Orphan drug denied reimbursement in health technology assessment

Contributed by **Advokatfirman Lindahl**

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Facts

A pharmaceutical company recently applied to the Dental and Pharmaceutical Benefits Agency (TLV) for a pricing and reimbursement decision. The Swedish reimbursement system is product based as opposed to indication based. However, it is possible to limit reimbursement to a certain indication or patient group.

The medicinal product at issue has been approved for two heart conditions:

- pulmonary arterial hypertension (PAH), for which there are other approved treatments; and
- chronic thromboembolic pulmonary hypertension (CTEPH), for which it has orphan drug status and is the only approved treatment. CTEPH is a fatal condition when left untreated.

Decision

Swedish reimbursement legislation provides that a prescription-only medicine is included in the reimbursement scheme if there are no other available medicines or therapies considered to be significantly more effective.

The TLV stated that the fact a medicinal product is the only approved product for a certain indication does not automatically mean that it will be granted reimbursement.

It further referred to the fact that PAH-specific treatments are widely used for the off-label treatment of CTEPH, which was not contested by the pharmaceutical company.

The TLV concluded that while indirect comparisons between treatments are associated with a high degree of uncertainty, it considered the CTEPH product to be equivalent to the PAH-specific treatments. In this comparison, the CTEPH product was considered cost effective only if the PAH-specific treatments had not produced a sufficient effect. Therefore, the CTEPH product was granted a limited reimbursement (ie, for the treatment of patients who had not responded to PAH-specific treatments).

The company appealed the decision to the Stockholm Administrative Court, arguing that its reasoning had been misrepresented in the TLV's decision. While the company did not contest the use of PAH treatments for CTEPH *per se*, it did contest that off-label use was cost effective. In accordance with clinical practice for the treatment of very severe and fatal illnesses that have no approved treatments, patients suffering from CTEPH have previously been treated with PAH-specific treatments because the lack of any treatment is ultimately fatal. Therefore, off-label use has previously been the only existing method to treat patients in accordance with clinical practice.

The company further referred to the 2014 European Society of Cardiology Guidelines on the diagnosis and management of acute pulmonary embolism, in which its CTEPH product was recommended as first choice (Class 1) for treatment. The guidelines also stated that off-label treatment may be considered. However, as the company pointed out, this treatment was given the second to lowest recommendation level possible (Class II(b)). Thus, the company argued that the TLV's finding that the CTEPH product and the comparator were equivalent was incorrect from a medicinal point of view.

Finally, the company argued that the limitation of reimbursement is contrary to Swedish pricing and reimbursement laws. The legislation states that a medicinal product will be included in the reimbursement scheme if there are no other available medicines or therapies considered to be significantly more effective. For the CTEPH indication, there had previously been no approved medicines or treatments available. The legislation explicitly states that a prescription-only medicine

must be included in the pricing and reimbursement system given that there are no other medicines or treatments available and that, after an assessment of efficacy and adverse events, the product can be significantly more effective for its purpose.

The company stated that the TLV had not given it sufficient time to submit data on comparisons between the CTEPH product and placebo treatment – something which the TLV had offered the company at a very late stage of the application process – and that as a result the treatments were entirely different and the comparison was therefore incorrect.

Comment

The EU Regulation on Orphan Medicinal Products (141/2000) was adopted to promote the development of effective treatment for patients suffering from rare diseases. The regulation aims to encourage investment in the research, development and marketing of orphan medicinal products. It therefore grants market exclusivity for 10 years after marketing authorisation has been granted.

Regarding rare diseases, the off-label use of orphan products is quite extensive, as the conditions are generally severe and/or chronic, and sometimes even terminal.

The TLV's position is that the legislative requirement of 'significantly more effective treatment' can be interpreted to include medicinal products which have not been approved for certain indications, even if new approved products for that indication have been introduced on the market. This appears to be the first pricing and reimbursement decision in Sweden in which a product under off-label use has been used as a comparator in the TLV's health technology assessment. However, it seems that this type of decision has been more been common in other European jurisdictions, such as the United Kingdom.

The issue in the case at hand is noteworthy, as it includes the extensive off-label use of medicinal products with orphan drug status and the fact that this line of reasoning from the reimbursement authorities undermines market exclusivity and one of the incentives of the EU Regulation on Orphan Medicinal Products (ie, to encourage investment in the research, development and marketing of orphan medicinal products).

A judgment is likely to be given at the end of 2015.

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