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ORIGINAL RESEARCH ARTICLE

Budget Impact Analysis of Oral Fisiogen Ferro Forte® versus Intravenous Iron for the Management of Iron Deficiency in Chronic Kidney Disease in Spain

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Abstract

Background 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 other clinical complications. Iron therapy represents one of the fundamentals of patients with CKD. Sucrosomial® oral iron allows Fisiogen Ferro Forte® to be used in all patients who are intolerant to treatment by the oral route of administration, or who present with malabsorption of conventional oral iron preparations.

Objective The main objective of this study was 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 who were candidates for intravenous iron due to a lack of response to oral iron, from the perspective of the Spanish healthcare system. Three subgroups of CKD patients were included in the analysis: predialysis, peritoneal dialysis, and post-transplant. The intravenous iron formulations Ferinject®, Venofer®, and Feriv® were considered appropriate comparators to be used in the model. National data on the prevalence of CKD for the three subgroups of patients were obtained from the literature, and input data on drug utilization and outpatient hospitalizations associated with iron administration were obtained by consulting nephrologists. Nephrology experts were also asked about resources used during medical visits and monitoring tests. Based on the unit costs for each iron therapy and the 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 due to an increase in Fisiogen Ferro Forte® and a decrease in intravenous iron have been estimated at €398,685, €180,937, and €195,842 over 4 years for the predialysis, peritoneal dialysis, and post-transplant groups, respectively.

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

Key Points

The increase in the use of Fisiogen Ferro Forte® leads to overall budget savings for the Spanish National Health Service over 4 years.

1 Introduction

Chronic kidney disease (CKD) is an emerging health problem throughout the world. According to the results of the EPIRCE study, designed to determine 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 in Spain have experienced some degree of CKD [1]. Factors such as aging of the population, the high prevalence of cardiovascular risk factors (e.g. diabetes, hypertension or dyslipidemia), or early diagnosis are some of the reasons for this increase in the incidence of CKD [1].

Iron deficiency is a frequent complication of CKD that is associated with a decrease in hemoglobin levels that is

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related to a decrease in the quality of life of patients and an increase in the risk of 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 is already present in the early stages of the disease. In the more advanced stages, and in patients receiving dialysis, approximately 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 the route of choice, but according to the latest Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [4], published in 2014, there is insufficient scientific evidence to affirm that the intravenous route is superior to oral administration in patients with CKD who are not subject to hemodialysis.

Treatment with conventional iron salts, administered orally, can often ineffectively resolve the medical situation. Patients with CKD used to present with a generalized inflammatory state, making the absorption of iron salts very difficult. This difficulty in absorption involves numerous problems relating to tolerability, causing problems in achieving good therapeutic compliance.

Despite this, in dialysis patients oral iron can be the more appropriate route for preserving the venous tree by the time hemodialysis is required.

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 a diet that can decrease their bioavailability even more, such as tannins, polyphenols and phytates. It also reduces the irritation often caused by iron compounds in the gastric mucosa, and allows its absorption, bypassing the hepcidin-dependent pathways involved in conventional iron absorption, being M cells from the reticuloendothelial system, a key pathway also contributing to its absorption, in an inflammatory context [5, 6].

Sucrosomial® oral iron allows for Fisiogen Ferro Forte® to be used in all patients who are intolerant to treatment by the oral route of administration, or who present with malabsorption of conventional oral iron preparations [5, 6]. The distinguishing features of Fisiogen Ferro Forte® make it possible to use it in all patients who are intolerant to oral treatment or who present with malabsorption of conventional oral iron preparations in which bioavailability is excessively limited, thus guaranteeing therapeutic adherence to treatment with oral iron and the consequent recovery of blood parameters [7–11].

Two pharmacoeconomic analyses [12, 13] have been published whereby the drugs assessed were all intravenous iron solutions. These studies have shown that ferric carboxymaltose (Ferinject®) provides savings from the perspective of the National Health Service (NHS) because of the shorter duration of intravenous administration compared with the other iron solutions assessed in those 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 stages of CKD, from the perspective of the Spanish NHS, by using a budget impact model (BIM).

2 Methods

2.1 Model Development and Structure

The BIM was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) from the perspective of the Spanish NHS. We assessed differences among three subgroups of patients who could benefit from the use of Fisiogen Ferro Forte®. Each subgroup represented a specific stage of CKD: predialysis, peritoneal dialysis, and post-transplant. The intravenous iron formulations Ferinject®, Venofer®, and Feriv® were considered appropriate comparators to be used in the model, given they constitute the iron deficiency maintenance treatment options in patients who do not respond to oral iron treatment due to absorption or intolerance problems. The model analyzed drug utilization for each subgroup of patients receiving iron supplementation based on their maintenance dose and the number of doses required per year to treat the iron deficiency and its consequences, as well as outpatient hospitalizations (day hospital stay of a few hours, sometimes minutes) associated with the administration of intravenous iron formulations. Other use of medical resources 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 analyzed subgroup, who control iron deficiency with 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 2017 Euros.

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.

2.2 Model Input Variables

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

2.3 Target Population

To estimate the target population comprising CKD patients with iron deficiency who were candidates for intravenous iron supplementation, the algorithm reported in Fig. 1 was applied. A literature review was performed to identify the prevalence of CKD for each stage of disease: 0.03% among the Spanish adult population (predialysis) [14], and 0.11% among the Spanish population (stage 5D) [15]. Within the last group, 5.5% corresponded to patients in peritoneal dialysis, and 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 presented with iron deficiency was estimated for each stage of disease, based on data provided by a panel of experts in nephrology: 65% predialysis, 82.5% peritoneal dialysis, and 50% post-transplant. Furthermore, the percentage of adult patients who were candidates for intravenous iron supplementation was also estimated for each stage of disease and also based on data provided by a panel of experts in nephrology: 52.5% predialysis, 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 also be taken into account that using the anemia data provides more restrictive results than using the iron deficiency data.

2.4 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 intravenous iron formulations, the number of 3-month treatments per year for Fisiogen Ferro Forte®, and the unit costs per dose in Euros, 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 2017 Euros.

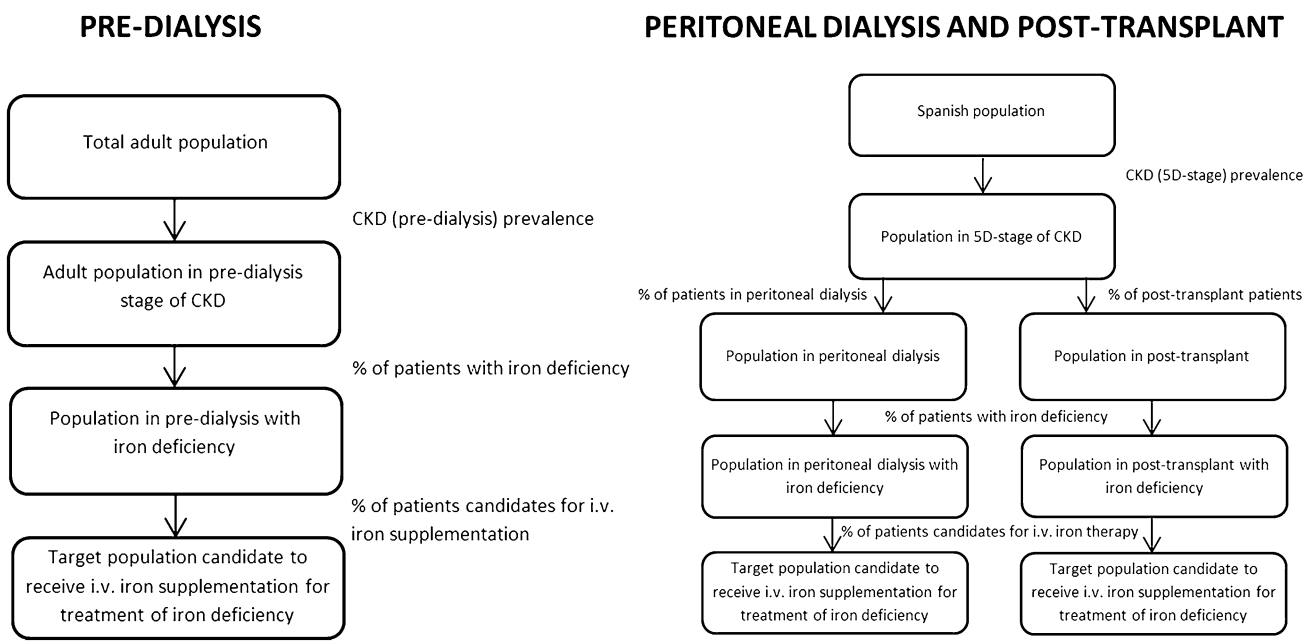

Fig. 1 Target population of the study. *CKD* chronic kidney disease, *i.v.* intravenous

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

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

2.5 Medical Resource Utilization and Costs

Healthcare resource utilization, and costs included in the model, were outpatient hospitalizations associated with the administration of the intravenous iron formulations, 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 and the nurse, and the laboratory tests, were obtained from the tariffs list of Valencia.

2.6 Budgetary Impact Analysis

Our model has estimated annual drug and healthcare resource costs per patient and has allowed us to calculate the annual cost per patient for each treatment option, in 2017 Euros. 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 maintenance iron therapy for the treatment of iron deficiency was obtained for 2017–2020. The actual market shares for 2017 were based

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

Stage of disease	Annual resources	Ferinject®	Venofer®	Feriv®	Fisiogen Ferro Forte®	2017 unit costs (€)
Predialysis	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
	Hemoglobin level monitoring	4	4	6	5	€9.58
	Annual cost (€)	107.52	107.52	161.28	134.40	–
	Total cost per patient (€)	663.52	1415.93	1103.05	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
	Hemoglobin level monitoring	6	12	6	6	€9.58
	Annual cost (€)	161.28	184.16	161.28	161.28	–
	Total cost per patient (€)	785.82	1492.57	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
	Hemoglobin level monitoring	4	12	12	4	€9.58
	Annual cost (€)	107.52	184.16	184.16	107.52	–
	Total cost per patient (€)	663.60	1492.57	1459.51	594.79	–

TSAT transferrin saturation

on data from IMS (IMS Health, unpublished data) regarding the actual distribution of iron products (Table 3). This current scenario was compared with an alternative scenario in which the economic impact was conducted when considering an increase in the use of Fisiogen Ferro Forte®. This increase has been calculated following the growing use of Fisiogen Ferro Forte® over the last years. The BIM was based on the difference found between the alternative and current scenarios.

2.7 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 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; variations of 50% were applied to parameters for which no ranges were identified in the published literature.

Table 3 Market shares: base-case analysis and alternative scenario

	2017 (%)	2018 (%)	2019 (%)	2020 (%)
Base-case analysis				
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				
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

3 Results

We present the results of the BIM separately for the different stages of disease, i.e. predialysis, peritoneal dialysis, and post-transplant. The results show the economic impact of the treatment of iron deficiency and low hemoglobin levels in the different CKD stages, from 2017 to 2020, for the whole of Spain.

3.1 Predialysis

In our model, based on the prevalence of iron deficiency and low hemoglobin in patients with CKD in the predialysis stage and using intravenous iron, it would be expected that, in 2017, 3700 patients diagnosed with iron deficiency and CKD received treatment with intravenous iron. Based on population trends, this number will decrease slightly to 3683 patients in 2020 (Table 4).

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

When the market share of Fisiogen Ferro Forte® was increased by 3, 5, 8, and 10% in 2017, 2018, 2019, and 2020, respectively, matched with a reduction in the share of

Table 4 Target population for intravenous iron treatment

Stage of disease	Target population	2017	2018	2019	2020
Predialysis	Adult patients with CKD in the predialysis stage	10,843	10,825	10,807	10,792
	Adult patients with CKD in the predialysis stage who have iron deficiency	7048	7036	7025	7015
	Adult patients with CKD in the predialysis stage who have iron deficiency and are candidates for intravenous iron	3700	3694	3688	3683
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	2837	2833	2828	2823
	Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency	2340	2337	2333	2329
	Adult patients with stage 5D CKD in peritoneal dialysis who have iron deficiency and are candidates for intravenous iron	1989	1986	1983	1980
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 and are candidates for intravenous iron	1328	1326	1324	1322

CKD chronic kidney disease

Table 5 Results of the base-case budget impact analysis

		2017 (€)	2018 (€)	2019 (€)	2020 (€)	Total (€)
Predialysis	*Current scenario*					
	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					
	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*					
	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					
	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*					
	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					
	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

intravenous 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 in the modified market shares, with an annual increase of Fisiogen Ferro Forte® and decrease of intravenous iron, were expected to be €376,041 over 4 years (Table 5).

At the patient level, the average annual cost per patient in the current scenario decreases from €1166 to €1104 in 2017–2020, and the cost per patient would be less, at €1064, in the alternative scenario. With the increase in the market share of Fisiogen Ferro Forte®, the average cost per patient over the period 2017–2020 was €25 lower, with €1135 annual costs per patient compared with the current scenario of €1109 (Table 5).

Table 6 One-way sensitivity analysis for the predialysis 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 the predialysis 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 the predialysis stage who have iron deficiency and are 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

CKD chronic kidney disease

3.2 Peritoneal Dialysis

In our model, based on the prevalence of iron deficiency in patients with CKD stage 5D (peritoneal dialysis) and using intravenous iron, it would be expected that, in 2017, 1989 patients diagnosed with iron deficiency, low hemoglobin, and CKD received treatment with intravenous iron. Based on population trends, this number will decrease slightly to 1980 patients in 2020 (Table 5).

In the base-case analysis in the current scenario, before the increase in the market share of Fisiogen Ferro Forte®, the total economic impact for treatment with intravenous 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 in 2017, 2018, 2019, and 2020, respectively (Table 6).

When the market share of Fisiogen Ferro Forte® was increased by 3, 5, 8, and 10% in 2017, 2018, 2019, and 2020, respectively, matched with a reduction in the share of intravenous 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 intravenous iron, was expected to be €122,490 over 4 years (Table 5).

At the patient level, the average annual cost per patient in the current scenario decreases from €1114 to €1030 in 2017–2020, and the cost per patient would be less, at €1006, in the alternative scenario. With the increase in the market share of Fisiogen Ferro Forte®, the average cost per patient over the period 2017–2020 was €15 lower, with €1072 annual costs per patient compared with the current scenario of €1056 (Table 5).

3.3 Post-transplant

In our model, based on the prevalence of iron deficiency in patients with stage 5D CKD with functioning kidney transplant and using intravenous iron, it would be expected that, in 2017, 1328 patients diagnosed with iron deficiency and CKD received treatment with intravenous iron. Based on population trends, this number will decrease slightly to 1322 patients in 2020 (Table 5).

In the base-case analysis in the current scenario, before the increase in the market share of Fisiogen Ferro Forte®, the total economic impact for treatment with intravenous 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 in 2017, 2018, 2019, and 2020, respectively (Table 5).

When the market share of Fisiogen Ferro Forte® was increased by 3, 5, 8, and 10% in 2017, 2018, 2019, and 2020, respectively, matched with a reduction in the share of intravenous 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 intravenous iron, was expected to be €167,031 over 4 years (Table 5).

At patient level, the average annual cost per patient in the current scenario decreases from €1367 to €1324 in 2017–2020, and the cost per patient would be less, at €1275, in the alternative scenario. With the increase in the market share of Fisiogen Ferro Forte®, the average cost per patient over the period 2017–2020 was €32 lower, with €1345 annual costs per patient compared with the current scenario of €1314 (Table 5).

3.4 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 intravenous iron, the market share for Fisiogen Ferro Forte®, and the monthly cost of Fisiogen Ferro Forte®. The results of varying each parameter are shown in Tables 6, 7, and 8.

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

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

4 Discussion

This study compares the costs of three intravenous 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: predialysis, peritoneal dialysis, and post-transplant. The results of the budget impact analysis suggest that the increasing use of Fisiogen Ferro Forte® would result in a 4-year adjusted total budget savings for the Spanish NHS of €376,041, €898,928, and €206,708 for the predialysis, peritoneal dialysis, and post-transplant groups, respectively, at a national level. The main reason for these budget impact results is that the growing use of Fisiogen Ferro Forte®, as an orally administered iron, does not involve

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 and are 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

CKD chronic kidney disease

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 and are 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

CKD chronic kidney disease

the healthcare center or healthcare professional during the administration process.

In this pharmacoeconomic analysis, we have only considered the Spanish NHS perspective, which involves drug acquisition and intravenous administration costs, as well as healthcare professionals, possible laboratory tests needed, and outpatient hospitalizations associated with the administration of intravenous iron formulations. However, we have not considered the society perspective, which includes patient transportation costs and patient working days lost.

In their pharmacoeconomic analysis on the treatment of iron deficiency with Ferinject® in Spain, Rubió-Terrés et al. [12] have considered both perspectives. The results obtained from the NHS perspective show that the use of Ferinject® for the treatment of iron deficiency would generate a savings of €183, compared with the use of iron dextran, and from €131 to €164 compared with the use of iron sucrose. From the society perspective, cost savings would be €262 and €143– €177, respectively.

One of the strengths of our analysis is that due to the lack of published clinical input data on drug use, medical resource utilization, and treatment with intravenous iron, this study was based on real-world use of these treatments as input data were based on the expert opinion of nephrologists working in different Spanish hospitals. However, the opinion of these experts may have caused bias in the study since only a few experts were involved, and did 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 a day's stay in hospital for administration of intravenous iron, treatment with Fisiogen Ferro Forte® would clearly produce even more important savings than those already obtained, without considering these costs.

5 Conclusions

The results from our analysis suggest that an increase in the market share of Fisiogen Ferro Forte® of 3, 5, 8, and 10% over 4 years, with a decrease in the use of intravenous iron, would result in a €376,041, €898,928, and €206,708 decrease in the overall budget for the predialysis, peritoneal dialysis, and post-transplant groups, respectively, over the period 2017–2020. These savings would be possible due to lower-than-expected drug costs and healthcare resource utilization costs. Although it has been shown that the economic impact of iron deficiency treatment will increase over 4 years due to population growth, it has also been shown that the increase in the use of Fisiogen Ferro Forte® for the treatment of iron deficiency will reduce the average annual cost per patient by an average of €24 over 4 years.

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Compliance with ethical standards

Conflicts of interest Josep Darbà is employed by the University of Barcelona, and Meritxell Ascanio is an employee of BCN Health Economics & Outcomes Research S.L., an independent contract health economic organization that has received research funding from Zambon.

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