

Cost Analysis of IV and SC Immunoglobulins Used in the Treatment of Primary Immunodeficiency Diseases in Spain

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Introduction

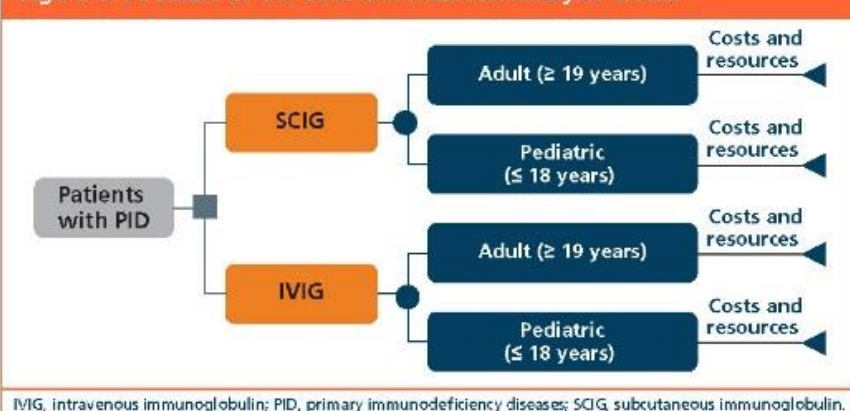
- Various immunoglobulin replacement therapy (IGRT) products are available in both subcutaneous immunoglobulin (SCIG) and intravenous immunoglobulin (IVIG) formulations in Spain for the treatment of primary immunodeficiency diseases (PID).
- In Spain, IVIG is typically administered in a day hospital (ie, outpatient facility) every 3 to 4 weeks, whereas SCIG may be administered at home every week to every 1 to 4 weeks.
- Although IVIG and SCIG formulations offer similar efficacy,^{1,2} their characteristics may influence patients and physicians in choosing IGRT. Such considerations include patients' preferences for route of administration, location of administration (eg, home or medical facility), and dosing frequency.
- This analysis calculated and compared the annual costs of IVIG and SCIG as part of the pharmaceutical service delivered by the Spanish National Healthcare System (SNS) for the treatment of PID.

Methods

Model Structure and Overview

- A cost-minimization analysis was developed based on the decision tree shown in Figure 1.
- The model included both direct (immunoglobulin, premedication, hospital administration, home training, and dispensing) and indirect (work absenteeism) costs.
- The analysis was from an SNS and societal perspective and estimated costs for 1 year of IGRT.
- A literature review was conducted to establish that SCIG and IVIG had equivalent efficacy—a finding that was supported by a noninferiority trial¹ and meta-analysis².
- The analysis considered the cost of SCIG and IVIG per the mean dose established by clinical consensus, multiplied by the ex-factory price per milligram of each immunoglobulin dose.

Figure 1. Structure of the Cost-Minimization Analysis Model



IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

Population Assumptions

- Usage ratios of SCIG and IVIG and each treatment in each category available in Spain were determined by expert consensus (Table 1).

Table 1. Usage Ratios of SCIG and IVIG

Immunoglobulin Replacement Therapies	Usage Ratio, %
Facilitated SCIG 10% ³	19.1
Conventional SCIG 20% ⁴	10.0
Total, SCIG	29.1
IVIG 5% ⁵	39.1
IVIG 5% ⁶	2.7
IVIG 10% ⁷	4.5
IVIG 10% ⁸	24.5
Total, IVIG	71.8

IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

- The age distribution of 52.5% adult (≥ 19 years old) and 47.5% pediatric (≤ 18 years old) cases was based on European Society for Immunodeficiencies database estimates for Europe⁹; detailed age distributions are shown in Table 2.

- Usage ratios of SCIG and IVIG treatment were applied equally across all age groups.

Table 2. Age Distribution of Patients With PID

Age Group Populations	Percentage
Adult ≥ 19 years	52.5
19–64 years	79.5
≥ 65 years	20.5 ^b
Pediatric ≤ 18 years	47.5
< 5 years	6.6
5–9 years	29.3
10–15 years	43.1
16–18 years	21.0 ^b

^aData supplied by ESID are based on a population older than 59 years.
^bData supplied by ESID are based on a population aged 16–19 years.
ESID, European Society for Immunodeficiencies; IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

Body weight

- Mean weight for adults was assumed to be 70 kg¹⁰.
- For pediatric patients, mean weight was categorized into 4 age groups (< 5 years, 12.38 kg; 5–9 years, 25.88 kg; 10–15 years, 47.04 kg; 16–18 years, 62.16 kg)¹¹.

Employment and school attendance

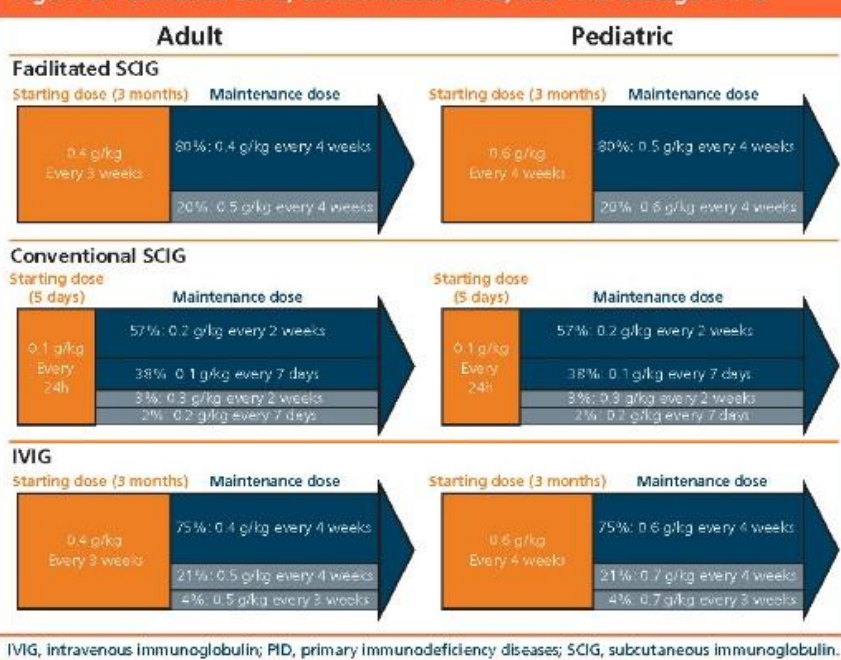
- 44.6% of adults with PID were assumed to be employed. This number was based on the overall employment rate of the general Spanish population,¹² and employment among adults with PID estimated by clinical experts from the Spanish Association of Patients with Primary Immunodeficiencies.
- All pediatric patients were assumed to attend school; we assumed that 63.7% of parents or guardians of pediatric patients (who may be responsible for transporting/accompanying the child to treatment) were employed¹².

Model Inputs

IG dosage

- Prescribing information for each IGRT product provides a range or interval for dosing. Therefore, mean doses were based on the expert consensus of clinical experts.
- Assuming that patients were treatment naïve, the model recommended initiation and maintenance doses of IGRT, based on each product's prescribing information, to be used.
- Dosage and dosing frequencies (shown in Figure 2) were calculated separately due to differences in the prescribing information for conventional and facilitated SCIG.

Figure 2. Facilitated SCIG, Conventional SCIG, and IVIG Dosage in PID



IVIG, intravenous immunoglobulin; PID, primary immunodeficiency diseases; SCIG, subcutaneous immunoglobulin.

Administration

- All IVIG infusions and 1–5% of SCIG infusions were assumed to be administered in a day hospital; all other SCIG infusions were assumed to be administered in the patient's home.
 - The cost of the infusion in the day hospital was assumed to include all services provided and materials used.
 - Typically, an experienced professional teaches a patient or caregiver at-home SCIG treatment administration within 3–4 hospital training sessions (mean 3.5 days).
 - Patients or caregivers were assumed to visit the hospital pharmacy 4 times per year (4 days) to obtain the SCIG doses.
- ### Premedication
- Due to the higher rate of systemic reactions associated with IVIG compared with SCIG,^{2,13} expert consensus was used to estimate that 15% of patients receiving IVIG would require premedication as shown in Table 3.

Table 3. Dosage of Premedication Administered With IVIG

Drug/Drug Type	Population	Route of Administration (% of Patients)	Dose
Acetaminophen	Adult	Intravenous (50)	1000 mg
	Adult	Oral (50)	1000 mg
Corticosteroid	Adult	Intravenous (100)	15 mg/kg
	Pediatric	Intravenous (100)	100 mg
Antihistamine	Adult	Intravenous (100)	6 mg
	Pediatric	Intravenous (100)	0.15 mg/kg

IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Direct costs

- The costs for the day hospital for adults (€175.45) and pediatric (€228.64) patients and time for pharmacy dispensing (€29.84) were obtained from the eSalud database of local costs, considering an average of the individual costs available¹⁴.

Indirect costs

- Work absenteeism (hours) for adult patients receiving IVIG was assumed to include time spent in the day hospital and travel time.
- For employed adult patients receiving SCIG, work absenteeism was related to training sessions, SCIG infusion in the day hospital (for a small percentage of patients), and travel to the hospital for training or infusions.
- These activities and time also applied to working parents or guardians of pediatric patients.
- An average hourly wage (€14.04) based on National Statistics Institute data was applied to all work absenteeism time¹⁵.
- Time consumed for treatments is shown in Table 4.

Table 4. Expenditure of Time for Immunoglobulin Treatments

Resource	Facilitated SCIG	Conventional SCIG	IVIG
Adult preparation and infusion	1.75 h	1.25 h	3.50 h
Pediatric preparation and infusion	1.00 h	1.25 h	3.50 h
Administration of premedication	–	–	0.50 h
Travel to hospital	0.75 h ^a	0.75 h ^a	0.75 h
Dispensing of drugs	0.50 h	0.50 h	–

^aOnly for SCIG infusions that are administered in the hospital.
IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Unit costs

- All costs were valued in 2018 euros.
- Costs of immunoglobulins were determined from the ex-factory price following the application of the deduction established by Royal Decree-Law 8/2010¹⁶.
- All unit costs were obtained from the Bot PLUS 2.0 database¹⁷.

- School absenteeism and lost leisure time were also calculated to show the impact of IGRT administration on patients' and caregivers' time; however, they were not included in the indirect cost calculation because there was no associated cost.

Results

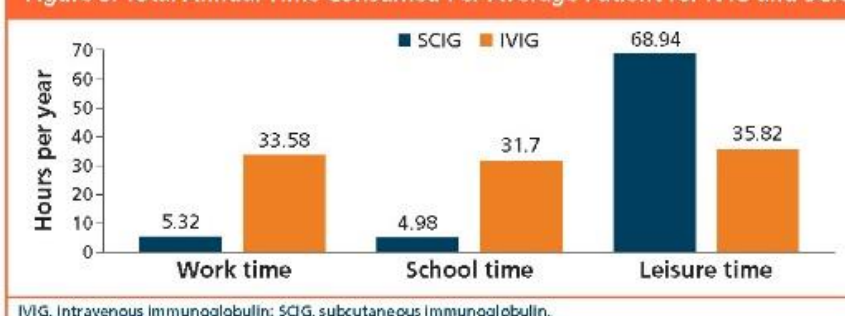
- The annual cost per average patient for SCIG was €4266 lower than that for patients taking IVIG (Table 5).
- Lower costs of hospital administration (Δ: –€2688) and immunoglobulin (Δ: –€1927) were the largest contributors to this difference.
- However, this was somewhat offset by the costs of training for home administration (Δ: €695) and dispensing (Δ: €58.27), which did not apply to IVIG.
- Annual indirect costs were lower for SCIG compared with IVIG (Δ: –€396.73).
- Patients receiving SCIG were estimated to spend 21.9 fewer hours per year on their treatments compared with those receiving IVIG (Figure 3).
- Total annual costs for SCIG were lower for both pediatric (Δ: –€2522) and adult (Δ: –€1744) patients compared with IVIG (Figure 4).

Table 5. Total Annual Cost and Time Consumed Per Average Patient for IVIG and SCIG

	SCIG	IVIG	Difference
Total cost (€)	14 465.63	18 731.81	–4266.17
Direct health costs	14 390.90	18 260.35	–3869.45
Immunoglobulin	13 531.39	15 458.86	–1927.47
Premedication	0	7.12	–7.12
Hospital administration	106.34	2794.37	–2688.03
Training for home-based SCIG	694.90	0	694.90
Dispensing	58.27	0	58.27
Indirect costs	74.73	471.45	–396.73
Total time (h)	79.24	101.10	–21.86
Work	5.32	33.58	–28.26
Infusion	2.43	23.65	–21.22
Travel	2.89	9.92	–7.04
School	4.98	31.70	–26.72
Infusion	2.17	22.33	–20.16
Travel	2.81	9.37	–6.56
Leisure	68.94	35.82	33.12
Infusion	58.11	25.23	32.88
Travel	3.02	10.59	–7.57
Dispensing	7.81	0	7.81

IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Figure 3. Total Annual Time Consumed Per Average Patient for IVIG and SCIG



IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Figure 4. Total Annual Direct and Indirect Costs Per Average Patient for IVIG and SCIG by Age Group



IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Conclusions

- In this cost-minimization model of IGRTs for PID in Spain, the annual cost per patient of SCIG was lower than IVIG, largely driven by hospital administration costs and IG dosage and costs.
- Patients receiving SCIG were estimated to spend fewer hours per year on their treatments than those receiving IVIG, resulting in lower indirect costs.

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