



Economic assessment of oral Fisiogen Ferro Forte® versus intravenous iron for the management of iron deficiency in Crohn's disease in Spain

MERITXELL ASCANIO¹, JOSEP DARBÀ²

¹BCN Health Economics & Outcomes Research S.L., Barcelona, Spain; ²Universitat de Barcelona, Barcelona, Spain.

Abstract

Objectives: To assess the economic impact of the oral iron Fisiogen Ferro Forte® for the management of iron deficiency in Crohn's disease patients in Spain.

Methods: A 4-year budget impact model was developed for the period 2018-2021 for Crohn's disease patients with iron deficiency candidates for intravenous iron supplementation due to a lack of response to oral iron therapy from the Spanish Healthcare System perspective. Ferinject®, Venofer® and Feriv® were the intravenous iron formulations considered as appropriate comparators to be used in the model. National data on Crohn's disease prevalence was obtained from the literature. Input data on drug utilization and outpatient hospitalizations associated with iron administration were obtained by consulting experts in gastroenterology from different Spanish hospitals. 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: Crohn's disease patients treated with intravenous iron for iron deficiency were estimated at 1,309 in 2018 with a slightly decrease to 1,302 in 2021. The average annual budget savings with an increase of Fisiogen Ferro Forte® and a decrease of i.v. iron was estimated at €242,752 over four years.

Conclusions: The increase in the use of Fisiogen Ferro Forte® leads to overall savings of €242,752 in the budget impact for the Spanish NHS over 4 years.

Key words: Iron deficiency, Crohn's disease, inflammatory bowel disease, economic analysis, costs, budget impact model.

Resumen

Objetivos: Evaluar el impacto económico del hierro oral Fisiogen Ferro Forte® para el tratamiento de la deficiencia de hierro en pacientes con enfermedad de Crohn en España.

Métodos: Se desarrolló un modelo de impacto presupuestario de 4 años para el período 2018-2021 para los pacientes con enfermedad de Crohn y deficiencia de hierro, candidatos a la administración de suplementos de hierro por vía intravenosa debido a la falta de respuesta a la terapia de hierro oral desde la perspectiva del Sistema de Salud Español. Ferinject®, Venofer® y Feriv® fueron las formulaciones de hierro intravenoso consideradas como comparadores apropiados para este modelo. Los datos nacionales sobre la prevalencia de la enfermedad de Crohn se obtuvieron de la literatura. Los datos sobre el uso de fármacos y las hospitalizaciones ambulatorias asociadas con la administración de hierro se obtuvieron mediante la consulta de expertos en gastroenterología de diferentes hospitales españoles. También se consultó a los expertos sobre el número de visitas médicas y de pruebas de monitorización. Se obtuvo el coste total del tratamiento por paciente asociado a cada producto en base a los costes unitarios para cada terapia de hierro y los recursos utilizados. Se estimó el impacto en el presupuesto global de aumentar el uso de Fisiogen Ferro Forte®.

Resultados: Los pacientes con enfermedad de Crohn y deficiencia de hierro tratados con hierro intravenoso se estimaron en 1.309 en 2018, con un ligero descenso a 1.302 en 2021. El ahorro en el presupuesto anual promedio con un aumento de Fisiogen Ferro Forte® y una disminución de hierro intravenoso se estimó en 242.752 € en cuatro años.

Conclusiones: El aumento en el uso de Fisiogen Ferro Forte® conlleva un ahorro general de 242.752 € en el presupuesto del Sistema Nacional de Salud Español en cuatro años.

Palabras clave: Deficiencia de hierro, enfermedad de Crohn, enfermedad inflamatoria intestinal, análisis económico, costes, modelo de impacto presupuestario

INTRODUCTION

Inflammatory bowel disease (IBD) represents a group of intestinal disorders that cause prolonged inflammation of the digestive tract, including Crohn's disease and ulcerative colitis¹.

In Europe, according to the results of Burish et al.² the incidence of Crohn's disease has increased from 1.0 per 100,000 person-years in 1962 to 6.3 per 100,000 person-years in 2010. A systematic review conducted in 2012 reported higher values of Crohn's disease incidence with a rate of 12.7 per 100,000 person-years³. This last study has also reported a prevalence of 322 per 100,000 persons in 2012 for Crohn's disease.

In Spain, according to the results of a study that has had the collaboration of GETECCU as well as professionals and key experts in the field at a national and international level, associations of patients and heads of public administrations at the state and regional level, ulcerative colitis and Crohn's disease are the intestinal conditions with the highest incidence and prevalence in IBD, with approximately 58% and 42% of cases in Spain, respectively⁴.

Iron deficiency is a frequent extraintestinal complication caused by a continuous blood loss from chronically inflamed intestinal mucosa and iron and B12 deficiency as a result of impaired absorption caused by duodenal inflammation, intestinal resection, or severe disease activity¹.

Treatment with conventional oral iron salts can often not effectively resolve the medical situation due to the difficulty in achieving a good therapeutic compliance because of the numerous problems of tolerability that patients with Crohn's disease present as a consequence of their inflammatory state. Because of that, the preferred route of iron administration is the intravenous route⁵.

Autor para correspondencia

Meritxell Ascanio
 BCN Health Economics & Outcomes
 Research S.L., Travessera de Gràcia, 62, 5-6;
 08006 Barcelona, Spain.
 E-mail: meritxell.ascanio@bcnhealth.com



In order to avoid the appearance of adverse effects without compromising the already low bioavailability of iron some new technologies have been developed. The coverage of iron in sucrosomes reduces the irritation that iron compounds produce in the gastric mucosa and it allows its absorption bypassing the hepcidin-dependent pathways involved in conventional iron absorption, with M cells from reticuloendothelial system being a key pathway contributing to its absorption also in an inflammatory context. It also reduces the interactions of iron compounds with other components of the diet that can decrease even more their bioavailability, such as tannins, polyphenols and phytates^{6,7}.

Sucrosomial[®] oral iron allows for Fisiogen Ferro Forte[®] to be used in all those patients who are intolerant to treatment by oral route administration, or who present malabsorption of conventional oral iron preparations^{6,7}.

The distinctive characteristics of Fisiogen Ferro Forte[®] allow to use it in all those patients who present malabsorption of conventional oral iron preparations whose bioavailability is excessively limited or who turn out to be intolerant to oral treatment, thus guaranteeing therapeutic adherence to treatment with oral iron and the consequent recovery of blood parameters⁸⁻¹².

Two pharmacoeconomic analyses^{13,14} about iron deficiency management in Spain have been published whereby 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 this study, we assessed the estimated economic impact due to the increase in the market share of Fisiogen Ferro Forte[®] for the management of iron deficiency in patients with Crohn's disease from the perspective of the Spanish NHS by using a budget impact model.

METHODS

Model Development and Structure

A budget impact model (BIM) was elaborated in Microsoft Excel from the Spanish National Health Service perspective. The model evaluated differences among patients with Crohn's disease who can benefit from the use of Fisiogen Ferro Forte[®]. Spain and six Spanish regions (Galicia, Andalusia, Valencia, Catalonia, Madrid and the Basque Country) were considered in our model. The iron formulations used as comparators in the model were those 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. In this case we have considered Ferinject[®], Venofer[®] and Feriv[®].

The model analysed the outpatient hospitalizations related with the administration of i.v. iron formulations, as well as 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. The mean number of events for medical visits and iron deficiency monitoring tests required per year were also considered in the model as other medical resources used.

The global budget impact of the expected uptake of Fisiogen Ferro Forte[®], as well as the differences in product and medical costs associated with each treatment option were estimated from 2018 to 2021.

The model included prevalent Crohn's disease patients, who cannot receive oral iron and, therefore, control iron deficiency with an iron maintenance treatment. A panel of experts from different Spanish hospitals make available information on medical resources associated with iron maintenance therapy (outpatient hospitalizations, medical visits and monitoring tests) and drug utilization. Annual costs of drugs and medical resources associated with iron maintenance therapy were reported in Euros (EUR 2018).

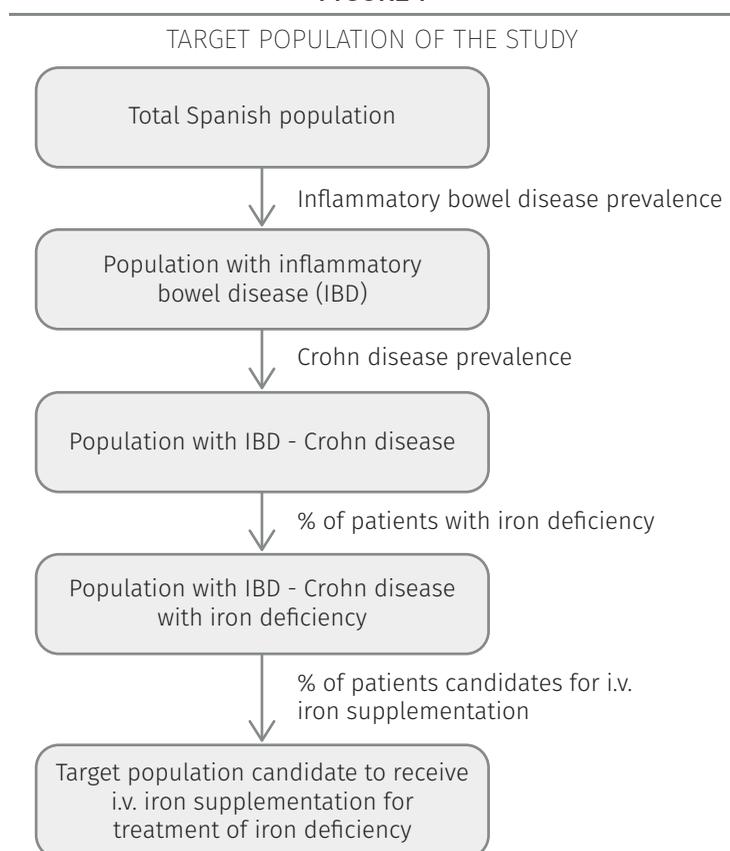
The model generated estimates the annual cost per patient including medical and drug costs to calculate the global budget impact based on market shares and prevalence data.

Model Input Variables

Target population

The algorithm showed in Figure 1 was used to estimate the target population comprising Crohn's disease patients with iron deficiency candidates for i.v. iron supplementation. A literature review was performed to identify the prevalence of Crohn's disease among the Spanish population¹⁵. The estimate for Crohn's disease 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 based on a panel of experts in gastroenterology (25%), as well as the percentage of adult patients who are candidates for i.v. iron supplementation (15%).

FIGURE 1



It must be taken into account that, due to the lack of data regarding iron deficiency prevalence in Crohn's disease patients, anemia data have been considered. Moreover, it should be considered that the use of anemia data provides more restrictive results than the use of iron deficiency data.

Drug treatments and costs

The number of doses needed per drug per year and the maintenance doses related with each treatment for patients having iron supplementation were estimated based on data from clinical practice by a panel of two clinical experts in gastroenterology from different Spanish hospitals (Table 1). The pharmacological treatment cost for each iron product per year was calculated based on the number of 3-month treatments per year of Fisiogen Ferro Forte®, the average number of doses per year for the i.v. iron formulations and the unit cost per dose in EUR. The drug prices were obtained from a Spanish Database of Pharmacists¹⁷ and were expressed in EURO 2018.

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

Medical visits, monitoring tests and outpatient hospitalizations associated with the administration of i.v. iron formulations were included in the model (Table 2). The medical resources associated with each drug were based on the consultation of an expert panel of gastroenterologists and unit costs were obtained from the regional tariff lists of Madrid and Valencia (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

The model has estimated healthcare resource and annual drug cost per patient and enabled



TABLE 1

DRUGS, PRESENTATIONS, COSTS PER DOSE, USAGE PERCENTAGES

Drugs	Dose per year (mg)	Dose per visit (mg)	Number of doses	Drug cost	% of patients using the dose
Ferinject®	1000 mg	500 mg	2	200.40 €	77%
	1500 mg	500 mg	3	300.60 €	23%
Venofer®	600 mg	200 mg	3	69.41 €	20%
	1200 mg	200 mg	6	138.81 €	80%
Feriv®	1500 mg	200 mg	7	123.93 €	100%
		100 mg	1		
Treatments per year				Drug cost per year	% of patients
Fisiogen Ferro Forte®	1 treatment of 3 months			69.76 €	70%
	2 treatments of 3 months			139.52 €	20%
	3 treatments of 3 months			209.28 €	8%
	4 treatments of 3 months			279.04 €	2%

TABLE 2

DRUG COST, MEDICAL RESOURCE UTILISATION AND UNIT COSTS AND AVERAGE COST PER PATIENT PER YEAR

Annual resources	Ferinject®	Venofer®	Feriv®	Fisiogen Ferro Forte®	Unit costs in € 2018
Drug cost (€)	226.88 €	141.02 €	146.28 €	99.06 €	-
Medical visits					
Specialist physician	4	4	12	4	66.50 €
Primary Care	2	2	2	2	39.82 €
Nurse	2.2	10.8	8	0	21.37 €
Annual cost (€)	393.30 €	576.44 €	1,048.60 €	345.64 €	-
Day hospital Annual cost (€)	73.96 €	509.08 €	365.31 €	0.00 €	-
Laboratory tests					
Study of ferric metabolism (TSAT and ferritin)	4	4	4	4	17.92 €
Haemoglobin level monitoring	4	4	4	4	9.93 €
Annual cost (€)	111.40 €	111.40 €	111.40 €	111.40 €	-
Total cost per patient in €	805.53 €	1,337.93 €	1,671.59 €	668.72 €	-

us to determine the annual cost per patient in EUR 2018 for each treatment option. The budget impact for 2018-2021 for the maintenance iron therapy for the treatment of iron deficiency was obtained using the target population, the annual average cost per patient and the current market shares for the products included in this study.

The current market shares were based on data of IMS on the actual distribution of iron products (Table 3). The economic impact was conducted considering an increase in the use of Fisiogen Ferro Forte® comparing the current scenario with the alternative scenario. This economic impact has been calculated following the growing of Fisiogen Ferro Forte®

TABLE 3

MARKET SHARES (%): BASE CASE ANALYSIS AND ALTERNATIVE SCENARIO

Base case analysis	2018	2019	2020	2021
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	2018	2019	2020	2021
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%

during the last years. The BIM was based on the difference found between the alternative scenario and the current scenario.

Deterministic sensitivity analysis

A deterministic sensitivity analysis has been conducted in order to assess the robustness of the model. The main variables were included in this sensitivity analysis to include all the possible scenarios. 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.

RESULTS

We present the results of the BIM for Crohn's disease patients. The results show the economic impact of the treatment of iron deficiency and low haemoglobin in Crohn's disease patients from 2018 to 2021 for the total of Spain.

According to our model based on the prevalence of iron deficiency and low haemoglobin in Crohn's disease patients and i.v. iron use, it would be expected that 1,309 patients in 2018 diagnosed with iron deficiency and Crohn's disease will receive treatment with i.v. iron. Based on population growth this number

decreases slightly to 1,302 patients in 2021 (Table 4).

In the current scenario for the base case analysis, before the Fisiogen Ferro Forte® market share increase, the total economic impact for the treatment with i.v. iron for patients with iron deficiency and Crohn's disease was estimated at €1.88 million, €1.88 million, €1.88 million and €1.87 million for the years 2018, 2019, 2020 and 2021, respectively (Table 5).

In the alternative scenario, with an increase in the market share of Fisiogen Ferro Forte® to 3%, 5%, 8% and 10% in 2018, 2019, 2020 and 2021 respectively, and a reduction in the share of the i.v. iron, the total economic impact was estimated at €1.85 million, €1.83 million, €1.80 million and €1.78 million in 2018, 2019, 2020 and 2021 respectively (Table 6). At the end, the total budget savings for the NHS with the modified market shares with an annual increase of Fisiogen Ferro Forte® and decrease of i.v. iron were expected to be €242,752 over the next four years (Table 5).

At patient level, the average annual cost per patient in the current scenario increases from 2018 to 2021 from €1,434 to €1,439 due to demographic changes in the population. In the alternative scenario the average annual cost decreases to €1,367. The average cost per patient over the period 2018-2021 with the increase in the market share of Fisiogen Ferro



TABLE 4

TARGET POPULATION FOR INTRAVENOUS IRON TREATMENT

Target population	2018	2019	2020	2021
Patients with inflammatory bowel disease	83,109	82,980	82,840	82,692
Patients with inflammatory bowel disease – Crohn disease	34,906	34,851	34,793	34,731
Patients with inflammatory bowel disease – Crohn’s disease who have iron deficiency	8,726	8,713	8,698	8,683
Patients with inflammatory bowel disease – Crohn’s disease who have iron deficiency candidates for intravenous iron	1,309	1,307	1,305	1,302

TABLE 5

RESULTS OF THE BASE CASE BUDGET IMPACT ANALYSIS

Current scenario	2018	2019	2020	2021	Total
Ferinject®	134,333 €	150,546 €	166,584 €	182,653 €	634,116 €
Venofer®	665,851 €	587,001 €	508,333 €	429,708 €	2,190,892 €
Feriv®	1,077,405 €	1,138,861 €	1,200,195 €	1,261,186 €	4,677,646 €
Fisiogen Ferro Forte®	0 €	0 €	0 €	0 €	0 €
Total cost (€)	1,877,589 €	1,876,408 €	1,875,111 €	1,873,546 €	7,502,654 €
Alternative scenario	2018	2019	2020	2021	Total
Ferinject®	123,789 €	133,000 €	138,557 €	147,682 €	543,028 €
Venofer®	648,338 €	557,857 €	461,782 €	371,623 €	2,039,601 €
Feriv®	1,055,524 €	1,102,450 €	1,142,035 €	1,188,617 €	4,488,625 €
Fisiogen Ferro Forte®	21,837 €	36,339 €	58,045 €	72,426 €	188,648 €
Total cost (€)	1,849,488 €	1,829,646 €	1,800,419 €	1,780,348 €	7,259,902 €
Budget impact savings	-28,101 €	-46,761 €	-74,692 €	-93,198 €	-242,752 €

Forte® was €46 lower than in the current scenario.(Table 5).

Deterministic sensitivity analysis

One-way sensitivity analyses were conducted to examine how variations in key model parameters might affect the results of the base case analysis. The parameters that were modified 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 this sensitivity analysis are shown in Table 6.

The model was most sensitive to the percentage of patient candidates to i.v. iron, resulting

in the largest overall decrease in budget impact of €323,670.

The model was also sensitive to the percentage of patients with iron deficiency and the market share of Fisiogen Ferro Forte®, resulting in overall decrease in budget impact of €291,303 and €280,081, respectively.

DISCUSSION

This study compares the costs of an oral iron product (Fisiogen Ferro Forte®) and three i.v. iron products (Ferinject®, Venofer® and Feriv®) and estimates the budget impact for the treatment of iron deficiency in Crohn’s disease patients with iron deficiency. The budget

TABLE 6

ONE-WAY SENSITIVITY ANALYSIS FOR THE MOST INFLUENTIAL VARIABLES IN THE BUDGET IMPACT MODEL

Model parameter	Value in model	Sensitivity analysis	2018	2019	2020	2021	Total
Base case			-28,101 €	-46,761 €	-74,692 €	-93,198 €	-242,752 €
Adult patients with IBD – Crohn’s disease who have iron deficiency	25%	20%	-22,480 €	-37,409 €	-59,754 €	-74,559 €	-194,202 €
		30%	-33,721 €	-56,113 €	-89,631 €	-111,838 €	-291,303 €
Adult patients with IBD – Crohn’s disease who have iron deficiency candidates for intravenous iron	15%	10%	-18,734 €	-31,174 €	-49,795 €	-62,132 €	-161,835 €
		20%	-37,467 €	-62,348 €	-99,590 €	-124,264 €	-323,670 €
Market share projection (Fisiogen Ferro Forte® increase)	3% - 5% - 8% - 10%	2% - 4% - 6% - 8%	-18,734 €	-37,409 €	-56,019 €	-74,559 €	-186,720 €
		3% - 6% - 9% - 12%	-28,101 €	-56,113 €	-84,029 €	-111,838 €	-280,081 €
Fisiogen Ferro Forte® monthly cost	20.22 €	10.11 €	-30,045 €	-49,998 €	-79,862 €	-99,649 €	-259,554 €
		30.33 €	-26,156 €	-43,525 €	-69,522 €	-86,748 €	-225,950 €

impact analysis results suggest that the increase in the use of Fisiogen Ferro Forte® would result in a four-year adjusted total budget savings for the Spanish NHS of €242,752 for patients with Crohn’s disease and iron deficiency.

The main reason for these economic results is that the increasing use of Fisiogen Ferro Forte®, as an orally administered iron, does not involve the healthcare centre or healthcare professional during the administration process.

In this pharmacoeconomic study the only perspective considered was the Spanish NHS perspective, which involves the drug acquisition cost and the i.v. administration cost, as well as the healthcare professionals and the possible laboratory tests needed. We have not considered the society perspective, which will include patients transportation cost and patients working days losses.

Rubió-Terrés et al¹³, in their cost analysis of iron deficiency therapy with i.v. ferric carboxymaltose versus iron dextran and iron sucrose in Spain have considered both perspectives. The results obtained from the NHS perspective shown that the use of Ferinject® in the treatment of iron deficiency involve savings 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.

The results obtained in our study should be considered conservative since, if indirect costs were determined, such as the loss of working hours due a day’s stay in hospital for administration of i.v. iron, the treatment with Fisiogen Ferro Forte® would involve even more important savings than those already obtained without considering indirect costs.

CONCLUSIONS

The results from our analysis suggest that the increase of Fisiogen Ferro Forte® of 3%, 5%, 8% and 10% over four years and the decrease in the use of i.v. iron would result in a €242,752 decrease in the overall budget over the period 2018-2021 for Crohn’s disease patients. These savings would be possible due to lower than expected drug costs and healthcare resource utilisation costs. The use of Fisiogen Ferro Forte® for the treatment of iron deficiency will reduce the average annual cost per patient by an average of €46 over four years.



REFERENCES

ACKNOWLEDGEMENT

The authors want thank the gastroenterology experts, Dr. Guillermo Bastida and Dr. Virginia Robles for their participation in this study.

Conflicts of interest

This study was sponsored by Zambon. JD is employed by the University of Barcelona. MA is an employee of BCN Health Economics & Outcomes Research S.L., Barcelona, Spain, an independent contract health economic organization that has received research funding from Zambon.

- 1 Kaitha S, Bashir M, Ali T. Iron deficiency anemia in inflammatory bowel disease. *World J Gastrointest Pathophysiol* 2015; 6(3):62-72.
- 2 Burisch J, Munkholm P. The epidemiology of inflammatory bowel disease. *Scand J Gastroenterol.* 2015; 50(8):942-51.
- 3 Molodecky NA, Soon S, Rabi DM, Ghali WA, Ferris M, Chernoff G, Benchimol EI, Panaccione R, Ghosh S, Barkema HW, Kaplan GG. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology.* 2012;142(1):46-54.
- 4 Enfermedad Inflamatoria Intestinal: situación actual y retos asistenciales. Ernst & Young, S.L. 2016. Available at: [http://www.ey.com/Publication/vwLUAssets/EY-informe-enfermedad-inflamatoria-intestinal/\\$FILE/EY-enfermedad-inflamatoria-intestinal-situacion-actual-y-retos-asistenciales.pdf](http://www.ey.com/Publication/vwLUAssets/EY-informe-enfermedad-inflamatoria-intestinal/$FILE/EY-enfermedad-inflamatoria-intestinal-situacion-actual-y-retos-asistenciales.pdf) (Accessed 12th of June 2018).
- 5 Gasche C, Berstad A, Befrits R, Beglinger C, Dignass A, Erichsen K, Gomollon F, Hjortswang H, Koutroubakis I, Kulnigg S, Oldenburg B. Guidelines on the diagnosis and management of iron deficiency and anemia in inflammatory bowel diseases. *Inflamm Bowel Dis.* 2007;13(12):1545-53.
- 6 Brilli E, Lipinski P, Barnadas R, Camacho M, Fabiano A, Giordano G, Equitani F, Tarantino G. Sucrosomial Iron Absorption Involve M Cells Interaction. *Blood* 2017; 130 (suppl 1): 2217.
- 7 Fabiano A, Brilli E, Fogli S, Beconcini D, Carpi S, Tarantino G, Zambito Y. Sucrosomial® iron absorption studied by in vitro and ex-vivo models. *Eur J Pharm Sci.* 2018;111:425-31.
- 8 Parisi F, Berti C, Mandò C, Martinelli A, Mazzali C, Cetin I. Effects of different regimens of iron prophylaxis on maternal iron status and pregnancy outcome: a randomized control trial. *J Matern Fetal Neonatal Med.* 2017;30(15):1787-92.
- 9 Mafodda A, Giuffrida D, Prestifilippo A, Azzarello D, Giannicola R, Mare M, Maisano R. Oral sucrosomial iron versus intravenous iron in anemic cancer patients without iron deficiency receiving darbepoetin alfa: a pilot study. *Support Care Cancer.* 2017;25(9):2779-86.
- 10 Giordano G, Mondello P, Tambaro R, Perrotta N, D'amico F, D'aveta A, Berardi G, Carabellese B, Patriarca A, Corbi GM, Di Marzio L. Biosimilar epoetin α is as effective as originator epoetin- α plus liposomal iron (Sideral®), vitamin B12 and folates in patients with refractory anemia: A retrospective real-life approach. *Mol Clin Oncol.* 2015;3(4):781-4.
- 11 Pisani A, Riccio E, Sabbatini M, Andreucci M, Del Rio A, Visciano B. Effect of oral liposomal iron versus intravenous iron for treatment of iron deficiency anaemia in CKD patients: a randomized trial. *Nephrol Dial Transplant.* 2014;30(4):645-52.
- 12 Ciudin A, Simó-Servat O, Balibrea JM, Vilallonga R, Hernandez C, Simó R, Mesa J. Response to oral sucrosomial iron supplementation in patients undergoing bariatric surgery. The BARI-FER study. *Endocrinol Diabetes Nutr.* 2018; 65:17-20.
- 13 Rubio-Terrés C, López ÁF, Montero AF, Vega JM, Castelao AM, Gisbert JP, Valera MQ, Baines JP. Análisis farmacoeconómico del tratamiento de la deficiencia de hierro con hierro carboximaltosa (Ferinject®) en España. *PharmacoEconomics Spanish Research Articles.* 2010;7(3):109-17.
- 14 Martín JE. Análisis coste-beneficio de la utilización de Ferinject. 2014.
- 15 Ondategui S. Enfermedad Inflamatoria Intestinal: situación actual y retos asistenciales. *EY Building a better working world.* 2016.
- 16 Instituto Nacional de Estadístico (INE). Proyecciones de población a corto plazo. 2011-2021 Available at: <http://www.ine.es/jaxi/menu.do?type=pcaxis&path=%2Ft20%2Fp269%2F2011-2021&file=pcaxis&L=> (Accessed 25th of May 2018).
- 17 Consejo General de Colegios Oficiales de Farmacéuticos. BOT plus web. 2012. Available at: <https://botplusweb.portalfarma.com/> (Accessed 12th of December 2017).
- 18 Orden 731/2013, de 6 de septiembre, del Consejero de Sanidad, por la que se fijan los precios públicos por la prestación de los servicios y actividades de naturaleza sanitaria de la Red de Centros de la Comunidad de Madrid. Available at: www.madrid.org/wleg/servlet/Servidor?opcion=VerHtml&nmnorma=8275&cdestado=P (Accessed 12th of December 2017)
- 19 Llei 12/2015, de 29 de desembre, de mesures fiscals, de gestió administrativa i financera, i d'organització de la Generalitat de la Comunitat Valenciana. Available at: www.dogv.gva.es/datos/2015/12/31/pdf/2015_10410.pdf (Accessed 12th of December 2017)
- 20 IMS Health. Market shares 2008-2016. Not published.