

Discussion paper

RARE DISEASES AND MEDICAL DEVICES IN THE EUROPEAN UNION

Rare diseases have been identified as a priority area for Community action within the framework for action in the field of public health. The European Parliament and the Council have adopted decision No 1295/188/EC of 29 April 1999 adopting a program of Community action on rare diseases within the framework for action in the field of public health.

For the purpose of this program, rare diseases are defined as life threatening or chronically debilitating diseases, which are of such low prevalence that special combined efforts are needed to address them so as to prevent significant morbidity, perinatal or early mortality or a considerable reduction in an individual's quality of life or socio-economic potential.

This low prevalence is generally recognised as being less than 5 per 10.000 in the Community.

Treatment options for rare diseases can include two types of products:

***Drugs and
Medical Devices.***

The Regulation (EC) N° 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products was approved on December 16th, 1999 and published in the Official Journal of the European Communities on January the 22nd, 2000.

This new legislation is based on the fact that :

“some conditions occur so infrequently that the cost of developing and bringing to market a medicinal product to diagnose, prevent or treat the condition would not be recovered by the expected sales of the medicinal product. The pharmaceutical industry would be unwilling to develop the medicinal product under normal market conditions; these medicinal products are called "orphan"”.

The notion of social justice underpinning this legislation supports the concept that it is equally desirable to advance effective treatments for individuals with rare disorders as for those with more common conditions.

The EU Parliament has expressed in this regulation the desire to have an open and transparent Community procedure for the designation of potential medicinal products as orphan medicinal products. Objective criteria have been established and are based on the prevalence of the condition (5/10.000) for which diagnosis, prevention or treatment is sought.

The orphan drug regulation is the result of an unwritten contract between society (or the Governments in their capacity as the expression of society's will) and the pharmaceutical industry to undertake R&D programs "without return on investment" in exchange of financial supports and a period of market exclusivity.

In 1992, the US Food and Drug Administration issued final regulations implementing the designation mechanism for the Orphan Drug Act.

However, while the EU legislation recognises that patients suffering from rare conditions should be entitled to the same quality of treatment as other patients, and therefore has adopted the Orphan Drug regulation No 141/2000 in order to stimulate the research, development and bringing to the market of appropriate medications by the pharmaceutical industry, *no such incentive has been given to the Medical Device Industry.*

Yet, there are several rare diseases or conditions that can only be treated by or with the help of (often implantable) medical devices, e.g. Parkinson's disease not any more adequately controlled by medications, severe spasticity in Multiple sclerosis patients. The development of high technology medical devices is very costly and R&D intensive. The risk of obtaining no return on investment for R&D on devices for rare diseases is real.

The current exclusion of Medical Devices from the EU Orphan Medicinal Products legislation means that similar incentives do not exist for such treatments as for those that are drug-based. Thus, patients whose rare conditions can only be effectively treated with or with the help of medical devices, are facing an unequal situation.

This leads to the recognition that the existing legislation on Orphan Drugs and Medical Devices needs to be up-dated in order to stimulate the often very costly and intensive research and development bringing to the market of new device-based therapies able to meet the unmet medical needs in the field of rare disorders.

The US Food and Drug Administration has recognised the fact that for diseases and conditions affecting small populations, a device manufacturer's R&D costs can exceed its market returns, thereby creating an impediment to the development of such a device. By promulgating its Humanitarian Use regulations for devices, effective October 1996, the US created an incentive for the development of devices for use in the treatment or diagnosis of conditions affecting a small number of individuals.

Examples of Medical Devices used for rare diseases

Definition of rare disease used:

Decision No 1295/99/EC of the EU Parliament and of the Council on the Programme of Community Action on Rare Diseases : prevalence of 5 per 10.000 in the Community.

Medical Devices

Medical Devices cover a very wide range of products: aids for disabled, active implantable devices, anaesthetic/respiratory devices, dental devices, electromedical, hospital equipment, imaging, in vitro diagnostics, ophthalmic and optical devices, passive implantable devices, single use devices, surgical instruments.

For the definition of Medical Devices we refer to the European legislation for Medical Devices: Council Directive 90/385/EEC regarding Active Implantable Medical Devices and Council Directive 93/42/EEC concerning Medical Devices.

Examples

- *Deep Brain Stimulation for the treatment of Parkinson's disease:*

This therapy involves the use of an active implantable medical device to deliver mild electrical stimulation to structures deep within the brain for patients with uncontrolled Parkinson's disease. The therapy blocks the abnormal brain signals that are related to Parkinson's disease symptoms. The therapy is reversible and can be used bilaterally. The parameters for stimulation can be adjusted to increase efficacy and decrease or eliminate side effects.

This therapy is intended in patients who are diagnosed with Parkinson's disease not adequately controlled by medications and in patients disabled by dyskinesias and motor fluctuations associated with pharmaceutical treatment for Parkinson's disease. The neurologists estimate that the number of patients eligible for this therapy is about 4,5/10.000 in the EU Community. The incidence is 0,6/10.000.

- *Implantable programmable drug delivery pumps:*

A programmable, implantable drug delivery pump is used for the intrathecal administration of Baclofen for patients with Multiple Sclerosis with severe spasticity.

Baclofen has a low blood/brain barrier penetration, with high systemic absorption, low CNS absorption and a lack of preferential spinal cord distribution. Thanks to the intrathecal administration, the solution of Baclofen is directly delivered into the intrathecal space where fluid flows around the spinal cord. The drug is directly delivered to where it is needed in the spinal cord, does not circulate throughout the body in the blood and the dose needed is about 1/100th of the oral dose. This helps minimise the unacceptable systemic side effects, such as muscle weakness, sleepiness, and nausea/vomiting, headaches or dizziness that often accompany oral medication at those doses effective for severe spasticity.

The prevalence of MS in the EU Community is about 7/10.000. Of all patients with MS, about 13% develop severe spasticity and can be eligible for the Intrathecal Baclofen treatment. This means a prevalence of about 1/10.000.

Clinical studies are being carried out for the use and adaptation of the implantable drug delivery pumps for the administration of new orphan drugs for other rare diseases. These drugs are inactive when not administered with the implantable drug delivery pump that brings the drug exactly at the site of action.

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