could HTA bodies and payers be more extensively involved** to support early access to medicines with CMA?

f) What **other aspects** need **to be addressed to improve the perception of CMA**?

Keep in mind: **holistic approach** and a **link with other on-going initiatives** such as the adaptive pathways pilot project, the parallel scientific advice, the update of the CHMP guideline on accelerated assessment.