WRITTEN QUESTION E-2144/01
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to the Commission

Subject: Orphan Drug Directive - marketing authorisation for the treatment of Fabry's Disease

When drafting and discussing the Orphan Drug Directive, nobody apparently considered the possibility that two products for the same indication could be submitted at the same moment. This however seems to have happened in July 2000 for Fabry's Disease. Both products received from the COM (Committee for Orphan Medicines) an orphan drug status. Moreover, they were both given by the CPMP (Committee for Proprietary Medicinal Products) a 'positive opinion' for granting marketing authorisation on 29 March 2001. Since Directive EC65/65, the criteria on which a pharmaceutical product has to be evaluated for marketing authorisation are quality, safety and efficacy. The efficacy of a pharmaceutical product has to be proven on the basis of clinical studies with validated endpoints for clinical benefits, and not based on non-validated so-called 'surrogate markers'. In this case, one product, Replagal, showed clinical benefits by reducing pain, improved renal function and a reduction of the cardiac mass. Another product, Fabrazyme, has not been able to document clinical benefits, but only effect on a non-validated 'surrogate marker'. This latter fact has also been stated by the company itself as well as its principal investigator.

1. How can a product receive a positive opinion for marketing authorisation in Europe, based on non-validated surrogate markers, when it has failed to demonstrate clinical benefits? Even more remarkable, how could this happen when the other product has documented significant clinical benefits, with a probably better safety profile?

2. How can it be in the interests of patients with a debilitating orphan disease to be treated with a product approved on a non-validated surrogate marker, when they have to wait for the outcome of future studies to know if there may be a clinical benefit, especially in the case where another product is scientifically proven to have clinical benefits?

3. Why has the letter from TKT Europe 5S of December 21 2000, dealing with this matter and sent to your Directorate c/o Pharmaceuticals and Cosmetics Unit, never officially been answered, with regard to the use of non-validated surrogate markers? One might assume that the transparency of the process could be served with an early answer?

4. Does this positive opinion from the CPMP for a product with effects only on a non-validated surrogate marker, reflect a shift in policy on allowing marketing authorisations in Europe, and if so, why has this not been publicly communicated to the industry and medical community?