General Court of European Union Confirms Withdrawal Of Orphan Medicine Status Because Cancer Medicine Elotuzumab No Longer Offers Significant Benefit Over Alternative Treatment

On 5 December 2018, the General Court of the European Union (the "GC") dismissed a request for annulment of a decision of the European Commission (the "Commission") which had found that elotuzumab no longer met the criteria for designation as an orphan medicinal product.

Bristol-Myers Squibb ("BMS") had obtained the designation of elotuzumab as an orphan medicinal product indicated for the treatment of multiple myeloma, a bone marrow cancer, under Regulation No 141/2000 on orphan medicinal products. BMS later submitted to the European Medicines Agency ("EMA") an application for marketing authorisation ("MA") for elotuzumab under the brand name Empliciti®. However, before the MA was granted, Amgen had secured an MA for Kyprolis® (carfilzomib), a new medicine with a similar indication.

On 11 May 2016, BMS obtained an MA for Empliciti® but was implicitly advised that its medicine had lost the orphan medicinal product status on the grounds that this medicine no longer satisfied the criterion of significant benefit pursuant to Article 3(1)(b) of Regulation No 141/2000, especially when compared with Kyprolis®. BMS disagreed and brought an action for annulment of that decision before the GC.

BMS's action for annulment focused on the alleged infringement of Article 5(12)(b) of Regulation No 141/2000. According to that provision, a designated orphan medicinal product will be removed from the Community Register of Orphan Medicinal Products if it no longer meets the criteria for orphan medicine status of Article 3(1). The criterion at issue in this case was whether Empliciti® would offer a significant benefit to those affected by the relevant condition which alternative treatments would not be able to match.

BMS put forward three major arguments.

(1) First, BMS contended that Kyprolis® must not be taken into account in the review of the significant benefit because it had been authorised after the submission of the application for an MA for Empliciti®. According to BMS, this approach called

into question compliance with the principle of proportionality and was also unfair because it meant that BMS had not had sufficient time to collect all the necessary data.

The GC dismissed this argument and, relying on its ruling in *Now Pharm* v *Commission*, T-74/08, held that the orphan medicine in question has to be compared with all medicinal products that were authorised in the EU, without exception, and that both Articles 5(12) and 7(3) of Regulation No 141/2000 provide as the deadline for the examination of the designation criteria (i.e., the date on which the Commission is to determine whether the orphan medicine satisfies the requirements for orphan medicine status), the grant date of the MA and not that of the application for the MA.

The GC also decided that the principle of proportionality had not been breached because the assessments concerning the significant benefit criterion were carried out objectively and from a purely scientific point of view.

(2) Second, BMS advanced the somewhat contorted argument that conclusive evidence should show that Empliciti® is no longer of significant benefit, not that it is of significant benefit.

The GC disagreed again and referred once more to the obligation under Articles 5(12)(b) and 7(3) of Regulation No 141/2000 to review the orphan medicine criteria before granting an MA and for the decision-making bodies, namely EMA's Committee for Orphan Medicinal Products ("COMP") and the Commission, to carry out a complete re-evaluation of the designation criteria on a scientifically sound basis.

(3) Third, BMS argued that the test for the assessment of significant benefit is overly rigid. According to BMS, the COMP should have (i) conducted a more global assessment, focusing on all of the evidence that could substantiate its claim of significant benefit; (ii) used the general criterion of benefit for the patient; and (iii) applied a standard of proof that did not require conclusive proof and could allow for estimates and assumptions based on the available data, especially when taking into account the relevant circumstances, including the practical impossibility for the applicant to produce new comparative data.

The GC did not buy BMS's argument and, deferring to the work carried out by the COMP, simply stated that the COMP had worked accurately as was evidenced by the proper functioning of the COMP, the internal consistency of the opinion and the statement of reasons in support of the decision. The GC was satisfied that the scientific findings were linked to the conclusions drawn with regard to the fulfillment of the orphan medicine criteria.

On this basis, BMS's action was dismissed. Still, BMS obtained something of a consolation prize in that the GC held the Commission liable for the procedural costs. According to the GC, the Commission had not acted as a reasonably careful administrator in adopting its decision on the loss of orphan medicine status only implicitly. The GC made it clear that the Commission should have taken its withdrawal decision in an express form.

While on its facts, the decision of the Commission and its endorsement by the GC would seem legitimate, the judgment will be met with a degree of anxiety by industry as it is facing a Commission review of Regulation No 141/2000. This is because the orphan medicine rules and other measures in support of pharmaceutical innovation draw criticism from certain quarters, including social security payers. The industry therefore feels it stands to lose from the Commission review.

Case T-329/16, Bristol-Myers Squibb Pharma v. European Commission and European Medicines Agency

14 January 2019