

# **NATIONAL POLICY FOR TREATMENT OF RARE DISEASES**

*Ministry of Health and Family Welfare*

*Government of India*

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## EXECUTIVE SUMMARY

### Rare Diseases

A rare disease is a health condition of low prevalence that affects a small number of people compared with other prevalent diseases in the general population. It is estimated that globally around 6000 to 8000 rare diseases exist with new rare diseases being reported in the medical literature regularly. However, 80% of all rare disease patients are affected by approximately 350 rare diseases.

Paradoxically, though rare diseases are of low prevalence and individually rare, collectively they affect a considerable proportion of the population in any country, which according to generally accepted international research is – between 6% and 8%. Rare diseases include genetic diseases, rare cancers, infectious tropical diseases and degenerative diseases. 80% of rare diseases are genetic in origin and hence disproportionately impact children.

There is no universally accepted definition of a rare disease. Different countries define rare diseases differently. However, the common considerations in the definitions are primarily, disease prevalence and to varying extent - severity and existence of alternative therapeutic options. India must arrive at its own definition suited to its need, based on a careful consideration of prevalence, disease severity and study-ability.

### Rare Diseases as a public health issue in India

The field of rare diseases is complex, heterogeneous, continuously evolving and suffers from a deficit of medical and scientific knowledge. So far about 450 rare diseases have been recorded in India. Globally as well as in India, rare diseases pose a significant challenge to public health systems in terms of – difficulty in collecting epidemiological data, which in turn impedes arriving at burden of diseases and cost estimations, difficulty in research and development, making correct and timely diagnosis, complex tertiary level management involving long term care and rehabilitation and unavailability and prohibitive cost of treatment.

Rare diseases constitute a significant economic burden independent of a country's size and demographics, arising from increased healthcare spending. As resources are limited,

there is a macroeconomic allocation dilemma due to opportunity cost of funding rare disease treatment: on one hand, health problems of a much larger number of persons can be addressed by allocating a relatively smaller amount, on the other, much greater resources will be required for addressing health problems of a relatively smaller number of persons.

### **Need for a Policy**

Rare diseases are, in most cases, serious, chronic, debilitating and life threatening illnesses, often requiring long-term and specialised treatments/management. In addition, they often result in some form of handicap, sometimes extremely severe. Moreover, they disproportionately impact children: 50% of new cases are in children and are responsible for 35% of deaths before the age of 1 year, 10% between the ages of 1 and 5 years and 12% between 5 and 15 years.

The impact on families is often catastrophic in terms of emotional as well as financial drain, as the cost of treatment is prohibitively high. As a result, parents of children suffering from rare diseases, whose treatment cost were not being covered by insurance or otherwise not being reimbursed, filed writ petitions in the Delhi High Court, seeking directions that the government provide the treatment for free. The High Court of Delhi in W.P. (C) No. 4444/2016, W.P. (C) No. 7730/2016, and W.P. (C) No. 7729/2013, directed the Ministry of Health & Family Welfare to frame a “national policy on treatment of rare diseases’.

The National Health Policy 2017 also underscores the need for management of rare/orphan diseases. For the above reasons, a policy is necessary to devise a multipronged and multisectoral approach to build India’s capacity to tackle rare diseases comprehensively, in areas of – epidemiological data for estimating burden, arriving at a definition and for cost estimation of treatment; research and development for treatment and diagnostic modalities, including through international/regional collaborations; training of health care providers; awareness generation; creating conducive environment for drug development and measures for ensuring affordability of treatment etc.

## **Policy Direction**

The GOI appointed high level committees to make recommendations towards formulation of 'Policy on treatment of Rare Diseases'. The committees made several recommendations, which have been incorporated in this Policy. The Policy highlights the measures and steps, both in the short as well as in the long term, that need to be taken to deal comprehensively with rare diseases. However, recognizing the exorbitant cost of treatment for rare diseases, the policy seeks to strike a balance between access to treatment with health system sustainability.

### **A. Immediate Measures**

- Constituting an Inter-ministerial Consultative Committee to coordinate and steer the initiatives of different ministries and departments on rare diseases as laid out in this Policy
- Constituting a Technical cum Administrative Committee at Central as well as State levels, for management of corpus funds and developing technical guideline/criteria for - which rare diseases to fund, to what extent, review of treatment etc.
- Creating a corpus fund at Central and State Level for part funding treatment of rare diseases on the basis of technical criteria developed by the Technical cum Administrative Committee
- Creating a Web-based application for online application process to access the corpus funds
- Creating a patient registry for rare diseases housed in ICMR
- Arriving at a definition of rare diseases suited to India
- Developing materials for generating awareness in the general public, patients and their families and health care providers.
- Developing and conducting training programmes of health care providers on rare diseases
- Constituting a Rare Diseases Cell within MoHFW, ICMR and DoP in Ministry of Chemicals and Fertilizers respectively to be the 'nodal' on rare diseases in their respective ministries and departments

**B. Long term measures: The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization -**

- Put systems in place for reporting and data collection
- Conduct epidemiological studies to estimate prevalence of rare diseases
- Take measures to improve research and development for treatment, diagnostic modalities, care and support including assistive devices, drug development for rare diseases etc.
- Take measures, legislative or otherwise, for encouraging local manufacturing of drugs for rare diseases
- Take legal and other measures to control the prices of drugs for rare diseases to ensure its affordability and health system sustainability
- Encourage funding support from Public Sector Undertakings (PSUs) and corporate sector and exploring other options for sustainable funding for the corpus
- Ensure insurance coverage for rare genetic disorders
- Allow import of Enzyme Replacement Therapies (ERTs) and remove import duty on them as well as on assistive devices
- As a strategy for early diagnosis of rare diseases, explore formulating a plan for piloting, and rolling out testing for rare genetic diseases in newborns, in tandem with development and standardization of diagnostic modalities and availability of treatment
- Develop standardized protocols for diagnosis and treatment/management of rare diseases, to be revised in conformity with evolving diagnosis and treatment landscape
- Strengthen laboratory networks for diagnosis of rare diseases
- Accredite centres for diagnosis and treatment of rare diseases which could be developed as Centres of Excellence (CoE) over a period of time, in a phased manner

- As a preventive strategy, explore feasibility of a plan for providing and progressively scaling up pre-conception and antenatal genetic counseling and screening in a targeted manner, or otherwise, to provide option to parents to prevent conception or birth of a child with a rare genetic diseases
- Drug Controller General of India (DCGI) to consider feasibility of amending Drugs and Cosmetics Act or otherwise taking measures under it, to include appropriate provisions on drugs for rare diseases, including provisions to facilitate clinical trials and import of ERTs.

### **A multi-sectoral convergent approach to tackling rare diseases**

The Policy delineates the role of several ministries in achieving the measures envisaged. Each Ministry and concerned department(s) is required to develop an implementation framework on measures to be taken by them on their sector wise response to tackling rare diseases.

## **1. Introduction**

### **1.1 What are Rare Diseases?**

A rare disease is a health condition of a particularly low prevalence that affects a small number of people compared with other prevalent diseases in the general population. There is no universally accepted definition of rare diseases and the definitions usually vary across different countries. However, the common considerations in the definitions are primarily, disease prevalence and to varying extent - severity and existence of alternative therapeutic options (1).

It is estimated that globally around 6000 to 8000 rare diseases exist with new rare diseases being reported in the medical literature regularly (2,3,4,5). However, 80% of all rare disease patients are affected by approximately 350 rare diseases (6).

Paradoxically, though rare diseases are of low prevalence and individually rare, collectively they affect a considerable proportion of the population in any country, which according to generally accepted international research is – between 6% and 8% (7,8). Rare diseases include genetic diseases, rare cancers, infectious tropic diseases and degenerative diseases (9). 80% of rare diseases are genetic in origin, and thus are present throughout a person's life, even if symptoms do not immediately appear.

### **1.2 Definitions of rare diseases across jurisdictions**

WHO defines rare disease as often debilitating lifelong disease or disorder condition with a prevalence of 1 or less, per 1000 population. However, different countries have their own definitions to suit their specific requirements and in context of their own population, health care system and resources. In the US, rare diseases are defined as a disease or condition that affects fewer than 200,000 patients in the country (6.4 in 10,000 people). EU defines rare diseases as a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people. Japan identifies rare diseases as diseases with fewer than 50,000 prevalent cases (0.4%) in the country.

**Table 1: Definitions of Rare Disease in different countries**

S No.	Country	Per 10,000 population
1	USA	6.4
2	Europe	5.0
3	Canada	5.0
3	Japan	4.0
4	South Korea	4.0
5	Australia	1.0
6	Taiwan	1.0

*Source: The I.C. Verma Sub-Committee Report 'Guidelines for Therapy and Management'*

### **1.3 The Indian Scenario**

India, like many other developing countries, currently has no standard definition of rare diseases and data on prevalence. Since there is no epidemiological data, there are no figures on burden of rare diseases and morbidity and mortality associated with them.

If we apply the international estimate of 6% to 8% of population being affected by rare diseases, to India, we have between 72 to 96 million people affected by rare diseases in the country, which is a significant number. However, this is at best a general estimate (10) and India will need to arrive at its own estimate and definition of rare diseases, derived chiefly from prevalence data, which is currently lacking.

So far only about 450 rare diseases have been recorded in India from tertiary care hospitals (10). The most common rare diseases include Haemophilia, Thalassemia, Sickle-cell Anaemia and Primary Immuno Deficiency in children, auto-immune diseases, Lysosomal storage disorders such as Pompe disease, Hirschsprung disease, Gaucher's disease, Cystic Fibrosis, Hemangiomas and certain forms of muscular dystrophies.

## **2. Rare Diseases as a public health issue**

The field of rare diseases is complex and heterogeneous and suffers from a deficit of medical and scientific knowledge. The landscape of rare diseases is constantly evolving as there are new rare diseases and conditions being identified and reported regularly in medical literature. Apart from a few rare diseases, where significant progress has been made, the field is still at a nascent stage. For a long time, doctors, researchers and policy makers were unaware of rare diseases and until very recently there was no real research or public health policy concerning issues related to the field. This poses formidable challenges in development of a comprehensive policy on rare diseases. Nevertheless, it is important to take steps, in the short as well as long term, with the objective of tackling rare diseases in a holistic and comprehensive manner.

### **2.1 Lack of epidemiological data**

Data on how many people suffer from different rare diseases in India is lacking. The cases identified so far have been diagnosed at tertiary hospitals (11). The lack of epidemiological data on incidence and prevalence of rare diseases impedes understanding of the extent of the burden of rare diseases and development of a definition. It also hampers efforts to arrive at correct estimation of the number of persons suffering from these diseases and describe their associated morbidity and mortality. In such a scenario, the economic burden of most rare diseases is unknown and cannot be adequately estimated from the existing data sets (12).

Although extremely challenging, considering the complexity of various diseases and the difficulty in diagnosis, there is a clear need to undertake systematic epidemiological studies to ascertain the number of people suffering from rare diseases in India.

### **2.2 Varying definitions and prevalence thresholds**

The use of inconsistent definitions and diverse terminology can result in confusion and inconsistencies and have implications for access to treatment and for research and development (1). According to a study which reviewed and analysed definitions across jurisdictions, most definitions, as discussed above, appear to consider disease

prevalence, but other criteria also apply sometimes, such as - disease severity, whether the disease is life-threatening, whether there are alternative treatment options available, and whether it is heritable (1). The study found that relatively few definitions (30%) included qualifiers relating to disease severity and/or a lack of existing treatments, whereas most definitions (58%) included a prevalence threshold. The average prevalence thresholds used to define rare diseases ranged among different jurisdictions from 5 to 76 cases/100,000 people, with a global average prevalence threshold of 40 cases/ 100,000 people. The study concluded that attempts at harmonising the differing definitions, should focus on standardizing objective criteria such as prevalence thresholds and avoid qualitative descriptors like severity of the disease.

However, it has been contested that disease prevalence alone may also not be an accurate basis for defining rare diseases, as it does not take into account changes in population over time. Hence, some have suggested that a more reliable approach to arriving at a definition could be based on the factors of – a) location - a disease which is uncommon in one country may be quite common in other parts of the world; b) levels of rarity - some diseases may be much more rare than other diseases which are also uncommon; and c) study-ability - whether the prevalence of a disease lends itself to clinical trials and studies (13).

This underscores the need for further research to better understand the extent of the existing diversity of definitions for rare diseases and to examine the scope of arriving at a definition which is best suited to conditions in India. It shall be done on a priority basis as soon as sufficient data is available.

### **2.3 Diagnosis of rare diseases**

Diagnosis of a rare condition may take upto several years, owing to difficulty in diagnostic modalities and lack of awareness among doctors. For many rare diseases, no diagnostic method exists, or diagnostic facilities are unavailable (14). Traditional genetic testing can only address a few genes at a time. As a result, physicians must often

provide their best guess on which genes to investigate. If the test is negative, further testing will be required, which is an expensive and time-consuming process.

There is a lack of awareness about rare diseases in general public as well as in the medical profession. Many doctors lack appropriate training and awareness to be able to correctly and timely diagnose and treat these conditions (15). According to a recent report, it takes patients in United States (US) an average of 7.6 years and patients in United Kingdom (UK) an average of 5.6 years to receive an accurate diagnosis, typically involving as many as eight physicians (four primary care and four specialists). In addition, two to three misdiagnoses are typical before arriving at a final diagnosis (16). Delay in diagnosis or a wrong diagnosis increases the suffering of the patients exponentially. There is an immediate need to create awareness among general public, patients and their families and doctors, training of doctors for better diagnosis, standardisation of diagnostic modalities, developing of new diagnostic tools and investment in gene therapy.

#### **2.4 Challenges in research and development**

A fundamental challenge in research and development for the majority of rare diseases is that there is relatively little known about the pathophysiology or the natural history of these diseases. Rare diseases are difficult to research upon as the patient pool is very small and it often results in inadequate clinical experience. Therefore, the clinical explanation of rare diseases may be skewed or partial. The challenge becomes even greater as rare diseases are chronic in nature, where long term follow up is particularly important. As a result, rare diseases lack published data on long-term treatment outcomes and are often incompletely characterised (17).

This makes it necessary to explore international and regional collaborations for research, collaborations with the physicians who work on any rare disease and with patient groups and families dealing with the consequences of these disorders. This will help gain a better understanding of the pathophysiology of these diseases, and the therapeutic effects that would have a meaningful impact on the lives of patients. There is also a need to review and where possible modify, clinical trial norms keeping in mind

the particular challenges in rare diseases, without compromising on the safety and quality of the drugs or diagnostic tools.

## **2.5 Challenges in treatment**

### **2.5.1 Unavailability of treatment**

Availability and access to medicines are important to reduce morbidity and mortality associated with rare diseases. Despite progress in recent years, effective or safe treatment is not available for most of the rare diseases. Hence, even when a correct diagnosis is made, there may not be an available therapy to treat the rare disease. There are between 7000 - 8000 rare diseases, but less than 300 have therapies available to treat them (18). About 95% rare diseases have no approved treatment and less than 1 in 10 patients receives disease specific treatment (19). Where drugs are available, they are prohibitively expensive, placing immense strain on resources of families, health systems and donor agencies alike.

### **2.5.2 Prohibitive cost of treatment**

As the number of persons suffering from individual rare diseases is small, they do not constitute a significant market for drug manufacturers to develop and bring to market drugs for them. For this reason, rare diseases are also called 'orphan diseases' and drugs to treat them are called "orphan drugs". Where, they do make drugs to treat rare diseases, they sell them at extremely high costs, statedly, to recoup the cost of research and development. At present very few pharmaceutical companies are manufacturing drugs for rare diseases globally and there are no domestic manufacturers in India. Due to the high cost, the government has not been able to provide these drugs for free. It is estimated that for a child weighing 10 kg, the annual cost of treatment for some rare diseases, may vary from Rupees 18 Lakhs to 1 crore 70 lakhs (discussed in detail in Chapter 3). Further, the methodology for evaluating treatment of rare diseases is often still in experimental phase, impeding assessment of clinical relevance and cost effectiveness.

Several countries have through legislation like Orphan Drug Act (ODA), provided incentives to drug manufactures to encourage them to manufacture drugs for rare

diseases. The most powerful incentive for drug manufacturers is the grant of 7 to 10 years of exclusive marketing rights including protection from imports, if a drug gets 'orphan drug' status. This means that pharmaceutical companies can price their drugs without fear of competition. This has changed the nature of drug development. The number of requests for orphan drug designation has quadrupled since 2000. The result has been a boom in drug sales and profits. In fact, almost a third of drugs for rare diseases now exceed £1bn in annual sales. The global orphan drugs market is expected to reach £144bn by 2020, and account for 19% of total branded prescription drug sales (20).

The average price of a drug for rare diseases exceeds \$100,000 a year. According to reports, while legislations on orphan drug development, like the US Orphan Drug Act, have facilitated development of orphan drugs, they have not been able to check the prices of these drugs, which has led to grave concerns for health system sustainability. For instance, the cystic fibrosis drug, Kalydeco (ivacaftor) is priced at £14,000 per patient per month. In fact, each one of the world's 10 most expensive drugs, is a drug to treat some rare disease, with Soliris (eculizumab) being the most expensive at £340,000 per patient per year. Although these drugs are prescribed to fewer patients, their extremely high prices can result in revenues equivalent to traditional blockbuster drugs. Publicly listed pharmaceutical companies that are orphan drug market authorisation holders are associated with higher market value and greater profits than companies not producing drugs for rare diseases (21)

Over the years many drugs have won 'orphan drugs' status even if they are not new or represent a scientific breakthrough. An inexpensive off-patent drug approved by the FDA for one condition, but widely prescribed as an "off-label" treatment for a rare disease, can be transformed into a big moneymaker. The accompanying 7 to 10 years of monopoly status can mean large price hikes for a drug that was already in wide use (22, 23, 24). For instance, older medicines for rare diseases like imatinib used to treat chronic myeloid leukemia can cost over USD 100,000 a year in developed countries (25). In India, public health safeguards in the patent law that restrict evergreening patents

have allowed Indian generic manufacturers to manufacture and supply this drug at far lower prices.

The exorbitant prices of drugs for rare diseases has led to concerns even in the developed countries about maintaining sustainability of the rare diseases funding/reimbursement programmes (26, 27). The exorbitant prices have led to calls for transparency in setting prices of drugs and for price control (28, 29, 30) and have even prompted scrutiny and congressional inquiries (31, 32). This should be a matter of careful consideration for any legislative or policy measures adopted in India for promotion of drug development for rare diseases. There is a pressing need for multi-pronged strategies to make drugs more affordable – by taking measures to lower the prices of drugs, encourage generic and local manufacturing of drugs and encourage PSUs to manufacture drugs for rare diseases.

## **2.6 Need to balance competing priorities of public health in resource constrained settings**

Rare diseases constitute a major economic burden independent of a country's size and demographics; these costs arise from increased healthcare spending and lost productivity (33, 34, 35). The exorbitant prices of medicines, are important considerations in public health policy development with reference to treatment for rare diseases. In resource constrained settings, it is pertinent to balance competing interests of public health for achieving optimal outcome for the resources allocated. As resources are limited, there is a macroeconomic allocation dilemma: on one hand, health problems of a much larger number of persons can be addressed by allocating a relatively smaller amount, on the other, for funding treatment of rare diseases, much greater resources will be required for addressing health problems of a relatively smaller number of persons. This raises questions of fairness and reasonability. However, it also raises issues of ethics and equity of opportunity for patients to benefit, in the interest of patients suffering from rare diseases. Hence any policy on treatment of rare diseases will have to strike a balance between access to treatments with health system sustainability.

### **3. Development of Policy for Treatment of Rare Diseases**

Rare diseases are, in most cases, serious, chronic, debilitating and life threatening, often requiring long and specialised treatments. In addition, they often result in some form of handicap, sometimes extremely severe (36). Rare diseases place a huge physical, psychological, and socioeconomic burden on patients and their families.

At least 80% of rare diseases have an identified genetic origin (37) and hence disproportionately impact children. 50% of new cases are in children and are responsible for 35% of deaths before the age of 1 year, 10% between the ages of 1 and 5 years and 12% between 5 and 15 years (38).

Rare diseases present a major challenge to population health and, untreated, are likely to contribute to large social and economic losses, affecting more than the individual, since often family members must forego employment outside the home in order to care for their sick relatives. In contrast, patients on treatment, are unlikely to require other high cost procedures such as pain management and surgery (39). Further, it is impossible for most families to fund treatment of rare diseases, without any governmental support.

The impact on families is often catastrophic in terms of emotional as well as financial drain, as the cost of treatment is prohibitively high. This has compelled parents of children suffering from rare diseases, whose treatment cost were not being covered by insurance or otherwise not being reimbursed, in approaching the courts seeking directions that the government provide the drugs for free, so that the treatment could continue. The High Court of Delhi in W.P. (C) No. 4444/2016, W.P. (C) No. 7730/2016, and W.P. (C) No. 7729/2013, had directed the Ministry of Health & Family Welfare to frame a “national policy on treatment of rare diseases’.

#### **3.1 Committees appointed by the government to make recommendations for framing a policy on rare diseases**

Pursuant to the orders of the Hon’ble Court, the GOI had constituted committees with the objective to make suggestions towards framing of a ‘national policy on treatment of

rare diseases’. Similarly, the Government of NCT of Delhi had also appointed a high powered interdisciplinary committee on rare diseases. The various committees that were appointed were:

- Committee under Professor V.K. Paul, Head, Department of Pediatrics, AIIMS, New Delhi – ‘Prioritisation of Therapy for Rare Genetic Disorders’
- Sub-committee on rare diseases in India, under Prof. I.C. Verma, Director, Institute of Medical Genetics Genomics, Sir Ganga Ram Hospital – ‘Guidelines for Therapy and Management’
- A high powered interdisciplinary Committee on rare diseases under the Chairpersonship of Dr. Deepak K. Tempe, Dean, Maulana Azad Medical College (MAMC), New Delhi

### 3.1.1 The V.K. Paul Committee Report

in their Report ‘prioritisation of therapy for rare genetic disorders’, the Committee attempts to elaborate on the available therapies and prioritisation for genetic disorders based on resources, cost of therapy (one time vs. long term), outcome (evidence-based), quality of life and published guidelines.

**Table 2: The Committee categorised genetic disorders into three categories and made recommendations for each category**

S No.	categories	Recommendations
1	Disorders amenable to one time treatment (curative)	<p>Prioritise funding for this category as:</p> <ul style="list-style-type: none"> <li>• One-time treatment cost ranges from 5 – 20 lacs, which is much less compared to long term therapy</li> <li>• Treatment outcome is good</li> <li>• Facilities for treatment are available in both private and public sector with good expertise and outcome</li> </ul>

		<ul style="list-style-type: none"> <li>• Funding should also include support for follow up therapy</li> <li>• Ceiling on existing funding limit should be made flexible</li> </ul>
2	Disorders requiring long term/life-long therapy	<ul style="list-style-type: none"> <li>• Cost of therapy for most disorders in this category is prohibitive and families cannot afford it without some support</li> <li>• Prioritise disorders in this category based on documented treatment outcome eg. Gaucher's disease type 1</li> <li>• Develop objective criteria for inclusion and exit from therapy and for assessing response to and progress on therapy</li> <li>• Identify institutes with sufficient manpower, facilities and expertise to manage these diseases</li> </ul>
3	Disorders for which no known therapy is currently available but requires supportive care	<ul style="list-style-type: none"> <li>• Supportive therapy is the only available option</li> <li>• Need to provide care and support services</li> </ul>

As about 80% of rare diseases are genetic in nature, the Committee recommended that it is important to provide genetic counseling and offer prenatal testing to the families with genetic disorders, as it will provide them an option about giving birth to children with rare diseases.

### 3.1.2 The I.C. Verma Sub - committee Report

The Sub-committee reviewed the burden and definitions of rare diseases globally as well as in India, availability of drugs and treatment options for various rare diseases, cost estimation and evidence on treatment outcomes. It considered the challenges in

treatment of rare diseases, reviewed the funding mechanisms for treatment of rare diseases in several countries and made recommendations for mechanisms of approving and regulating access and other inputs for formulating a national plan on rare diseases.

The Sub-committee specifically evaluated the availability and efficacy of treatment and cost of rare disorders of immediate relevance in India, namely - Lysosomal Storage Disorders (LSDs), which is treatable with Enzyme Replacement Therapies (ERTs). The LSDs include – Gaucher Disease, Mucopolysaccharidosis (MPS) Type 1 (Hurler-Schie), MPS Type II (Hunter), MPS Iva, MPS VI, Pompe Disease and Fabry Disease.

The sub-committee calculated the annual cost of the available therapies for a 10 kg child.

**Table 3. Approximate Annual Cost of ERTs**

Disease	Enzyme	Weight of the patient	Approximate annual cost (INR)*
Gaucher	Cerezyme (Genzyme)	10kg	39,84,768
Gaucher	Velaglucerase (Shire)	10kg	71,86,340
Gaucher	Taliglucerase	-	No information available
MPS 1	Aldurazyme (Genzyme)	10kg	46,78,464
Pompe	Myozyme (Genzyme)	10kg	48,94,368
Fabry	Fabrazyme (Genzyme)	10kg	18,29,712
MPSII	Elaprase (Shire)	10kg	44,00,000
MPSII (0.5mg/kg/week) Vial 2mg	Hunterase (Green Cross-Korea) 3mg/6ml (0.5mg/ml) vial 1,43,520/- per vial	10kg	1,72,22,400
MPS VI (1mg/kg every week)	Naglazyme (USD 1755 per vial)	10kg	1,09,51,200

Vial 5mg			
MPS IV (2mg/kg/every week) Vial 5mg	Vimizim (USD 1068/Vial)	10kg	1,33,28,640

\*including customs duty, CVD. Taxes, Octroi etc.

Source: I.C. Verma Sub-committee Report

The Sub-committee similarly evaluated the treatment, efficacy and cost of Inborn Errors of Metabolism (ELMs).

The Sub-committee notes that various countries have used different approaches for funding treatment for rare diseases. As treatment is out of reach of most families, many countries cover the cost through their National Health Services, for instance, most of the European countries. In USA once a therapy is approved by the FDA, the insurance companies cover the cost. In many emerging economies, the government funds the treatment of rare diseases, for instance in Egypt, Thailand, Argentina, Chile, Peru, Serbia, Malaysia and Philippines.

It therefore, concludes that there is a need for the government to play a role in evolving a funding mechanism for treatment of rare diseases and made recommendations for formulation of a national policy for treatment of rare diseases.

### 3.1.3 The D.K. Tempe Committee Report

The Committee considered the prohibitive costs of treatment and competing priorities of public health and resource allocation; inadequate prevalence data; and still unravelling diagnostic and treatment landscape. It suggested that the national policy should cover treatment in a phased manner, starting with rare genetic disorders, for which treatment with good clinical outcome is available. The policy could be progressively revised with increased knowledge and clarity about epidemiological data, diagnostic and treatment options, evidence on clinical outcomes, reduced cost of drugs, etc.

Expanding on the challenge of economic evaluation and resource allocation for rare diseases, the committee gave the example of cost of ERTs to treat LSDs (Gaucher, Pompe,

Fabry etc.) and stated that Enzyme Replacement Therapy (ERTs) is very costly and life-long and the public health system cannot support it in a cost-effective way with its own funds. The annual recurring cost of one patient with ERT could range from 1.8 – 17.0 lakhs per kg of body weight. This means that for a child weighing 10kgs, the cost would be between 18 lakhs to 1 crore 70 lakhs. This is a huge cost in a resource constrained public health system. This amount could treat 400 TB or 400 HIV patients in a year (40). This cost could also potentially treat 10-100 patients with Type 1 diabetes (annual cost estimated at Rs.18,000/- based on a study in South India in 2011) (41), which is also a lifelong and life threatening disease. This cost could also potentially prevent 10,000 malaria cases a year or prevent almost 600 under five children from being hospitalised with pneumonia annually.

Thus, the committee cautioned that when resources in the public health system are limited, appropriate choices need to be made taking into account the larger canvas of health problems that affect the population and the economic consequences of each life saved.

In conclusion, acknowledging the severity and impact of rare diseases on patients and their families; the directions of the Hon'ble High Court of Delhi and the consequent recommendation of the government sub-committee, there is a need to chalk out a roadmap for facilitating access to treatment for rare diseases. However, keeping in mind the prohibitive cost of treatment and the other formidable challenges as discussed above, appreciated from the perspective of public health principle of evidence informed resource allocation for garnering optimal outcome for the resources allocated, makes it imperative that the same be done in a phased manner.

### **3.2 Policy Recommendations**

The committees made several recommendations towards formulation of a 'national policy for treatment of rare diseases'. The recommendations go beyond treatment funding and takes a more holistic approach towards rare diseases, encompassing suggestions towards - prevention, awareness creation, training, research and development in treatment and diagnosis, development and manufacturing of drugs for rare diseases at affordable prices, provision of insurance coverage etc.



The recommendations fall in the domain of several ministries and departments, which is recognition of the fact that an effective response to rare diseases will require a comprehensive and convergent intersectoral effort. The Policy Directions in the next section reflect on this recognition and delineates the roles for ministries and departments, in addition to the Ministry of Health and Family Welfare.

## **4. Policy Direction**

In light of the severity and impact of rare diseases on patients and their families and the directions of the High Court of Delhi, the policy for facilitating access to treatment for rare diseases has been prepared. The recommendations of the government appointed committees have been considered while making this policy.

### **4.1. Implementation Mechanism**

The Policy highlights the measures and steps that ought to be taken immediately and also those that can be implemented progressively in phases. It also highlights the role of various ministries and departments, which at present is indicative and can be further extended based on adequate evidence and data gathered from epidemiological studies and research.

The Policy envisages setting up a Consultative Committee for implementing the policy in coordination with various ministries and departments. There will also be a Technical cum Administrative Committee within MoHFW, both at the Central and State Levels, for handling the corpus fund. The ministries, including MoHFW will design their own roadmap for implementation of the activities indicated below.

### **4.2 Strategies for implementation**

#### **A. Immediate/short term Measures**

- Constituting an inter-ministerial Consultative Committee at National Level to be led by MoHFW, to co-ordinate, oversee and steer the activities and initiatives of the concerned ministries and departments on rare diseases.
- Constituting a Technical cum Administrative Committee at Central as well as State levels for management and release of corpus funds and for developing technical criteria/guidelines for determining 'which rare diseases to fund', 'to what extent', 'review of progress' etc.
- Creating a corpus fund at Central and State Level for treatment of rare diseases on the basis of technical criteria developed by the Technical cum Administrative

Committee at the centre

- Creating a Web-based application for online application process to apply for funding support from the corpus funds
- Creating a patient registry for rare diseases housed in ICMR
- Arriving at a definition of rare diseases suited to India
- On the basis of the current knowledge, developing materials for generating awareness in the general public, patients and their families and for training of health care providers. This ought to be revised with availability of new information and knowledge
- Constituting a Rare Diseases Cell within MoHFW, ICMR and DoP in the Ministry of Chemicals and Fertilizers to be the nodal for the activities related to rare diseases

**B. Long term measures - The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization, where required -**

- Putting systems in place for reporting and data collection
- Conducting epidemiological study to estimate prevalence of rare diseases
- Taking measures to improve research and development for drugs, diagnostic modalities and care and support including assistive devices
- Taking measures, legislative or otherwise, to create a conducive environment for local manufacturing of drugs for rare diseases
- Take legal and other measures to control the prices of drugs for rare diseases to ensure its affordability and for health system sustainability
- Encouraging funding support from Public Sector Undertakings (PSUs) and corporate sector and exploring other options for sustainable funding for the corpus
- Ensuring insurance coverage for rare genetic disorders
- Allowing import of ERTs and removing import duty on them as well as on assistive devices
- As a strategy for early diagnosis of rare diseases, explore formulating a plan for

piloting and depending on feasibility, rolling out progressively, testing for rare genetic diseases in newborns, in tandem with development and standardization of diagnostic modalities and availability of treatment

- Develop standardized protocols for diagnosis and treatment/management of rare diseases, to be revised in conformity with evolving diagnosis and treatment landscape
- Strengthen networks of laboratories for accurate diagnosis of rare diseases
- Accredite centres for diagnosis and treatment of rare diseases which could be developed as Centres of Excellence (CoE) over a period of time, in a phased manner
- As a preventive strategy, explore feasibility of making a plan for providing and progressively scaling up pre-conception and antenatal genetic counseling and screening in a targeted manner, or otherwise, to provide option to parents to prevent conception or birth of a child with a rare genetic disease

### **4.3 Role of ministries and departments**

The activities listed below are indicative and can be expanded depending on improvement in our knowledge and understanding of rare diseases and the type of response it will require, based on availability of data and evidence generated through research and studies.

#### **4.3.1 Ministry of Health and Family Welfare**

- a) Health Ministry to create a cell on rare diseases within itself, to be headed by a Joint Secretary. It will act as a nodal agency and coordinate all the activities of the Health Ministry on rare diseases.
- b) Indian Council of Medical Research (ICMR) to constitute a division or identify one of its existing divisions, to promote research and development in the field of rare diseases for diagnosis and treatment of rare diseases, including through international/regional collaborations. An initiative like open source drug discovery and research for rare diseases based on principles of public funding of research and access to any treatments arising from this to be available

'Intellectual Property (IP) – free' and open to competitive manufacturing should be looked into.

- c) Constitute an an Inter-Ministerial Consultative Committee to co-ordinate the activities of various ministries and departments on rare diseases
- d) Constitute an Administrative and Technical Committee at Central as well as State levels, for management of corpus funds and developing technical guideline/criteria for - which rare diseases to fund, to what extent, review of treatment etc.
- e) Create a patient registry with information to practitioners and a reporting system of any patient diagnosed with a rare disease. This will be housed in ICMR. Patient registries may serve as appropriate tools to aid in understanding the natural history and clinical characteristics of rare diseases and assess the long-term outcomes of treatment.
- f) Take measures to collect epidemiological data on rare diseases.
- g) Take measures to create awareness among medical professionals, patients and their families and general public on rare diseases.
- h) Develop and conduct training programme for doctors on diagnosis and management of rare diseases
- i) As a strategy for early diagnosis of rare diseases, explore formulating a plan for piloting and depending on feasibility, rolling out progressively, testing for rare genetic diseases in newborns, in tandem with development and standardization of diagnostic modalities and availability of treatment
- j) Strengthen network of laboratories to effectively and accurately diagnose rare diseases
- k) Drug Controller General of India (DCGI) to consider feasibility of amending Drugs and Cosmetics Act or otherwise taking measures under it, to include appropriate provisions on drugs for rare diseases, including provisions to facilitate clinical trials and import of ERTs.
- l) For patients in the BPL category who get diagnosed with rare diseases, make available for free, supportive services, whether in private or government hospital.

- m) ICD 11 classifies about 5000 rare diseases. The centres identified by the Central/State government for categorising rare diseases in India, need to group/put rare diseases under already identified disease classification under ICD 11. If any new rare disease is identified, steps will be taken by the Ministry for sending required evidence to WHO for inclusion of the disease under ICD classification.
- n) As a preventive strategy, consider feasibility of making a plan for providing and progressively scaling up pre-conception and antenatal genetic counseling and screening in a targeted manner, or otherwise, to provide option to parents to prevent conception or birth of a child with a rare genetic disease
- o) **Creating a National and State Level Corpus**
1. The Government of India (GOI) to set up a corpus fund with an initial amount of Rs. 100 crore towards funding treatment of rare genetic diseases. Resources allocated for treatment of rare diseases can be progressively scaled up with regular improvements in availability of epidemiological data, cost estimation studies and measures taken to encourage development of drugs and for reduction in prices of drugs.
  2. The States to have a similar corpus at the state level and the GOI will contribute funds towards the State corpus to the ratio of 60:40. It would be open to the states to contribute a larger amount to the corpus. This funding arrangement will be part of the PIP process.
  3. The corpus fund will be dedicated for rare disorders. However, it will not fund treatment for blood disorders (hemophilia, thalassemia and sickle cell anemia) as separate government programs for them exist already. Depending on need, the existing programmes for blood disorders shall be scaled up.
  4. The corpus will be used for only part funding of the entire treatment cost.
  5. To ensure sustainability of the corpus, the Public Sector Undertakings (PSUs) and corporate houses, to be encouraged to make contributions as per Section 135 and Schedule VII of the Companies Act as well as the provisions of the Companies (Corporate Social Responsibility Policy) Rules,

**p) Creating a web-based application for online application process**

To ensure timely decisions and release of funds, a web-based application would be developed for creating online mechanism for applying to the corpus. Central government will create this web-based application within 6-12 months of the release of this policy. It will have the details of the corpus and instructions and mechanism for applying for funding. It would be open to individuals institutions as well as state governments to apply for funds by entering details on the web application as per instructions provided.

**4.3.2 Ministry of Commerce, Department of Industrial Policy and Promotion (DIPP)**

- a) Constitute a Cell within DIPP to promote local development and manufacture of drugs for rare diseases at affordable prices
- b) Take legal/legislative measures for creating a conducive environment for indigenous manufacturing of drugs for rare diseases at affordable prices. For instance, ensuring strict scrutiny of patent applications related to rare diseases to ensure they meet the strict patentability of the Indian patent law and issuing compulsory licenses under Patents Act 2005, to ensure affordability of patented drugs for rare diseases.
- c) Encourage PSUs for local manufacturing of drugs for rare diseases

**4.3.3 Ministry of Chemicals and Fertilizers, Department of Pharmaceutical (DoP), National Pharmaceutical Pricing Authority (NPPA)**

Take measures to document and make publicly available the prices of drugs for rare diseases and work towards affordability of drugs for rare diseases, in consultation with the Ministry of Health and Family Welfare

**4.3.4 Ministry of Corporate Affairs**

Encourage PSUs and corporate houses to contribute to the corpus as per the Section 135 and Schedule VII of the Companies Act as well as the provisions of the Companies

(Corporate Social Responsibility Policy) Rules, 2014 (CRS Rules). Preventive and promotive health care is included in the list in the Schedule for CSR activities.

#### **4.3.5 Ministry of finance**

- a) Department of Revenue to consider removing import duty on ERTs as well as on assistive devices.
- b) Department of Financial Services to consider, on the basis of actuarial studies, whether insurance sector could cover cost of treatment of rare genetic diseases and amend the Insurance Act accordingly. It is necessary to bring in health insurance reforms through IRDA (Insurance Regulatory and Development Authority of India) and government intervention.

#### **4.3.6 Ministry of Labour and Employment**

Employees State Insurance Corporation (ESIC) to consider removing/increasing the ceiling limit on funding treatment for rare diseases.

#### **4.4 Implementation Framework on way forward**

Each Ministry and concerned departments should develop an implementation framework on action points to be taken by them on their sector wise response to tackling rare diseases. The implementation framework should have a clear targeted approach, complete with indicators and benchmarks (where applicable) and progressive realisation, to ensure demonstrability of progress.

#### **4.5 Setting Up of Committees**

##### **4.5.1 Constitution of Consultative Committee**

Government of India (GOI) to constitute a Consultative Committee headed by Secretary Health to oversee, coordinate and steer the initiatives taken by the different ministries and departments. Its meetings could be held at least once in a year.

##### **4.5.2 Constitution of Technical cum Administrative Committee**

- a) There will be a Central Technical cum Administrative Committee for the national

- corpus. It will be chaired by the Additional Secretary/Joint Secretary and have such technical experts as members as considered necessary.
- b) There will be Technical cum Administrative Committee at the State level for the State Corpus. It will be chaired by the Secretary and have such technical experts as members as considered necessary.
  - c) The Committees will meet once in three months.
  - d) The State corpus could be operated at the State level under the oversight of the Central Committee.

#### **4.5.3 The Broad Role of the Technical cum Administrative Committees:**

- a) Central Committee will come up with a definition of rare diseases for the purposes of this policy, which could be revised in conformity with increased information and knowledge about rare diseases.
- b) Central Committee will develop a priority list of rare disorders for which funding support will be considered, on the basis of – disease severity, availability of treatment, reasonably proven clinical outcome, cost data and cost effectiveness. It will develop the priority list with due regard to the recommendations of the government appointed committees.
- c) Central Committee will develop objective inclusion/exclusion criteria on the basis of which individual applications for funding support will be decided and the extent of funding to be provided will be determined. The inclusion/exclusion criteria will include household income of patient, curability of condition and cost effectiveness etc. This will also be developed according to the recommendations of the government appointed committee.
- d) The Central Committee will also develop criteria on the basis of which the progress of the patients whose treatment is funded from the corpus, will be reviewed.
- e) The Central Committee will develop protocols for diagnosis and treatment/management of rare diseases
- f) The Central and State Committees will identify and accredit institutions that will carry out diagnosis of rare diseases, and institutions that will provide treatment for rare diseases, and institutions that will both diagnose and treat rare diseases.

- g) The State Committees will review the applications received on the website and decide on the applications – whether to fund and fund to what extent - as per the details entered and the criteria developed by the Central Committee.
- h) The State Committees will also review the progress of the case, as per the criteria developed by the Central Committee and evaluate whether the clinical condition of the patient is being improved by the therapy.

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**Expert Committee Meeting ON Rare Diseases**  
***22<sup>nd</sup> March 2017***  
**Ministry of Health & Family Welfare**  
**New Delhi**

## **Participants**

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