BUDGET IMPACT ANALYSIS OF FISIOGEN FERRO FORTE® VERSUS INTRAVENOUS IRON FOR THE MANAGEMENT OF IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE IN SPAIN

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ABSTRACT

Background and Objective: Iron deficiency is a frequent complication of chronic kidney disease (CKD) that is associated with a decrease in the quality of life of patients and an increase in the risk of suffering other clinical complications. Iron therapy represents one of the fundamentals of patients with CKD. Sucrosomial® oral iron allows that Fisiogen Ferro Forte® can be used in all those patients who turn out to be intolerant to treatment by oral route or who present a malabsorption of conventional oral iron preparations. The main objective is to assess the economic impact of the oral iron Fisiogen Ferro Forte® for the management of iron deficiency in CKD patients in Spain.

Methods: A 4-year budget impact model was developed for the period 2017-2020 for CKD patients with iron deficiency candidates for intravenous iron due to a lack of response to oral iron from the Spanish Healthcare System perspective. Three subgroups of CKD patients were included in the analysis: pre-dialysis, peritoneal dialysis and post-transplant. Ferinject®, Venofer® and Feriv® were the intravenous iron formulations considered as appropriate comparators to be used in the model. National data on CKD prevalence for the three subgroups of patients were obtained from the literature. Input data on drug utilization and outpatient hospitalizations associated with iron administration were obtained by consulting nephrologists. Nephrology experts were also asked about resources of medical visits and monitoring tests. Based on the unit costs for each iron therapy and resources used, the total treatment cost per patient associated with each product was obtained to estimate the global budget impact of increasing the use of Fisiogen Ferro Forte®.

Results: The average annual budget savings with an increase of Fisiogen Ferro Forte® and a decrease of intravenous iron was estimated at €398,685, €180,937 and €195,842 over the next four years for pre-dialysis, peritoneal dialysis and post-transplant groups respectively.

Conclusions: The increase in the use of Fisiogen Ferro Forte® leads to overall savings of €775,464 in the budget for the Spanish NHS over the next 4 years.

Key points: The increase in the use of Fisiogen Ferro Forte® leads to overall savings in the budget for the Spanish NHS over the next 4 years.

1. INTRODUCTION

Chronic kidney disease (CKD) is an emerging health problem throughout the world. In Spain, according to the results of the EPIRCE study, designed to know the prevalence of CKD and promoted by the Spanish Society of Nephrology with the support of the Ministry of Health and Consumption, it was estimated that approximately 10% of the adult population suffered from some degree of CKD [1]. Factors such as the aging of the population, the high prevalence of cardiovascular risk factors in the population (such as diabetes, hypertension or dyslipidemia) or early diagnosis, would be the reason of this increase in the CKD incidence [1].

Iron deficiency is a frequent complication of CKD that is associated with a decrease in hemoglobin levels that is related also with a decrease in the quality of life of patients and an increase in the risk of suffering other clinical complications, including a significant increase in cardiovascular risk [2]. The main cause of anemia in CKD is the inadequate production of endogenous erythropoietin, a hormone that acts on the differentiation and maturation of the precursors of the red blood cells. In addition, iron deficiency already appears in early stages of the disease. In more advanced phases and in patients on dialysis, around 90% of patients have an iron deficiency [3].

In the therapeutic approach of iron deficiency associated with renal failure, iron therapy represents one of the main treatment modalities of patients with CKD. In patients undergoing hemodialysis, the intravenous route is of choice but according to the latest KDIGO guidelines [4], published in 2014, there is not enough scientific evidence to affirm that the intravenous route is superior to oral administration in patients with CKD, not subject to hemodialysis.

Treatment with conventional iron salts, administered orally, can often not effectively resolve the medical situation. Patients with CKD used to present a generalized inflammatory state making iron salts absorption very difficult. The absorption difficulty involves numerous problems of tolerability causing problems in achieving a good therapeutic compliance.

Despite this, in dialysis patients, oral iron can be especially the appropriate route to the need to preserve the venous tree by the time they need to enter into a hemodialysis process.

The development of new technologies, such as the coverage of iron in sucrosomes, to avoid the appearance of adverse effects without compromising the already low bioavailability of iron is a very topical issue. This new technology reduces the possible interactions of iron compounds with other components of the diet that can decrease even more their bioavailability, such as tannins, polyphenols and phytates.

It also reduces the irritation often caused by iron compounds in the gastric mucosa and it allows its absorption bypassing the hepcidin-dependent pathways involved in conventional iron absorption, being M cells from reticuloendothelial system a key pathway contributing to its absorption also in an inflammatory context [5,6].

Sucrosomial® oral iron allows that Fisiogen Ferro Forte® can be used in all those patients who are intolerant to treatment by oral route or who present a malabsorption of conventional oral iron preparations [5,6].

The distinguishing features of Fisiogen Ferro Forte® make it possible to use it in all those patients, who are intolerant to oral treatment or who present a malabsorption of conventional oral iron preparations whose bioavailability is excessively limited, thus guaranteeing therapeutic adherence to treatment with oral iron and the consequent recovery of blood parameters [7-11].

Different pharmacoeconomic analyses [12,13] have been published, where the drugs assessed were all intravenous (i.v.) iron solutions. These studies have shown that ferric carboxymaltose (Ferinject®) provide savings from the perspective of the national health service (NHS) because of the shorter duration of intravenous administration compared to the other iron solutions assessed in the studies.

In the current study, we evaluated the expected economic impact from the increase in the market share of Fisiogen Ferro Forte® for the management of iron deficiency in patients with different CKD stages from the perspective of the Spanish NHS by using a budget impact model.

2. METHODS

Model Development and Structure

The budget impact model (BIM) was developed in Microsoft Excel from the perspective of the Spanish NHS. We assessed differences among three subgroups of patients who can benefit from the use of Fisiogen Ferro Forte®. Each subgroup represents a specific stage of CKD: pre-dialysis, peritoneal dialysis and post-transplant. Ferinject®, Venofer® and Feriv® were the i.v. iron formulations considered as appropriate comparators to be used in the model, given that constitute the iron deficiency maintenance treatment options in patients who do not respond to oral iron treatment due to problems of absorption or intolerance. The model analysed drug utilization for each subgroup of patients receiving iron supplementation based on their maintenance dose and number of doses required per year to treat the iron deficiency and its consequences, as well as the outpatient hospitalizations (Day hospital stay of a few hours, sometimes minutes) associated with the administration of i.v. iron formulations. Other medical resources use was based on the mean number of events for medical visits and iron deficiency monitoring tests required per year. The differences in product and medical costs associated with each treatment option, as well as the global budget impact of the forecast uptake of Fisiogen Ferro Forte®, were estimated from 2017 to 2020.

The model included prevalent CKD patients estimated for each analysed subgroup, who control iron deficiency with an iron maintenance treatment but cannot receive oral iron. A panel of experts from different Spanish hospitals provided information on drug utilization and medical resources associated with iron maintenance therapy (outpatient hospitalizations,

medical visits and monitoring tests). Annual costs of drugs and medical resources associated with iron maintenance therapy were reported in Euros (EUR 2017).

The model generated estimates for the annual cost per patient including drug and medical costs to calculate the global budget impact based on market shares and prevalence data.

Model Input Variables

A panel of experts were consulted about some specific data that cannot be found in the literature or in the guidelines. In order to obtain the data requested, the experts have filled a questionnaire in which they were asked for data about epidemiology, treatments, dosage and healthcare resources use for the three subgroups of patients considered in this study.

Target population

To estimate the target population comprising CKD patients with iron deficiency candidates for i.v. iron supplementation the following algorithm was applied as shown in Figure 1. A literature review was performed to identify the prevalence of CKD for each stage of disease: 0.03% among the Spanish adult population (pre-dialysis) [14] and 0.11% among the Spanish population (stage 5D) [15]. Within the last group, a 5.5% correspond to patients in peritoneal dialysis and a 51.5% to post-transplant patients. The estimate for each stage of CKD has been extrapolated to the Spanish adult population obtained from the population projections conducted by the National Institute of Statistics (INE) [16]. The number of adult patients in Spain who present iron deficiency was estimated respectively for each stage of disease based on a panel of experts in nephrology: 65% (pre-dialysis), 82.5% (peritoneal dialysis) and 50% (post-transplant). The percentage of adult patients who are candidates for i.v. iron supplementation was estimated respectively for each stage of disease based on a panel of experts in nephrology: 52.5% (pre-dialysis), 85% (peritoneal dialysis) and 10% (post-transplant).

It must be taken into account that, due to the lack of data regarding iron deficiency prevalence in CKD patients, anemia data have been considered. In addition, it should be taken into account that using the anemia data provides more restrictive results than using the iron deficiency data.

Drug treatments and costs

The iron maintenance doses associated with each treatment for the different subgroups of patients receiving iron supplementation and the number of doses required per drug per year were estimated based on data from clinical practice by a panel of two clinical experts in nephrology from different Spanish hospitals (Table 1). Based on the average number of doses per year for the i.v. iron formulations, the number of 3-month treatments per year for Fisiogen Ferro Forte® and the unit costs per dose in EUR, the annual pharmacological treatment cost for each iron product was calculated. Prices were obtained from a Spanish Database of Pharmacists [17] and were expressed in EURO 2017.

Furthermore, we assumed that the increase of Fisiogen Ferro Forte® was offset by a decrease in the market share of the i.v. iron formulations.

Medical Resource Utilization and Costs

Healthcare resources utilisation and costs included in the model were outpatient hospitalizations associated with the i.v. iron formulations administration, medical visits and monitoring tests (Table 2). The medical resources associated with each drug were based on the consultation of an expert panel of nephrologists and unit costs were obtained from the regional tariff lists of Madrid [18] and Valencia [19] (Table 2). The costs for the primary care visit and the Day hospital stay were obtained from the tariffs list of Madrid and the costs for the specialist physician, the nurse and the laboratory tests were obtained from the tariffs list of Valencia.

Budgetary impact analysis

Our model has estimated annual drug and healthcare resource cost per patient and allowed us to calculate for each treatment option, the annual cost per patient in EUR 2017. Based on the annual average cost per patient, the target population and the actual market shares for the products included in this study, the budget impact of the maintenance iron therapy for the treatment of iron deficiency was obtained for 2017-2020. The actual market shares for 2017 were based on data of IMS [20] on the actual distribution of iron products (Table 3). This current scenario was compared with an alternative scenario in which the economic impact was conducted considering an increase in the use of Fisiogen Ferro Forte®. This increase has been calculated following the growing of Fisiogen Ferro Forte® during the last years. The BIM was based on the difference found between the alternative scenario and the current scenario.

Deterministic sensitivity analysis

A one-way sensitivity analysis has been conducted in order to assess the robustness of the model. In order to include all the possible scenarios, the main variables were included in this sensitivity analysis. The base case parameter for each variable was varied from the default value within reasonable lower and upper limits by using data from expert consultation and variations of 50% were applied to parameters for which no ranges were identified in the published literature.

3. RESULTS

We present the results of the BIM separately for the different stages of disease: pre-dialysis, peritoneal dialysis and post-transplant. The results show the economic impact of the treatment of iron deficiency and low haemoglobin in the different CKD stages from 2017 to 2020 for the total of Spain.

Pre-dialysis

In our model based on the prevalence of iron deficiency and low haemoglobin in patients with CKD in pre-dialysis stage, and i.v. iron use it would be expected that 3,700 patients in 2017 diagnosed with iron deficiency and CKD receive treatment with i.v. iron. Based on population trends this number decreases slightly to 3,683 patients in 2020 (Table 4).

In the base case analysis in the current scenario before the increase of the market share of Fisiogen Ferro Forte® the total economic impact for the treatment with i.v. iron for patients with iron deficiency and CKD in pre-dialysis stage was estimated at €4.31 million, €4.23 million, €4.15 million and €4.06 million for the years 2017, 2018, 2019 and 2020, respectively (Table 5).

When the market share of Fisiogen Ferro Forte® was increased to 3%, 5%, 8% and 10% in 2017, 2018, 2019 and 2020 respectively, matched with a reduction in the share of the i.v. iron, the total economic impact was estimated at €4.27 million, €4.16 million, €4.03 million and €3.92 million in 2017, 2018, 2019 and 2020 respectively (Table 6). Overall, the total budget savings with the modified market shares with an annual increase of Fisiogen Ferro Forte® and decrease of i.v. iron were expected to be €376,041 over the next four years (Table 5).

At patient level, the average annual cost per patient in the current scenario decreases from 2017 to 2020 from €1,166 to €1,104 and further, the cost per patient would be less with €1,064 in the alternative scenario. The average cost per patient over the period 2017-2020 with the increase in the market share of Fisiogen Ferro Forte® was €25 lower with €1,135 annual costs per patient than in the current scenario with €1,109 (Table 5).

Peritoneal dialysis

In our model based on the prevalence of iron deficiency in patients with CKD stage 5D (peritoneal dialysis), and i.v. iron use it would be expected that 1,989 patients in 2017 diagnosed with iron deficiency and low haemoglobin and CKD receive treatment with i.v. iron. Based on population trends this number decreases slightly to 1,980 patients in 2020 (Table 5).

In the base case analysis in the current scenario before the increase of the market share of Fisiogen Ferro Forte® the total economic impact for the treatment with i.v. iron for patients with iron deficiency and CKD stage 5D (peritoneal dialysis) was estimated at €2.22 million, €2.16 million, €2.10 million and €2.04 million for the years 2017, 2018, 2019 and 2020 respectively (Table 6).

When the market share of Fisiogen Ferro Forte® was increased to 3%, 5%, 8% and 10% in 2017, 2018, 2019 and 2020 respectively, matched with a reduction in the share of the i.v. iron, the total economic impact was estimated at €2.20 million, €2.13 million, €2.06 million and €1.99 million in 2017, 2018, 2019 and 2020 respectively (Table 6). Overall, the total budget savings with the modified market shares with an annual increase of Fisiogen Ferro Forte® and decrease of i.v. iron was expected to be €122,490over the next four years (Table 5).

At patient level, the average annual cost per patient in the current scenario decreases from 2017 to 2020 from €1,114 to €1,030 and further, the cost per patient would be less with €1,006 in the alternative scenario. The average cost per patient over the period 2017-2020 with the increase in the market share of Fisiogen Ferro Forte® was €15 lower with €1,072 annual costs per patient than in the current scenario with €1,056 (Table 5).

Post-transplant

In our model based on the prevalence of iron deficiency in patients with stage 5D CKD with functioning kidney transplant, and i.v. iron use it would be expected that 1,328 patients in 2017 diagnosed with iron deficiency and CKD receive treatment with i.v. iron. Based on population trends this number decreases slightly to 1,322 patients in 2020 (Table 5).

In the base case analysis in the current scenario before the increase of the market share of Fisiogen Ferro Forte® the total economic impact for the treatment with i.v. iron for patients with iron deficiency and stage 5D CKD with functioning kidney transplant was estimated at €1.82 million, €1.79 million, €1.77 million and €1.75 million for the years 2017, 2018, 2019 and 2020 respectively (Table 5).

When the market share of Fisiogen Ferro Forte® was increased to 3%, 5%, 8% and 10% in 2017, 2018, 2019 and 2020 respectively, matched with a reduction in the share of the i.v. iron, the total economic impact was estimated at €1.79 million, €1.76 million, €1.72 million and €1.66 million in 2017, 2018, 2019 and 2020 respectively (Table 5). Overall, the total budget savings with the modified market shares with an annual increase of Fisiogen Ferro Forte® and decrease of i.v. iron was expected to be €167,031over the next four years (Table 5).

At patient level, the average annual cost per patient in the current scenario decreases from 2017 to 2020 from €1,367 to €1,324 and further, the cost per patient would be less with €1,275 in the alternative scenario. The average cost per patient over the period 2017-2020 with the increase in the market share of Fisiogen Ferro Forte® was €32 lower with €1,345 annual costs per patient than in the current scenario with €1,314 (Table 5).

Deterministic sensitivity analysis

One-way sensitivity analyses were conducted to examine how changes in key model parameters might affect the results of the base case analysis. The parameters that were varied included the percentage of patients with iron deficiency, the percentage of patient candidates for i.v. iron, the market shares for Fisiogen Ferro Forte® and the monthly cost of Fisiogen Ferro Forte®. The results of varying each parameter are shown in Table 6-8.

The model was most sensitive to the percentage of patient candidates to i.v. iron for all the subgroups, resulting in the largest overall decrease in budget impact of €644,642, €951,806 and €310.063 for the pre-dialysis, peritoneal dialysis and post-transplant subgroups, respectively.

The model was also sensitive to the drug cost per month of Fisiogen Ferro Forte® for all the subgroups, resulting in overall decrease in budget impact of €478,355, €946,629 and €246,386 for the pre-dialysis, peritoneal dialysis and post-transplant subgroups, respectively.

4. DISCUSSION

This study compares the costs of three i.v. iron products (Ferinject®, Venofer® and Feriv®) and an oral iron product (Fisiogen Ferro Forte®) and estimates the budget impact for the treatment of iron deficiency in three groups of nephrology patients: pre-dialysis, peritoneal dialysis and post-transplant. Results of the budget impact analysis suggest that the increasing use of Fisiogen Ferro Forte® would result in a four-year adjusted total budget savings for the Spanish NHS of €376,041, €898,928 and €206,708 for pre-dialysis, peritoneal dialysis and post-transplant respectively at a national level.

The main reason for these budget impact results is that the growing use of Fisiogen Ferro Forte®, as it is an oral iron does not involve any use of the healthcare centre or healthcare professional during its administration.

In this pharmacoeconomic analysis we have only considered the Spanish NHS perspective, which involves the drug acquisition cost and the i.v administration cost, as well as the healthcare professionals,the possible laboratory tests needed and the outpatient hospitalizations associated with the administration of i.v. iron formulations. But we have not considered the society perspective, which will include patients transportation cost and patients working days losses.

Carlos Rubió-Terrés et al [5], in their pharmacoeconomic analysis of the treatment of iron deficiency with Ferinject® in Spain have considered both perspectives. The results obtained from the NHS perspective shown that the use of Ferinject® would generate a saving by treatment of iron deficiency of 183 € compared to iron dextran and from 131 € to 164 € compared to iron sucrose. From the society perspective, savings would be 262 € and 143 € to 177 €, respectively.

One of the strengths for our analysis is that due to the lack of published clinical input data on drug use, medical resource utilisation and treatment of i.v. iron this study was based on the real-world use of these treatments as input data was based on the expert opinion of

nephrologists working in different Spanish hospitals. However, these experts opinion may have caused a bias in the study since only a few experts have been involved, which do not cover all regions of Spain. The results obtained in our analysis can be considered conservative since if indirect costs were considered, such as the loss of working hours due to the stay in the day hospital for i.v. iron to be administered, clearly the treatment with Fisiogen Ferro Forte® would produce even more important savings than those already obtained without considering these costs.

5. CONCLUSIONS

The results from our analysis suggest that when the market share of Fisiogen Ferro Forte® increases of 3%, 5%, 8% and 10% for the next four years while the use of i.v. iron decreases, it would result in a €376,041, €898,928 and €206,708 decrease in the overall budget over the period 2017-2020 for pre-dialysis, peritoneal dialysis and post-transplant groups respectively. These saving would be possible due to lower expected drug costs and healthcare resource utilisation costs. Although the economic impact of iron deficiency treatment has shown to increase over the next four years due to population growth the increase in the use of Fisiogen Ferro Forte® for the treatment of iron deficiency shows to reduce the average annual cost per patient with an average of €24 over the next four years.

Figure 1. Target population of the study

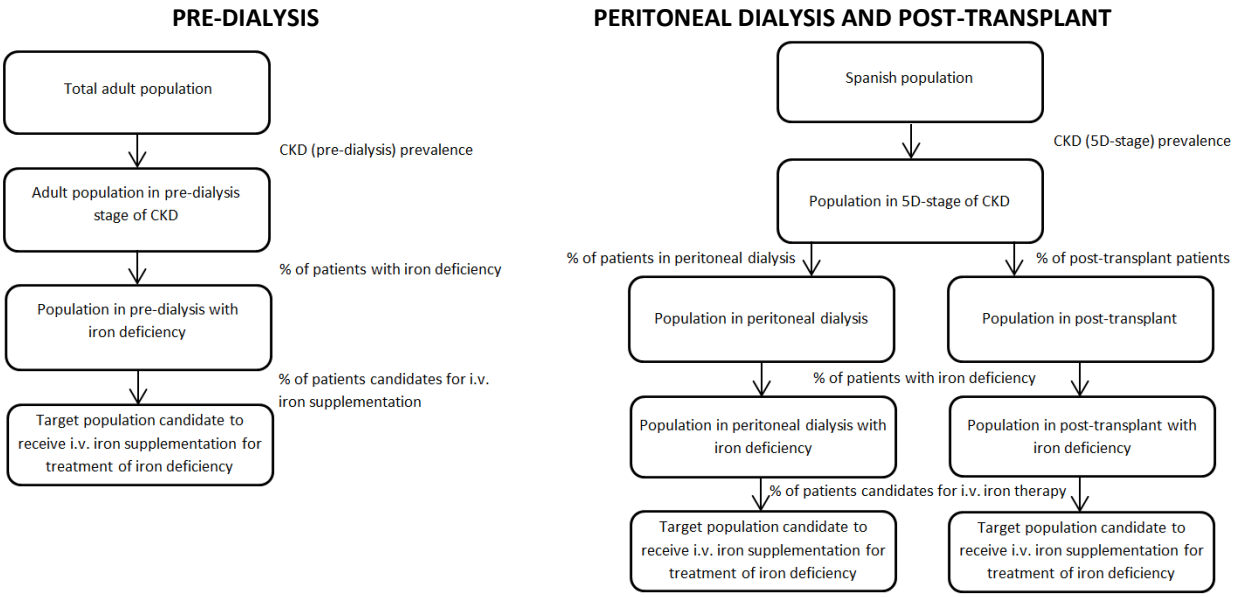

Table 1. Drugs, dosage, costs per dose, usage percentages

Stage of disease	Drugs	Dose per year (mg)	Dose per visit (mg)	Number of doses	Drug cost (€)	% of patients using the dose
Pre-dialysis	Ferinject®	500 mg	500 mg	1	100.20 €	10%
		1000 mg	500 mg	2	200.40 €	80%
		1500 mg	500 mg	3	300.60 €	10%
	Venofer®	1000 mg	200 mg	5	115.68 €	100%
	Feriv®	1000 mg	200 mg	5	82.62 €	10%
		1200 mg	200 mg	6	99.15 €	60%
		1600 mg	200 mg	8	132.20 €	30%
		Treatments per year			**Drug cost per year**	**% of patients**
	Fisiogen Ferro Forte ®	1 treatment of 3 months			63.69 €	5%
		2 treatments of 3 months			127.39 €	15%
		3 treatments of 3 months			191.08 €	20%
		4 treatments of 3 months			254.77 €	60%
		Dose per year (mg)	**Dose per visit (mg)**	**Number of doses**	**Drug cost (€)**	**% of patients using the dose**
Peritoneal dialysis	Ferinject®	500 mg	500 mg	1	100.20 €	40%
		1000 mg	500 mg	2	200.40 €	60%
	Venofer®	1000 mg	200 mg	5	115.68 €	100%
	Feriv®	600 mg	200 mg	3	49.57 €	20%
		800 mg	200 mg	4	66.10 €	60%
		1200 mg	200 mg	6	99.15 €	20%
		Treatments per year			**Drug cost per year**	**% of patients**
	Fisiogen Ferro Forte ®	1 treatment of 3 months			60.66 €	10%
		2 treatments of 3 months			121.32 €	30%
		3 treatments of 3 months			181.98 €	5%
		4 treatments of 3 months			242.64 €	55%
		Dose per year (mg)	**Dose per visit (mg)**	**Number of doses**	**Drug cost (€)**	**% of patients using the dose**
Post-transplant	Ferinject®	500 mg	500 mg	1	100.20 €	30%
		1000 mg	500 mg	2	200.40 €	60%
		1500 mg	500 mg	3	300.60 €	10%
	Venofer®	1000 mg	200 mg	5	115.68 €	100%
	Feriv®	1000 mg	200 mg	5	82.62 €	100%
		Treatments per year			**Drug cost per year**	**% of patients**
	Fisiogen Ferro Forte ®	3 treatments of 3 months			181.98 €	20%
		4 treatments of 3 months			242.64 €	80%

Table 2. Drug cost, medical resource utilisation and unit costs and average cost per patient per year

Stage of disease	Annual resources	Ferinject®	Venofer®	Feriv®	Fisiogen Ferro Forte®	Unit costs in € 2017
Pre-dialysis	**Drug cost (€)**	**203.36 €**	**130.48 €**	**126.65 €**	**213.37 €**	-
	Medical visits					
	Specialist physician	4	12	6	5	64.19 €
	Primary Care	0	2	0	0	38.45 €
	Nurse	2	5	6.5	0	20.63 €
	Annual cost (€)	**298.02 €**	**950.33 €**	**519.24 €**	**320.95 €**	-
	Day hospital Annual cost (€)	**54.62 €**	**227.60 €**	**295.88 €**	**0.00 €**	-
	Laboratory tests					
	Study of ferric metabolism (TSAT and ferritin)	4	4	6	5	17.30 €
	Haemoglobin level monitoring	4	4	6	5	9.58 €
	Annual cost (€)	**107.52 €**	**107.52 €**	**161.28 €**	**134.40 €**	-
	Total cost per patient in €	**663.52 €**	**1,415.93 €**	**1,103.05 €**	**668.72 €**	-
Peritoneal dialysis	**Drug cost (€)**	**162.69 €**	**130.48 €**	**81.83 €**	**185.01 €**	-
	Medical visits					
	Specialist physician	6	12	6	6	64.19 €
	Primary Care	0	2	0	0	38.45 €
	Nurse	1.6	5	4.2	0	20.63 €
	Annual cost (€)	**418.15 €**	**950.33 €**	**471.79 €**	**385.14 €**	-
	Day hospital Annual cost (€)	**43.70 €**	**227.60 €**	**191.18 €**	**0.00 €**	-
	Laboratory tests					
	Study of ferric metabolism (TSAT and ferritin)	6	4	6	6	17.30 €
	Haemoglobin level monitoring	6	12	6	6	9.58 €
	Annual cost (€)	**161.28 €**	**184.16 €**	**161.28 €**	**161.28 €**	-
	Total cost per patient in €	**785.82 €**	**1,492.57 €**	**906.08 €**	**731.43 €**	-
Post-transplant	**Drug cost (€)**	**183.03 €**	**130.48 €**	**97.42 €**	**230.51 €**	-
	Medical visits					
	Specialist physician	4	12	12	4	64.19 €
	Primary Care	0	2	2	0	38.45 €
	Nurse	1.8	5	5	0	20.63 €
	Annual cost (€)	**293.89 €**	**950.33 €**	**950.33 €**	**256.76 €**	-
	Day hospital Annual cost (€)	**49.16 €**	**227.60 €**	**227.60 €**	**0.00 €**	-
	Laboratory tests					
	Study of ferric metabolism (TSAT and ferritin)	4	4	4	4	17.30 €
	Haemoglobin level monitoring	4	12	12	4	9.58 €
	Annual cost (€)	**107.52 €**	**184.16 €**	**184.16 €**	**107.52 €**	-
	Total cost per patient in €	**663.60 €**	**1,492.57 €**	**1,459.51 €**	**594.79 €**	-

Table 3. Market shares (%): Base case analysis and alternative scenario

Base case analysis	2017	2018	2019	2020
Ferinject®	12.74%	14.30%	15.85%	17.41%
Venofer®	38.02%	33.57%	29.12%	24.66%
Feriv®	49.24%	52.13%	55.03%	57.93%
Fisiogen Ferro Forte®	0.00%	0.00%	0.00%	0.00%
Alternative scenario	**2017**	**2018**	**2019**	**2020**
Ferinject®	11.74%	12.63%	13.18%	14.08%
Venofer®	37.02%	31.90%	26.45%	21.33%
Feriv®	48.24%	50.46%	52.36%	54.60%
Fisiogen Ferro Forte®	3.00%	5.00%	8.00%	10.00%

Table 4. Target population for intravenous iron treatment

Stage of disease	Target population	2017	2018	2019	2020
Pre-dialysis	Adult patients with CKD in pre-dialysis stage	10,843	10,825	10,807	10,792
	Adult patients with CKD in pre-dialysis stage who have iron deficiency	7,048	7,036	7,025	7,015
	Adult patients with CKD in pre-dialysis stage who have iron deficiency candidates for intravenous iron	3,700	3,694	3,688	3,683
Peritoneal dialysis	Adult patients with CKD stage 5D	51,575	51,501	51,421	51,334
	Adult patients with stage 5D CKD in peritoneal dialysis	2,837	2,833	2,828	2,823
	Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency	2,340	2,337	2,333	2,329
	Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency candidates for intravenous iron	1,989	1,986	1,983	1,980
Post-transplant	Adult patients with CKD stage 5D	51,575	51,501	51,421	51,334
	Adult patients with stage 5D CKD with a functional transplant	26,561	26,523	26,482	26,437
	Adult patients with stage 5D CKD with a functional transplant who have iron deficiency	13,281	13,262	13,241	13,219
	Adult patients with stage 5D CKD with a functional transplant who have iron deficiency candidates for intravenous iron	1,328	1,326	1,324	1,322

Table 5. Results of the base case budget impact analysis

Pre-dialysis	**Current scenario**	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	312,791 €	350.492 €	387.858 €	425.438 €	1.476.579 €
	Venofer®	1,991,955 €	1.755.808 €	1.520.611 €	1.285.919 €	6.554.293 €
	Feriv®	2,009,730 €	2.124.054 €	2.238.610 €	2.353.294 €	8.725.688 €
	Fisiogen Ferro Forte®	0 €	0 €	0 €	0 €	0 €
	Total cost (€)	4,314,475 €	4.230.354 €	4.147.079 €	4.064.652 €	16.756.560 €
	Alternative scenario	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	288,239 €	309.642 €	322.603 €	343.983 €	1.264.468 €
	Venofer®	1,939,563 €	1.668.636 €	1.381.361 €	1.112.099 €	6.101.659 €
	Feriv®	1,968,915 €	2.056.145 €	2.130.131 €	2.217.884 €	8.373.074 €
	Fisiogen Ferro Forte®	74,232 €	123.509 €	197.297 €	246.278 €	641.317 €
	Total cost (€)	4,270,949 €	4.157.933 €	4.031.392 €	3.920.245 €	16.380.519 €
	Budget impact savings	-43,527 €	-72.421 €	-115.687 €	-144.407 €	-376.041 €
Peritoneal dialysis	**Current scenario**	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	199,142 €	223.208 €	247.016 €	999.610 €	1.668.977 €
	Venofer®	1,128,805 €	995.263 €	861.986 €	728.738 €	3.714.792 €
	Feriv®	887,483 €	938.230 €	988.879 €	1.039.242 €	3.853.835 €
	Fisiogen Ferro Forte®	0 €	0 €	0 €	0 €	0 €
	Total cost (€)	2,215,431 €	2.156.702 €	2.097.881 €	2.767.590 €	9.237.604 €
	Alternative scenario	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	183,511 €	197.193 €	205.457 €	219.011 €	805.172 €
	Venofer®	1,099,116 €	945.851 €	783.049 €	630.233 €	3.458.249 €
	Feriv®	869,460 €	908.234 €	940.960 €	979.444 €	3.698.097 €
	Fisiogen Ferro Forte®	43,648 €	72.644 €	116.049 €	144.817 €	377.158 €
	Total cost (€)	2,195,735 €	2.123.922 €	2.045.515 €	1.973.504 €	8.338.676 €
	Budget impact savings	-19,696 €	-32.780 €	-52.366 €	-794.086 €	-898.928 €
Post-transplant	**Current scenario**	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	107,201 €	120.156 €	132.972 €	145.815 €	506.145 €
	Venofer®	753,634 €	664.476 €	575.495 €	486.534 €	2.480.140 €
	Feriv®	954,423 €	1.008.998 €	1.063.467 €	1.117.628 €	4.144.516 €
	Fisiogen Ferro Forte®	0 €	0 €	0 €	0 €	0 €
	Total cost (€)	1,815,259 €	1.793.630 €	1.771.935 €	1.749.977 €	7.130.800 €
	Alternative scenario	**2017**	**2018**	**2019**	**2020**	**Total**
	Ferinject®	98,787 €	106.152 €	110.601 €	117.897 €	433.436 €
	Venofer®	733,812 €	631.487 €	522.794 €	420.768 €	2.308.862 €
	Feriv®	935,040 €	976.739 €	1.011.933 €	1.053.319 €	3.977.031 €
	Fisiogen Ferro Forte®	23,697 €	39.439 €	63.004 €	78.623 €	204.763 €
	Total cost (€)	1,791,336 €	1.753.817 €	1.708.332 €	1.670.607 €	6.924.092 €
	Budget impact savings	-23,922 €	-39.814 €	-63.603 €	-79.370 €	-206.708 €

Table 6. One-way sensitivity analysis for the pre-dialysis subgroup

One-way sensitivity analysis			Budget impact analysis				
Model parameter	**Value in model**	**Sensitivity analysis**	**2017**	**2018**	**2019**	**2020**	**Total**
Base case			-43,527 €	-72.421 €	-115.687 €	-144.407 €	-376.041 €
Adult patients with CKD in pre-dialysis stage who have iron deficiency	65%	50%	-33.482 €	-55.708 €	-88.990 €	-111.082 €	-289.263 €
		80%	-53.571 €	-89.133 €	-142.384 €	-177.732 €	-462.820 €
Adult patients with CKD in pre-dialysis stage who have iron deficiency candidates for intravenous iron	52,5%	15%	-12.436 €	-20.692 €	-33.053 €	-41.259 €	-107.440 €
		90%	-74.617 €	-124.150 €	-198.320 €	-247.555 €	-644.642 €
Market share projection (Fisiogen Ferro Forte® increase)	3% - 5% - 8% - 10%	2% - 4% - 6% - 8%	-29.018 €	-57.937 €	-86.765 €	-115.526 €	-289.245 €
		3% - 6% - 9% - 12%	-43.527 €	-86.905 €	-130.148 €	-173.288 €	-433.868 €
Fisiogen Ferro Forte® monthly cost	20.22 €	10.11 €	-55.370 €	-92.125 €	-147.163 €	-183.697 €	-478.355 €
		30.33 €	-31.684 €	-52.716 €	-84.211 €	-105.117 €	-273.728 €

Table 7. One-way sensitivity analysis for the peritoneal dialysis subgroup

One-way sensitivity analysis			Budget impact analysis				
Model parameter	**Value in model**	**Sensitivity analysis**	**2017**	**2018**	**2019**	**2020**	**Total**
Base case			-19,696 €	-32.780 €	-52.366 €	-794.086 €	-898.928 €
Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency	82,5%	80%	-19.099 €	-31.787 €	-50.780 €	-770.022 €	-871.688 €
		85%	-20.293 €	-33.773 €	-53.953 €	-818.149 €	-926.169 €
Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency candidates for intravenous iron	85%	80%	-18.538 €	-30.852 €	-49.286 €	-747.375 €	-846.050 €
		90%	-20.855 €	-34.708 €	-55.447 €	-840.796 €	-951.806 €
Market share projection (Fisiogen Ferro Forte® increase)	3% - 5% - 8% - 10%	2% - 4% - 6% - 8%	-13.131 €	-26.224 €	-39.275 €	-781.016 €	-859.646 €
		3% - 6% - 9% - 12%	-19.696 €	-39.336 €	-58.912 €	-807.155 €	-925.100 €
Fisiogen Ferro Forte® monthly cost	20.22 €	10.11 €	-25.217 €	-41.968 €	-67.043 €	-812.401 €	-946.629 €
		30.33 €	-14.176 €	-23.593 €	-37.689 €	-775.770 €	-851.228 €

Table 8. One-way sensitivity analysis for the post-transplant subgroup

One-way sensitivity analysis			Budget impact analysis				
Model parameter	**Value in model**	**Sensitivity analysis**	**2017**	**2018**	**2019**	**2020**	**Total**
Base case			-23,922 €	-39.814 €	-63.603 €	-79.370 €	-206.708 €
Adult patients with stage 5D CKD with a functional transplant who have iron deficiency	50%	40%	-19.138 €	-31.851 €	-50.882 €	-63.496 €	-165.367 €
		60%	-28.707 €	-47.777 €	-76.323 €	-95.244 €	-248.050 €
Adult patients with stage 5D CKD with a functional transplant who have iron deficiency candidates for intravenous iron	10%	5%	-11.961 €	-19.907 €	-31.801 €	-39.685 €	-103.354 €
		15%	-35.884 €	-59.721 €	-95.404 €	-119.055 €	-310.063 €
Market share projection (Fisiogen Ferro Forte® increase)	3% - 5% - 8% - 10%	2% - 4% - 6% - 8%	-15.948 €	-31.851 €	-47.702 €	-63.496 €	-158.997 €
		3% - 6% - 9% - 12%	-23.922 €	-47.777 €	-71.553 €	-95.244 €	-238.496 €
Fisiogen Ferro Forte® monthly cost	20.22 €	10.11 €	-28.514 €	-47.456 €	-75.811 €	-94.605 €	-246.386 €
		30.33 €	-19.331 €	-32.172 €	-51.394 €	-64.135 €	-167.031 €

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