EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

PHARM 707

PHARMACEUTICAL COMMITTEE
28 April 2016

Subject: **Update on Court cases**

Agenda item 1i

- **Case C-82/15P, Judgement of 3 December 2015, PP Nature Balance v Commission**

Background: With this appeal a company challenged specific aspects of the first instance ruling of the General Court in case T-189/13, which the Commission won.

The case concerns the results of a Union review procedure ('Article 31 referral') of tolperisone-containing medicinal products. This scientific of the product by the European Medicines Agency resulted in a Commission decision, which obliged Member States to delete certain indications from national marketing authorisations of those products.

Tolperisone is a centrally acting muscle relaxant first synthesized in 1956, and used in clinical practice since the 1960's. In 2011 Germany initiated an EU review procedure of those products under Article 31 of Directive 2001/83. Germany considered that the numerous reports of hypersensitivity reactions received in the post-authorisation phase were indicative of a safety concern which is not balanced by the limited evidence of efficacy. In its scientific opinion the European Medicines Agency concluded that the risk-benefit balance in certain indications is indeed no longer favourable and recommended variation of the marketing authorisations by deleting some indications. With its implementing decision of January 2013 the Commission followed the opinion and ordered Member States to vary the national marketing authorisations accordingly.

In April 2013 one of the marketing authorisation holders lodged an application under Article 263 TFEU for the partial annulment of the implementing decision of the Commission (Case T-189/13). The company contested the legality of the scientific opinion as well as the subsequent Commission decision. In December 2014 the General Court dismissed this action.

In January 2015, the company appealed the judgement before the Court of Justice claiming that the General Court made some errors of law. In its submission to the Court, the Commission considered those claims unfounded.

Main considerations of the Court of Justice:

The Court dismissed the appeal in its entirety and rejected all five pleas of the appellant.

The Court reiterated its constant case-law that Article 116 of Directive 2001/83, which sets the grounds for regulatory actions on marketing authorisations, has to be interpreted in the light of the precautionary principle. It is therefore sufficient for the Commission to point to serious doubts regarding the benefit/risk balance ("la Commission peut se limiter à fournir des indices sérieux et concluants, qui, sans écarter l'incertitude scientifique, permettent raisonnablement de douter de l'innocuité ou de l'efficacité du medicament", para. 24).

The Court also confirmed that a previous assessment of the same data by a national authority has no impact on whether that data should be considered as new for the purpose of the assessment at EU level: "aucune disposition de la directive 2001/83 n'interdit au comité des médicaments à usage humain, dans le cadre d'une procédure suivie au titre de l'article 31 de cette directive, de prendre en considération des informations pertinentes, au motif qu'elles ont déjà été soumises à l'appréciation d'une autorité nationale. Une telle interdiction serait d'autant moins compréhensible qu'elle conduirait à interdire à ce comité de prendre en considération les données scientifiques en possession d'une autorité compétente d'un État membre ayant justifié l'ouverture, à la demande de ce dernier, de la procédure visée à l'article 31 de cette directive" (para. 36).

- **Case C-138/15P, Judgement of 3 March 2016, TEVA v EMA**

Background: With this appeal Teva challenged specific aspects of the first instance ruling of the General Court in case T-140/12, which EMA won.

Glivec and Tasigna are similar medicinal products that have been developed by Novartis to treat an orphan disease. Despite being similar, both products were awarded with an independent 10-year market exclusivity period under the Orphan Regulation, as Tasigna – the second product - was found to be of significant benefit compared to Glivec. For Glivec the exclusivity period expired in 2011, while for Tasigna it is still running.

In 2011 Teva applied for a generic marketing authorisation of Glivec. EMA refused to validate this application as far as it covered therapeutic indications for which the orphan product Tasigna had been authorised. EMA considered that those indications are covered by the market exclusivity for Tasigna and that such validation would have led to a violation of the market exclusivity provided under Article 8(1) of the Orphan Regulation for Tasigna.

Not satisfied with this decision, Teva lodged an application under Article 263 TFEU for the annulment of EMA's decision not to validate the generic marketing authorisation application (case T-140/12). The Commission intervened in support of EMA.

In January 2015 the General Court dismissed this action. Subsequently, the company appealed before the Court of Justice claiming that the General Court made several errors of law. With its judgement, the Court dismissed the appeal and confirmed the position of EMA (and the Commission as intervener).

Main considerations of the Court:

The Court dismissed the appeal in its entirety and rejected all pleas of the appellant.

With its first plea, Teva took issue with the General Court's interpretation of the conditions for the application of the ten-year market exclusivity period under Article 8(1) of the Orphan Regulation. Teva had argued that where a company develops a second orphan product, which does not contain the same active substance as the first product, but

is nevertheless similar to that first product, that second product would not benefit from an independent market exclusivity period, if that second product was authorised under one of the derogations provided by Article 8(3).

As confirmed by the Court of Justice, the General Court was right to dismiss this argument. None of the provisions in the Orphan Regulation expressly provides that a marketing authorisation granted on the basis of Article 8(3) of Regulation No 141/2000 (ie. under the derogations) is to be denied the benefit of the ten-year period of exclusivity provided for in Article 8(1). (para. 30)

Regulation No 141/2000 does not contain any provision under which it is possible not to apply the ten-year period of market exclusivity to orphan medicinal products that have been granted marketing authorisation for certain therapeutic indications, with the exception of the situations set out in Article 8(2). As a consequence, where a similar medicinal product that has been granted marketing authorisation under Article 8(3) of Regulation No 141/2000 is an orphan product, it enjoys the market exclusivity provided in Article 8(1). (para. 31)

Contrary to the contentions of the Teva companies, that interpretation is neither illogical nor at odds with the purpose or scheme of Article 8 of Regulation No 141/2000. Paragraphs 1 and 3 of Article 8, although complementary, are different in scope and purpose. The fact that an orphan medicinal product enjoys the period of market exclusivity provided in Article 8(1) does not preclude a second, similar product which has been authorised in accordance with Article 8(3) being granted, in turn, market exclusivity, as long as it also fulfils the requirements set out in Article 3(1) for designation as an orphan medicinal product. (para. 32)

With its second plea, Teva contested the effects of this interpretation on the term of the market exclusivity period. Granting market exclusivity to the second similar product would lead to the prolongation the market exclusivity of the first product, in view of their similarity. According to Teva this has been demonstrated by EMA's refusal to validate generic marketing authorisation applications for copies of Glivec. The Court of Justice dismissed this argument and confirmed the finding of the General Court that

- there is no formal extension of the market exclusivity period of the first product due to the fact that market exclusivity was granted to a second similar product (para. 39);
- the market exclusivity period can only be curtailed on the basis of Article 8(2) and not on the basis of possible secondary effects which such market exclusivity may produce for other similar products.

Overall, the two rulings (first and second instance) provide clarity regarding the scope of the market exclusivity concept in case of authorisation of subsequent similar products.

➢ Interesting pending cases

Case **T-672/14** (A. Wolff v Commission), direct action seeking the partial annulment of the Commission decision in an Article 31 referral re: estradiol containing medicines;

Case **T-269/15** (Novartis v Commission), direct action seeking the annulment of the Commission decision to grant marketing authorisation to the medicinal product Vantobra;

Cases **T-235/15, T-718/15 and T-729/15**, access to document cases against EMA concerning the confidentiality of scientific opinions on similarity/clinical superiority under the Orphan Regulation and/or clinical study reports;

Case **T-80/16** (Shire v EMA), direct action seeking the annulment of EMA's decision not to validate an application for an orphan designation;

Case **C-629/15P (**and **C-630/15P)**, appeal of a pharmaceutical company against the General Court ruling in case T-472/12 and T-67/13 (Global marketing authorisation concept);

Case **C-114/15**, preliminary reference concerning the possibility of livestock farmers to (parallel) import veterinary medicinal products from other Member States;

Case **C-148/15**, preliminary reference concerning the applicability of the German system of fixed prices to products bought from non-German internet pharmacies;

Case **C-276/15**, preliminary reference concerning pharmacy preparations (Article 3 of Directive 2001/83);

Case **C-296/15**, preliminary reference concerning tendering practices of Slovenian hospitals with regard to the procurement of plasma products;

Case **C-621/15**, preliminary reference concerning the liability for medicinal products (Article 4 of Directive 85/374 - standard of proof).

Action to be taken:
For information