# An Integral Approach to Assess the 3 Human Normal Immunoglobulin formulations for Primary Immunodeficiency in Portugal: Combining Costs, Patient's Preferences, and HCP Choices

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#### INTRODUCTION

Primary immunodeficiency diseases (PID) are a group of rare, heterogeneous disorders composed of approximately 485 genetic conditions that impair the production or function of proteins with critical roles in the immune system.<sup>1</sup> According to the European Society for ImmunoDeficiencies (ESID) registry, 68% of PID patients receive Immunoglobulin (Ig) replacement therapy.<sup>2</sup>

In Portugal, a total of 487 PID cases were registered in 2022, of which 44% (n=214) were adults, which places Portugal as one of the TOP 6 Europe countries with the highest PID prevalence in 2022 (4.73/100.000 inhabitants).<sup>2</sup>

Currently, there are three immunoglobulin administration formulations commonly available, namely facilitated subcutaneous immunoglobulin replacement therapy (fSCIG), conventional subcutaneous immunoglobulin replacement therapy (cSCIG) and intravenous immunoglobulin replacement therapy (IVIG).<sup>3</sup> IVIG requires hospital administration, while both subcutaneous options allow for self-administration at home.<sup>4</sup> cSCIG often requires multiple injection sites and frequent infusion due to limited administration volume, while fSCIG (a dual-vial unit of immunoglobulin (IG) 10% and recombinant human hyaluronidase (rHuPH20)) allows for highrate, increased volume, and low-frequency administration (once every 3-4 weeks), potentially improving patient care, treatment adherence, and reducing healthcare costs.<sup>5,6</sup>

#### OBJETIVE

The aim of this study was to evaluate the available Ig formulations (fSCIG, cSCIG and IVIG) for the treatment of PID in children and adults in Portugal, considering three different dimensions: costs per treatment, patient preferences and healthcare professionals' choice.

### **METHODS**

A cost-minimization analysis (CMA) was performed to compare the costs for all IG formulations, assuming equivalent outcomes (efficacy and safety). The CMA was performed for both National Healthcare System (NHS) and societal perspectives over a two-year time horizon, based on a literature review and official sources (namely Instituto Nacional de Estatística, INFARMED reports, Organisation for Economic Co-operation and Development (OECD)). Healthcare resources, unit prices, and dosages were collected from official sources and literature. An expert panel was conducted with 3 hospital pharmacists of the most experienced healthcare centers treating PID patients in Portugal to validate the assumptions and healthcare resources used, ensuring its adequacy to the Portuguese reality, in 2024. Qualitative insights were also discussed in this panel, to capture HCPs preferences. Patient preferences were taken from the literature. Variables as treatment, travel, productivity, school absenteeism, leisure time costs, treatment criteria, outpatient care capacity, and patient preference were assessed.

### RESULTS

In Portugal, subcutaneous and intravenous routes of administration imply differences that must be evaluated. Some inputs found in the literature do not correspond with portuguese reality, namely the time spent during treatment management and some associated costs (all inputs included are presented in table 1). Direct medical, direct non-medical and indirect costs were assessed and validated by a group of portuguese experts. All data assessed for the first year of treatment are presented below.

	Mean weight (kg)	Average dose (g/kg/ month)	Frequency of ADM	Treatment frequency (year)	РМ	Treatment sites	Infusion time (h)	Training sessions time (h)	Number of TS	Dispensing time (h)	Dispensing rounds (year)*	Employed patients (adults)	Employed caregivers	Distance to hospital (km)	Travel time (h)
fSCIG	75 (adult) 30 (child)	0,4	Q4W	13	No	1	0,75	2	3	0,35	9	50%	72%	92,3	3,97
cSCIG			Q1W	52	No	3-4	1,5	2	3	0,35	9				
IVIG			Q4W	13	Yes	1	2,7	-	-	-	-				

Table 1 – Inputs considered in cost-minimization analysis

ADM (administration), PM (pre-medication), TS (training sessions assumed to enable self-administration), Q4W (every 4 weeks), Q1W (every week/seven days).

Note: The same price per gram was considered for the 3 formulations, as the vast majority of Igs available in Portugal have a comparable list price per gram.

\*The majority of inputs were similar between Portugal and the literature, except the frequency of pharmacy dispensing (need to ensure correct storage and controlled dosage for shorter periods of time).

### **QUANTITATIVE RESULTS**





	HCP dimension							
Current criteria assessed during treatment choice (in Portugal), ranked in order:								
		fSCIG cSCIG IVIG						
1	Direct medical costs associated with therapy price							
2	Outpatient care capacity (chair availability, healthcare professionals availability)							
3	Therapy supply guarentee							

**Direct medical costs (DMC)** include **Ig costs** (representing ≥96% or more of these costs), **premedication** costs, hospital administration, training sessions, pharmacy dispensing.

• 3% and 7% of DMC are related with hospital administration (IVIG context) in adults and children, respectively • Around 1% of DMC are related with patient training (first year of SCIG treatment context)

Less than 1% of DMC are related with hospital pharmacy dispensing



Subcutaneous formulations require the use of an infusion pump and consumables. Currently, in Portugal, only the cSCIG carries costs associated with the infusion pump and its consumables, which can amount to up to 4% of direct costs for the adult population and 10% for the pediatric population. However, these costs may vary amongst vendors and hospitals.

Subcutaneous formulations are less costly than IVIG formulation. Between those, fSCIG is the most affordable choice, since it does not include infusion pump and consumables costs for the NHS.

Average annual hours spent in Ig administration, per patient <sup>7,8,9</sup>



During the discussion of the literature-based data with the



Considering Healthcare Professionals' perspective, fSCIG seems to be the preferred therapy choice, since it enables to combine the majority of criteria.



#### Patient preference dimension

18,3% 20.7% 22,9% <mark>79,3%</mark> <mark>75,6%</mark> 72,6% <mark>72,3%</mark> 72,3%

Patient

preference

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**Direct &** 

Indirect

costs

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In addition to the criteria associated with the health system's capacity to respond, patient preferences are generally considered. Adherence to therapy by the pediatric population is a concern and the option that balances their preference is managed. In the absence of clinical contraindications, changing from intravenous to subcutaneous formulation is considered, especially considering the impact on their QoL and the associated costs. In the literature, 79% of PID patients ( $\geq$  16 years) prefer fSCIG when compared to their previous therapy, particularly because of its convenience and 75% of

Productivity losses	57h	87h	57h	group differer
Loss of leisure time	<b>38h</b>	<b>43h</b>	<b>106h</b>	spent subcut need to in Por
School absenteeism and loss of leisure time	<b>28h</b>	<b>86h</b>	96h	guaran patient the lite (direct aiven t
$\mathcal{A}$ <b>Adult patient</b>	fSCIG ~4 days	IVIG ~5 days	cSCIG ~7 days	fSCI
$\ \ ^{1}$ Pediatric patient	~1 day	~4 days	4 days	۱ <u>ـــ</u> ـ

of experts, some data was identified that would be nt in Portugal, with an impact on the number of hours on each route of Ig administration. When it comes to aneous formulations, the number of times patients to pick up their medication from the pharmacy is higher rtugal, as certain storage conditions need to be nteed, and stock needs to be managed for existing ts (apart from PID patients). These divergences from erature have a direct impact both in terms of costs and indirect) and in terms of time spent per patient, the travel required.

IG requires less of patients' personal time than IVIG and, specially, cSCIG formulation.

patients prefer fSCIG over cSCIG or IVIG<sup>10</sup> This Treatment Overall Total time Frequency Number overall conveniencespent for of ADM of needle preference and QoL impact should be widely explored sticks treatmen (monthly) (monthly) in Portugal. fSCIG CSCIG IVIG

On a patients' perspective, fSCIG formulation enables patients to combine their personal preferences with therapy choice.

> CONCLUSION fSCIG Considering the Portuguese context, the formulation presents itself as a cost-saving option for the NHS and society, for patients with PID. In addition, fSCIG Healthcare Professional seems to be the option favored by patients and is aligned choice with all HCP's treatment preferences.

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#### References

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