Medicines & Healthcare products Regulatory Agency

PCWP : Article 8.2 et al

September 2018

Daniel O'Connor (UK COMP representative)
On behalf of the COMP

CPRD NIBSC MHRA

Article 8.2

- Orphan regulation provides incentives for the research, development and placing on the market of designated orphan medicinal products
  - 10 year period of market exclusivity is very valuable to companies
- Little known and barely used provision in the orphan regulation that allows for the period of market exclusivity to be reduced to six years
- Called ‘Article 8.2’, where:
- ‘*Regulation provides that this period may be reduced to six years if, at the end of the fifth year, it is established, in respect of the medicinal product concerned, that the designation criteria laid down in Article 3 are no longer met, inter alia, where it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity*’
- There is a specific EC guideline on triggering Article 8.2

Article 8.2

- The procedure of Article 8(2) is triggered by information received from a Member State (MS) relating to a specific designation of an orphan medicinal product
- The procedure is not intended to be systematic for all orphan designated products
- Member States should only inform the European Medicines Agency if they have sufficient indications suggesting that the designation criteria are no longer met

C 242/8 EN Official Journal of the European Union 23.9.2008

Guideline on aspects of the application of Article 8(2) of Regulation (EC) No 141/2000 of the European Parliament and of the Council: Review of the period of market exclusivity of orphan medicinal products

(2008/C 242/07)

1. **INTRODUCTION**

Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products ([1]) entered into force on 28 April 2000. It lays down a Community procedure for the designation of medicinal products as orphan medicinal products and provides incentives for the research, development and placing on the market of designated orphan medicinal products.

'A medicinal product shall be designated orphan medicinal product if its sponsor can establish:

(a) that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10 thousand persons in the Community when the application is made (so-called "**prevalence**" criterion), **or**

Article 8.2

- The MS should provide the rationale for its doubts and include appropriate data justifying why at least one of the original designation criteria of the orphan medicinal product concerned may no longer be met

- Assessment is carried out within the EMA by the Committee on Orphan Medicinal Products (COMP)

- COMP will provide an opinion as to whether the market exclusivity should be maintained or reduced

- First step: If the initial designation criteria are still met, COMP will adopt an opinion recommending that the period of market exclusivity is not reduced

- Second step: If the original criteria are no longer met, COMP will review the other designation criteria of Article 3(1)

  – where the initial designation was based on prevalence, COMP will assess the return on investment of the product – profitability

Article 8.2

- If the available evidence is insufficient to establish with reasonable confidence whether or not the designation criteria continue to be met, COMP will recommend that the period of market exclusivity is not reduced

- The Commission will take a decision on whether market exclusivity is to be maintained or reduced, on the basis of the opinion of COMP

Only one example

- At the request of the UK, the COMP reviewed the criteria for orphan designation for Plenadren
- The COMP looked at the seriousness and prevalence of the condition and the existence of other methods of treatment, and whether the medicine is of significant benefit to patients with adrenal insufficiency
- Recommendation to maintain the period of market exclusivity at 10 years

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 April 2016
EMA/COMP/263073/2016
Committee for Orphan Medicinal Products

COMP assesses whether Plenadren still meets orphan designation criteria

Recommendation to maintain the period of market exclusivity at 10 years

During its meeting of 21 to 23 March 2016, the Committee for Orphan Medicinal Products (COMP) assessed whether Plenadren (hydrocortisone) still met the criteria for orphan designation as there appeared to be an increase in the prevalence of the condition.[1] Plenadren has been authorised in the European Union for the treatment of adrenal insufficiency since 3 November 2011. At the time, because Plenadren met the criteria for orphan designation, it was granted 10 years of market exclusivity in the EU.[2]

A Member State can ask that this period of market exclusivity be reduced to 6 years if at the end of 5 years the criteria for orphan designation no longer apply and the medicine is sufficiently profitable.

At the request of the United Kingdom, the COMP therefore reviewed the criteria for orphan designation for Plenadren. The Committee looked at the seriousness and prevalence of the condition and the existence of other methods of treatment. As other methods of treatment are authorised in the European Union (EU), the COMP also considered whether the medicine is of significant benefit to patients with adrenal insufficiency. As these criteria continue to be met, the COMP recommended that the 10-year period of market exclusivity granted to Plenadren in 2011 for the treatment of adrenal insufficiency should not be reduced.

COMP paper on defining the orphan condition

- Discusses challenging areas when delineating an orphan condition

- Four main sections:
  - Symptoms of a disease
  - Subsetting - severity/ stages and biomarkers
  - Iatrogenic and adverse reactions to a medicinal product
  - Treatment modalities

- Provides an at-a-glance chart of available guidance

COMMENT

Defining orphan conditions in the context of the European orphan regulation: challenges and evolution

Daniel J. O'Connor[1,12], Maria E. Sheean[2,3,12], Matthias P. Hofer[2,12], Stelios Tsigkos[2], Segundo Mariz[2], Laura Fregonese[2], Kristina Larsson[2], Virginie Hivert[4], Kerstin Westermark[5], Frauke Naumann-Winter[6], Violeta Stoyanova-Beninska[7], Ingeborg Barišić[8], Giuseppe Capovilla[9], Armando Magrelli[10] and Bruno Sepodes[11]*

The definition and acceptability of an orphan condition is pivotal for the assessment of European orphan medicinal product designation applications, and consequently the eligibility for incentives. Here, based on the experiences of the Committee for Orphan Medicinal Products, we discuss how to define orphan conditions in the context of the European regulatory framework.

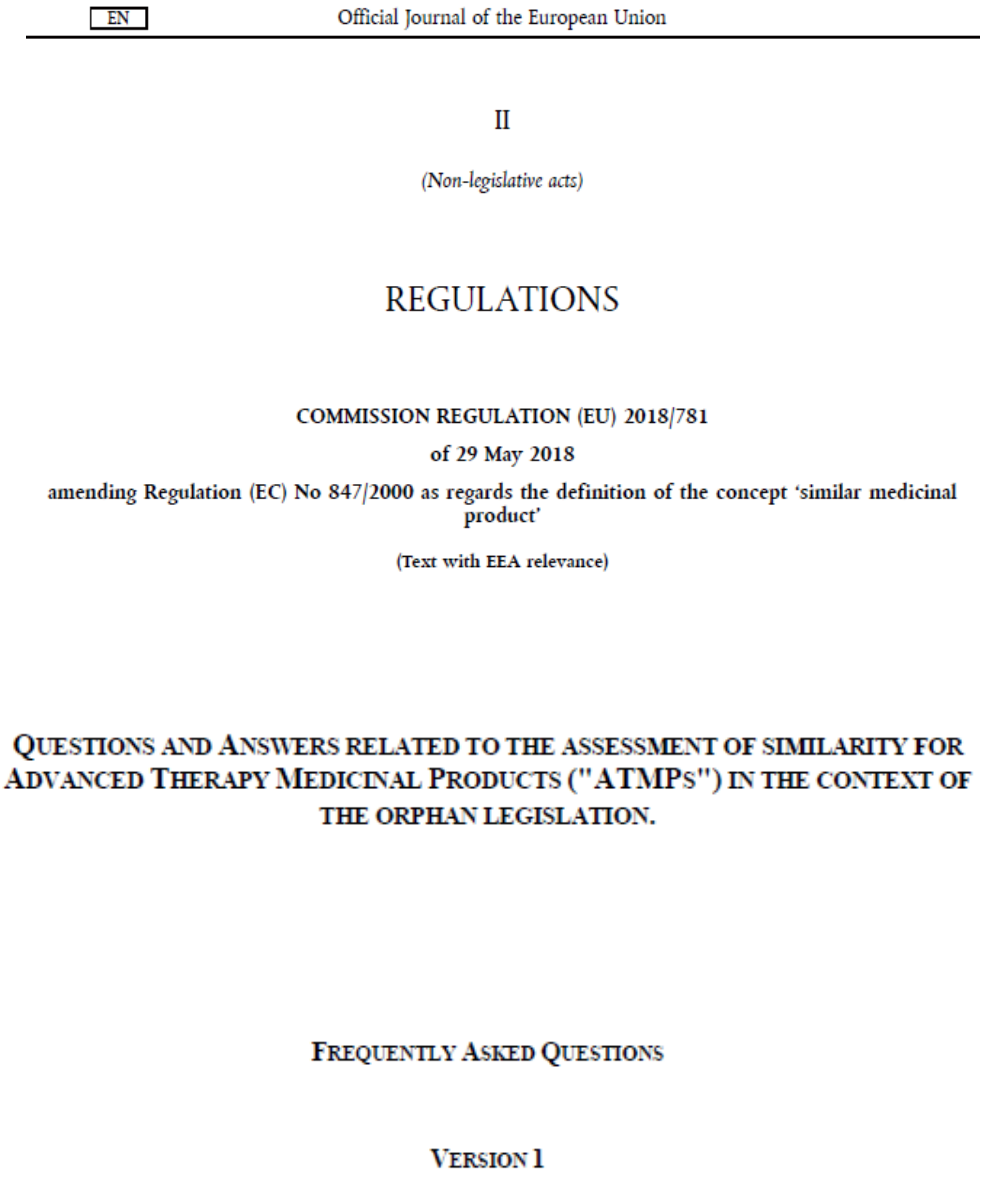
- Explains COMP decisions in the context of the EU orphan drug regulation and provides some discussion points to help future sponsors

EC activities

- Regulation (EC) No 847/2000 provides a definition of 'similar medicinal products' for the purposes of the application of the incentives provided under the Regulation

- Due to major developments in the field of biological medicines and technical progress including advanced therapy medicinal products (ATMPs), the definitions required adaption

- Two new documents released by the EC in May 2018 to reflect changing science



EN Official Journal of the European Union

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) 2018/781

of 29 May 2018

amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'

(Text with EEA relevance)

QUESTIONS AND ANSWERS RELATED TO THE ASSESSMENT OF SIMILARITY FOR ADVANCED THERAPY MEDICINAL PRODUCTS ("ATMPS") IN THE CONTEXT OF THE ORPHAN LEGISLATION.

FREQUENTLY ASKED QUESTIONS

VERSION 1

EMA activities

- An overview of the EU's orphan designation programme provided in a infographic →

- Questions and answers document addresses some common misunderstandings ↓

28 February 2018
EMA/551338/2017

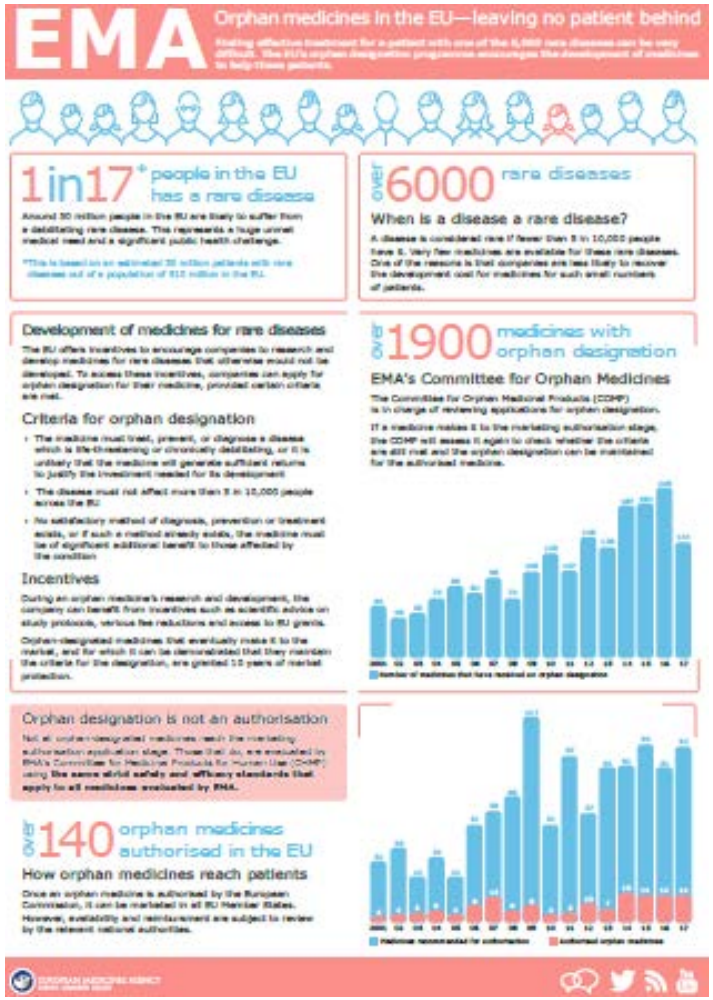
Rare diseases, orphan medicines

Getting the facts straight

EMA is eager for European citizens with rare diseases to have access to specific and effective medicines. The European Union's orphan legislation has been designed to help overcome the extra hurdles these medicines face to get on the market.

Broadly speaking, the orphan legislation foresees giving orphan designation for substances that could be used for treating, preventing or diagnosing a rare and serious condition. Orphan designation can help the medicine's developer advance the medicine to the stage where it can be authorised to be put on the market. Formal approval (marketing authorisation) is needed before a medicine can legally be marketed.

Misunderstandings often arise about orphan medicines and how orphan designation is given. The following questions and answers address some common ones.



Thank you

Dan O’Connor : daniel.oconnor@mhra.gov.uk

© Crown copyright 2013