

**SURVEY OF PEOPLE WHO HAVE FABRY DISEASE  
(2018)**

**EVALUATING THE DIRECT AND INDIRECT COSTS OF FABRY DISEASE<sup>1</sup>**

**May 2022**

**Contest**

Fabry disease is a sphingolipidosis, an inherited metabolic disorder that is caused by a deficiency of alfa-galactosidase A. This can cause angiokeratomas, acroparesthesias, corneal opacity, recurring bouts of fever, and renal or cardiac insufficiency.

In 2018, the Italian Anderson-Fabry Association commissioned C.R.E.A. Sanità to carry out an investigation into the disorder. The investigation involved the administration of a targeted questionnaire, aiming to collect a range of information to evaluate the disorder across various different aspects – for example, quality of life for the patient, types of treatment, support from the national health service and from charities and the relative costs of treatment.

In administering this questionnaire, Sinodè generated a database of information available in Excel format with 327 columns (information fields). Furthermore, it organized the preparation of all data relating to social issues and compiled data relating to the costs borne by both the National Health System and patients for the treatment of this disorder.

Anderson-Fabry disease is a rare genetic illness, characterised by an accumulation of specific lipids in various cells of the organism. It mostly affects the kidneys, nervous system and the cardiovascular system, and a patient's life expectancy can be up to thirty years less than the wider population. There are an estimated 60 - 125 new cases in Italy every year, with a total of 700 - 1,500 patients living with this disease.

Compared to the aforementioned incidence of people with Fabry disease, 106 patients responded to this questionnaire: based on the estimates of the prevalence of Fabry disease among the Italian population, this survey's coverage rate is within the range of 6.6% - 15.1%.

**Aims and Objectives**

The aim of this document is to demonstrate the direct and indirect costs borne by the State and the National Health System and by patients who have Fabry disease. This is achieved through the administration of a questionnaire (provided by the Italian Anderson-Fabry Association) which describes the methods used to determine costs.

**Data Sources, Documents and Useful Links**

Documents:

- Survey Questionnaire

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<sup>1</sup> This document was written by Sinodè s.r.l.

Data:

- Excel file with responses to questionnaires, filled in by patients or family members of those with Fabry disease

Links:

- <https://www.osservatoriomalattie.it/malattie-rare/malattia-di-fabry/14666-malattia-di-fabry-i-risultati-di-un-indagine-nazionale-sulla-qualita-della-vita-dei-pazienti>
- Further links can be found in the section “Methodology and Results”

### Critical Issues, Notes and Points to Consider

- The average amount associated with each healthcare service and its relative cost is calculated in reference to the number of patients who responded to the questionnaire (e.g., 106); it is therefore possible that some patients have a high usage of treatment at high cost (e.g., patients who undergo liver transplants) and others who have a low usage of treatment, as the illness has a lesser impact on the state of their health. The cost per patient is therefore calculated as an average value.
- The calculation of the average of services took into consideration the number of services accessed in the last twelve months by patients who had carried out diagnostic tests using the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont); there are no significant differences between the prices listed on the regional tariff pricings and the cost of services listed in the questionnaire; there was a discrepancy between the number of tests undertaken by a patient and the number of months that elapsed between undertaking the same test by the same patient (e.g. ID 1408 → Brain MRI: Specify the number of tests undertaken in the last 12 months → 6 tests – On average, every how many months do you undergo this test → 24); therefore for the calculation, the absolute number of sittings for tests undertaken in the last twelve months, as declared by patients was used.

### Methodology and Results

This analysis is based on the results of a questionnaire completed by 106 patients with Fabry disease. In addition to these data, it was necessary to consider data taken from other sources in order to calculate the direct and indirect costs borne on the National Health System and the patients themselves. This additional information is as follows:

- Identifying amounts related to state/regional benefits (e.g., Law 104, carers’ allowance, civilian indemnity allowance, school attendance benefit, etc.):
  - <https://www.inps.it/pages/standard/46178> (Law 104/1992)
  - <https://www.inps.it/prestazioni-servizi/indennita-di-accompagnamento-agli-invalidi-civili> (Civilian Invalidation Allowance)
  - <https://www.inps.it/prestazioni-servizi/indennita-mensile-di-frequenza> (school attendance benefit)
- Average wage per region: <http://www.indagodati.it/2021/05/28/redditi-2019/>
- Regional tariffs for specialised outpatient services<sup>2</sup>:

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<sup>2</sup> The calculation of the average of services took into consideration the number of services accessed in the last twelve months by patients who had carried out diagnostic tests via the current pricing tariff of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont). The calculation of this cost was carried out in this way as more than 50% of the total number of patients with Fabry disease reside (in decreasing order) in Lombardy,

- Veneto: Decree No. 47 of 22/05/2013 and successive amendments and integrations
- Lazio: DGR No.1059/1998 and successive amendments and integrations
- Emilia Romagna: DGR No. 1108/2011 and successive amendments and integrations
- Lombardy: DGR No. XI/4658 del 03/05/2021 and successive amendments and integrations
- Average cost of hospital admission per discharge for specialist visits (data produced from the Veneto Region in 2017)<sup>3</sup>
- Costs of medication (list price/ acquisition price from Health Authorities):
  - List: <https://www.torrinomedica.it/schede-farmaci/Fabrazyme/>
  - List: <https://www.torrinomedica.it/schede-farmaci/Replagal/>
  - List: <https://www.torrinomedica.it/schede-farmaci/Galafold/>
  - ULSS (Local Health Unit) 6 Vicenza: DDG No. 257 of 15/04/2016 ([https://www.aulss8.veneto.it/provvedimenti/delibera%20f ta 1 DDG 2016 257.pdf](https://www.aulss8.veneto.it/provvedimenti/delibera%20f%20ta%201%20DDG%202016%20257.pdf))
  - ASL (Local Health Authority) Rieti: DDG No. 62 of 18/12/2020 ([https://www.asl.rieti.it/fileadmin/delibere-n/2020/All. 1 osc-signed.pdf](https://www.asl.rieti.it/fileadmin/delibere-n/2020/All.1_osc-signed.pdf))
  - ULSS (Local Health Unit) 9 Scaligera: Management Decision No. 911 of 31/05/2018 ([https://trasparenza.aulss9.veneto.it//media/AULSS9/Trasparenza/Bandi di Gara/Verona Provveditorato/2018/CHIARA/galafold determina 911 del 31 05 2018.pdf](https://trasparenza.aulss9.veneto.it//media/AULSS9/Trasparenza/Bandi%20di%20Gara/Verona%20Provveditorato/2018/CHIARA/galafold%20determina%20911%20del%2031%2005%202018.pdf))
- Cost €/km: <http://www.raccontadati.it/2019/09/quanto-ci-costa-davvero-viaggiare-in-auto/>

The following summarises the break-down of costs that was revealed by analysing both the information provided by patients when filling in the questionnaire and the previously indicated sources:

- **Direct Costs borne by the State/ National Health System:** these are the direct and indirect costs which are borne by the State/National Health System of providing economic support or free or subsidised health services to patients
  - ***Costs of Assistance Benefits:*** these are the direct and indirect costs which are borne by the State/National Health System of providing monthly allowances or the expenditure of a patient's employer with regards to the number of day that the patient is not able to go to

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Emilia-Romagna, Veneto and Lazio; these Regions all have their own Regional pricing tariffs, which is a version of the national tariff price list. This method was used to calculate all outpatient costs.

<sup>3</sup> The calculation of this cost was carried out by applying the National DRG pricing tariffs based on hospital admissions in the Veneto Region. When calculating the cost of hospitalisation, it is not possible to apply one single tariff, but a combination of a series of factors (e.g., number of days of hospitalisation (both expected and over the expected number), type of DRG, discharge ward, intervention code, diagnosis codes, days of leave, inpatient treatment etc.); the methodology used took into account all factors that impact the calculation of the DRG based on actual hospitalisations that took place in the Veneto Region. For both ordinary hospitalisations and one-day admissions, the average cost of admission for each hospital unit reported in the survey. Based on the patients "interviewed", for each hospitalisation, average cost of admission per unit and number of admissions (as reported in the questionnaire), an average admission cost per patient was calculated.

For outpatient services, it was possible to accurately carry out this analysis as the questionnaire administered to patients collected each individual type of service rendered, each of which is associated with a specific tariff. However, for inpatients, the questionnaire only collected data regarding the hospital unit, which do not have an associated tariff price for admissions. Therefore, the analysis proved more accurate when taking into account the average cost per hospital unit, and using the actual value of each individual hospital admission as a starting point. It is important to mention that with one-day admissions in hospital, it is often necessary for the patient to be admitted more than once, and therefore the chosen methodology also established the number of times a patient was hospitalised and the real cost of one-day admission for each hospital unit, rather than simply considering the cost of one single hospital admission.

The costs related to any transplants were also looked at and calculated; there are few transplants carried out on patients with Fabry disease but the cost of hospital admission for transplants is considerable.

work:

- **Cost of Law 104/1992:** workers with severe disabilities or workers with family members with severe disabilities can qualify for paid leave; one day of work is based on the average gross income per region; from this average cost, the overall number of days that those who are eligible (as provided for by Law 104/1992) can claim was calculated
- **Cost of Civilian Invalidation Allowance:** invalidity is recognised to people who are living with severe disabilities (either congenital or acquired), which negatively impact their capacity to work or to study; the average cost per patient was calculated based on the average price laid out in Circular No. 148 of 10 December 2020
- **Cost of Carers' Allowance:** this is an economic benefit that is paid on demand for people with disabilities or invalidity for whom it has been ascertained that their mobility would be completely compromised without the help of a carer or the incapacity to carry out day-to-day activities; the average cost per patient was calculated based on the average value of the Carers' allowance as laid out in Circular No. 148 of 10 December 2020
- **Cost of School Attendance Benefit:** financial aid paid directly by INPS to young people living with disabilities up until they come of age. It aims to support and incentivise school attendance with the young patient and their social integration. The overall amount paid to the patient and the relative average cost per patient was calculated based on the amount paid by INPS and the total number of eligible patients

*The abovementioned costs were calculated as an average cost for those patients who have the right to assistance benefits, without accounting for those patients who receive no benefits and/or invalidity allowance (see the "Details of Precise cost" columns of the summary table at the end of this document).*

- **Cost of Outpatient Healthcare Services:** these are the direct and indirect costs which are borne by the State/National Health System of providing specialised outpatient assistance services; services may be either completely borne by the National Health System (for patients who are exempt due to low wage and/or illness) or partially borne by the National Health System (for patients who are not exempt, there is a health service fee ("ticket")):

- **Cost of Medical Appointments:** average cost of medical appointments per patient; through data reported in the questionnaire, the number of medical visits was taken into consideration, using it to calculate the average cost of a specific visit listed in the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont)
  - **Cost of Psychological Support:** average cost of therapy session per patient (responses to the questionnaire did not reveal a particularly high value for this type of support; in fact, the average yearly cost per patient for this entry is notably low)
  - **Cost of Diagnostic Services:** average cost of diagnostic services per patient; through data reported in the questionnaire, the number of diagnostic test services was taken into consideration, using it to calculate the average cost of a specific visit listed in the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont)
  - **Cost of Laboratory Services:** average cost of laboratory services per patient; through data reported in the questionnaire, the number of laboratory services was taken into consideration, using it to calculate the average cost of a specific visit of the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont); given that the questionnaire does not give a breakdown of the types of laboratory services used to monitor the health status of patients who have Fabry disease (as it does for medical visits and diagnostic tests) the protocol of the Local Health Authority of the City of Turin was used as a reference: ([https://www.malattierapiemonte.it/obj/files/dcmt/2021.5.18.10.45.35\\_17-IT.pdf](https://www.malattierapiemonte.it/obj/files/dcmt/2021.5.18.10.45.35_17-IT.pdf)); using this protocol, it was possible to identify the laboratory services used to monitor the health status of patients
  - **Cost of Rehabilitation:** average cost of sessions per patient (responses to the questionnaire did not reveal a particularly high value for this type of support; in fact, the average yearly cost per patient for this entry is notably low)
  - **Cost of Prosthetics and Assistive Products (e.g., wheelchairs, crutches, etc.):** average cost of assistive products used by patients (responses to the questionnaire did not reveal a particularly high value for this type of support; in fact, the average yearly cost per patient for this entry is notably low).
- **Cost of Inpatient Healthcare Services:** these are the direct and indirect costs which are borne by the State/National Health System of providing inpatient health services:
  - **Cost of ordinary hospitalisation:** average cost of ordinary hospitalisation per patient; through data reported in the questionnaire, the number of ordinary hospitalisations was taken into consideration, using it to calculate the average cost of hospitalisations of each specialist visit; a value for hospitalisation with the diagnosis code “Fabry disease” was also simulated, but the number of hospitalisations recorded in this way was insignificant
  - **Cost of Day-hospital (One-day Admission):** average cost of one-day admission per patient; through data reported in the questionnaire, the number of one-day admissions was taken into consideration, using it to calculate the average cost of hospitalisations of each specialist; a value for hospitalisation with the diagnosis code “Fabry disease” was also simulated, but the number was insignificant

- **Transplant Cost (kidney):** average cost of admission to hospital for a transplant per patient; through data reported in the questionnaire, the number of transplant admissions was taken into consideration, using it to calculate the average cost of admission to hospital for a transplant.
- **Cost of Medication and Administration:** these are the direct and indirect costs which are borne by the State/National Health System of providing and administering medication for the treatment of Fabry disease:
  - **Cost of Medication (Agalsidase Alfa, Agalsidase Beta, Migalastat):** these medications have a very high list price. Through an analysis carried out of deliberations released by various regional health authorities in Italy, it is possible to show the true acquisition cost of specific medication; these costs were then cross-referenced with data collected through the questionnaire and used to calculate the average yearly cost per patient
  - **Cost of Administration of Pharmacological Treatment in Hospital Structures<sup>4</sup>:** the cost of administering pharmacological treatment in hospital structures was calculated using the tariff pricing for accessing one-day admission in hospital with the MDC (Major Diagnostic Category) code 10 “Endocrine, Nutritional, and Metabolic System” illnesses; using this tariff pricing of €161.60 and cross-referencing it with data on the number of infusions administered to patients every year, it was possible to calculate the average yearly cost per patient
  - **Cost of Administration of Pharmacological Treatment at Home:** the cost of administration of pharmacological treatment at the patient’s home is accounted for by the cost of the medication itself; the deliberations<sup>5</sup> released by the Health Authorities that buy medications administered through infusion (Agalsidase Alfa, Agalsidase Beta) highlight the fact that the pharmaceutical companies provide an at-home administration service for patients with no extra cost to the health authorities.

*The abovementioned costs for administering pharmacological treatment were calculated as an average cost for those patients who use pharmacological treatment without taking into account the overall number of patients analysed (see the "Details of Precise Cost" columns of the summary table at the end of this document).*

- **Direct Costs borne by the Patient:** these are the costs that the patients must pay to access and/or use health services:
  - **Cost of Outpatient Healthcare Activities:** these are the direct costs which are borne by the patient of using specialist outpatient healthcare services; this section lists the costs borne by patients who are not exempt from the health service fee (“ticket”); these costs are minimal as almost all patients are exempt from paying due to low wages and/or illness and therefore

<sup>4</sup> From the number of inpatient admissions and outpatient services that were reported in the questionnaire, it is important to mention that the analysis did not report data on the number of visits to hospital structures for pharmacological treatment; however, this number can be assumed from the number of treatment sessions a patient underwent in hospital.

<sup>5</sup> [https://www.asllanusei.it/documenti/4\\_170\\_20121115125016.pdf](https://www.asllanusei.it/documenti/4_170_20121115125016.pdf)  
[https://www.aulss8.veneto.it/provvedimenti/delibera%20f%20ta\\_1\\_DD%2015\\_938.pdf](https://www.aulss8.veneto.it/provvedimenti/delibera%20f%20ta_1_DD%2015_938.pdf)  
[https://www.aulss8.veneto.it/provvedimenti/delibera%20f%20ta\\_1\\_DD%2021\\_1841.pdf](https://www.aulss8.veneto.it/provvedimenti/delibera%20f%20ta_1_DD%2021_1841.pdf)

do not pay any health service fees:

- **Cost of Medical Appointments:** average cost of medical appointments per patient; through data reported in the questionnaire, the number of medical appointments was taken into consideration, using it to calculate the average cost of each specific medical visit listed in the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont)
- **Cost of Psychological Support:** average cost per therapy session per patient
- **Cost of Diagnostic Services:** average cost of diagnostic services per patient; through data reported in the questionnaire, the number of diagnostic tests was taken into consideration, using it to calculate the average cost of each specific diagnostic test listed in the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont)
- **Cost of Laboratory Services:** average cost of laboratory services per patient; through data reported in the questionnaire, the number of laboratory services was taken into consideration, using it to calculate the average cost of each specific laboratory service listed the current tariffs of the four regions with the highest number of patients (Veneto, Lombardy, Emilia-Romagna, Piedmont)
- **Cost of Rehabilitation:** average cost of sessions per patient
- **Cost of Prosthetics and Assistive Products (e.g., wheelchairs, crutches, etc.):** average cost of assistive products used by patients
- **Cost of Transport:** average cost borne by patients to travel to treatment or support centres; based on the number of kilometres travelled as declared by patients in the questionnaire and on the average cost per kilometre travelled.

*The abovementioned costs for transport were calculated as an average cost for those patients, split between patients who were treated with medication in hospital structures and those who received treatment at home, either using oral treatment or non-pharmacological treatment (see the "Details of Precise Cost" columns of the summary table at the end of this document).*

- **Indirect Costs borne by the Patient:** these are the indirect costs which are borne by the patient due to days needed for medical treatment or days in which the patient needed help from family members and/or others to carry out day-to-day activities:

- **Indirect Cost borne by the Patient or Family Members:**
  - **Cost of Illness-related Absences from Work/Study:** average cost per patient for the missed days of work/school in order to manage their illness; this average cost was valued using the average cost of one day of work, calculated from the average gross annual income per region
  - **Cost of Illness-related Absences from Work/Study for Family Members/Friends:** average cost per patient for the days of work/school missed by family members/friends to support the patient in managing their illness; this average cost was valued using the average cost of one day of work
  - **Cost of Days of Domestic Help:** average cost per patient for the days during which the patients needed or would have needed domestic support; this average cost was calculated by looking at the number of days reported on the questionnaire administered to patients and the average hourly cost of a domestic helper (8 €/h<sup>6</sup>); in this calculation, two data records were deleted as they were incoherent with other values reported in the questionnaire.

The following page shows the results of this analysis of the survey (the percentage values given in each line are calculated in relation to the “Total Average Cost per Year per Patient”).

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<sup>6</sup> INPS Circular No. 16 of 01/02/2019 of the Central Revenue and Debt Collection Department.



**Summary of Average Annual Costs per Patient with Fabry Disease**

**Details of  
Precise Cost**

<b>Total Average Annual Cost per Patient</b>	<b>142,387 €</b>	<b>100.0%</b>
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<b>Total Direct Costs borne by the State/NHS Yearly Average per Patient</b>	<b>137,694 €</b>	<b>96.7%</b>
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<b>Direct Costs borne by the State/NHS</b>	<b>Cost of Assistance Benefits</b>	<b>4,168 €</b>	<b>2.9%</b>
	Cost of Law 104	1,733 €	1.2%
	Cost of Civilian Invalidation Allowance	2,072 €	1.5%
	Cost of Carers' Allowance	331 €	0.2%
	Cost of School Attendance Benefit	32 €	0.0%

Price w/ Assistance Benefits	Price w/o Assistance Benefits
4,591 €	0 €
4,307 €	0 €
8,763 €	0 €
3,442 €	0 €

<b>Direct Costs borne by the State/NHS</b>	<b>Cost of Outpatient Healthcare Activities</b>	<b>793 €</b>	<b>0.6%</b>
	Cost of Medical Appointments	97 €	0.1%
	Cost of Psychological Support	2 €	0.0%
	Cost of Diagnostic Services	497 €	0.3%
	Cost of Laboratory Services	175 €	0.1%
	Cost of Rehabilitation	19 €	0.0%
	Cost of Prosthetics and Assistive Products (e.g., Wheelchairs, crutches, etc.)	2 €	0.0%

<b>Direct Costs borne by the State/NHS</b>	<b>Cost of Inpatient Healthcare Services</b>	<b>2,288 €</b>	<b>1.6%</b>
	Cost of Ordinary Hospitalisation	499 €	0.4%
	Cost of Day-hospital (One-day Admission)	850 €	0.6%
	Cost of Transplants (Kidney)	939 €	0.7%

<b>Direct Costs borne by the State/NHS</b>	<b>Cost of Medication and Administration</b>	<b>130,445 €</b>	<b>91.6%</b>
	Cost of Medication (Agalsidase Alfa, Agalsidase Beta, Migalastat)	128,919 €	90.5%
	Cost of Administration of Pharmacological Treatment in Hospital Structures	1,526 €	1.1%
	Cost of Administration of Pharmacological Treatment at Home	0 €	0.0%

Price of Pharm. Treatment in Hospital	Price of Pharm. Treatment at Home
4,148 €	0 €
0 €	0 € <sup>7</sup>

<sup>7</sup> This cost is included within the cost of the medication itself – this is the case in situations (highly prevalent in this sample of respondents (3 out of 4 cases)) where the pharmaceutical company provided nursing staff to administer replacement enzyme therapy directly through IV. The cost of administering the medication was calculated using the hourly rate (as negotiated by the National Collective Contract for level D1) for the nursing staff of the Integrated Home Care Services (ADI) of the Local Health Authority, which is estimated at € 22.76.



<b>Total Direct Costs borne by the Patient Yearly average per Patient</b>	<b>583 €</b>	<b>0.4%</b>
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<b>Direct Costs borne by the Patient</b>	<b>Cost of Outpatient Healthcare Activities</b>	<b>41 €</b>	<b>0.0%</b>
	Cost of Medical Appointments	14 €	0.0%
	Cost of Psychological Support	0 €	0.0%
	Cost of Diagnostic Services	16 €	0.0%
	Cost of Laboratory Services	10 €	0.0%
	Cost of Rehabilitation	0 €	0.0%
	Cost of Prosthetics and Assistive Products (e.g., wheelchairs, crutches, etc.)	0 €	0.0%

**Price of Pharm. Treatment in Hospital**      **Price of Pharm. Treatment at Home**

<b>Direct Costs borne by the Patient</b>	<b>Cost of Transport</b>	<b>542 €</b>	<b>0.4%</b>
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995 €	278 €
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<b>Total Indirect Costs borne by the Patient Yearly average per Patient</b>	<b>4,111 €</b>	<b>2.9%</b>
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<b>Indirect Costs borne by the Patient</b>	<b>Indirect Costs borne by the Patient/Family Members</b>	<b>4,111 €</b>	<b>2.9%</b>
	Cost of Illness-related Absences from Work/Study	1,757 €	1.2%
	Cost of Illness-related Absences from Work/Study for Family Members/Friends	610 €	0.4%
	Cost of Days of Domestic Help	1,744 €	1.2%

### Final Thoughts

The total average yearly cost per patient is almost € 142,400.

The data highlights the good coverage of the National Health System for people with Fabry disease: in fact, out-of-pocket health service expenditure for patients themselves can be considered minimal with respect to the overall cost.

90.5% of all costs are related to the medication used for the treatment of this disorder. In that respect, it shows the savings possible thanks to the administration of pharmacological treatment at home for both the National Health System and the families (fewer transport costs and lost productivity).

Other significant issues are costs of assistance benefits (2.9%; €4,168 year/patient) and the indirect costs of managing the illness borne by the patient and family members (2.9%; €4,111 year/patient). Specifically, the survey showed the number of workdays missed due to managing the disease – this is also due to the lack of legal recognition of a patient's handicap status pursuant to article 3 of Law 104/1992<sup>8</sup>.

<sup>8</sup> The status of having a handicap was recognised to 33% of people pursuant to article 3 of Law 104/1992 (of whom 46% were recognised to have a serious handicap, pursuant to article 3 para. 3).