

LA INCORPORACIÓN DE LA EVALUACIÓN ECONÓMICA EN LOS INFORMES DE POSICIONAMIENTO TERAPÉUTICO

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BACKGROUND

- Therapeutic Positioning Reports (IPTs, Spanish acronym) are an essential tool to inform funding and pricing decisions for medicines in the Spanish healthcare system
- IPTs are exercises of comparative or joint evaluations of medicines based on scientific evidence
- IPTs were created in 2013 but did not initially incorporate the evaluation of efficiency
- A plan for the consolidation of IPTs approved in 2020 states that "**Economic evaluation (cost-utility, cost-effectiveness or cost minimisation analysis, according to available evidence) will be included in the IPT**"
- Aims: to explore the extent to which IPTs have incorporated the efficiency dimension and to critically analyse the EEs conducted to date

METHODS

- We identified IPTs that from June 2021 (first IPT with EE) until June 2023 incorporated an “Economic evaluation” section
 - Economic evaluations are included in IPTs **gradually**
 - Using minutes of the meetings of the Coordination Group of the Spanish Network for the Evaluation of Medicines (REvalMeD) we identify medicines included in the “**pilot**” of the Action Plan → they ought to include an EE
 - We also manually reviewed all published IPTs to identify IPT with an EE section
- We developed a data extraction sheet to collect the main characteristics of identified economic evaluations based on:
 - Recommended items to be reported in EEs (Husereau et al., 2022): CHEERS statement
 - Spanish guidelines on conducting EEs (López-Bastida et al., 2010; Ortega-Eslava et al., 2016)

RESULTS

- From June 2021 until the end of May 2023*, 173 IPTs have been published, of which 17 incorporated an EE section (**under 10% of IPTs**)

ATC group	IPTs	IPTs with EE section
Group A ALIMENTARY TRACT AND METABOLISM	12	1
Group B BLOOD AND BLOOD FORMING ORGANS	5	1
Group C CARDIOVASCULAR SYSTEM	6	0
Group D DERMATOLOGICALS	5	1
Group G GENITO URINARY SYSTEM AND SEX HORMONES	0	0
Group H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	4	1
Group J ANTIINFECTIVES FOR SYSTEMIC USE	13	1
Group L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	105	10
Group M MUSCULO-SKELETAL SYSTEM	5	1
Group N NERVOUS SYSTEM	11	1
Group R RESPIRATORY SYSTEM	2	0
Group S SENSORY ORGANS	3	0
Group V VARIOUS	2	0
TOTAL	173	17
% of IPTs incorporating an EE section		9.8%

~60% related to ATC group L

*We plan to update this review to include IPTs published until the end of June 2023

RESULTS – 17 IPTs with EE section

Drug	Latest version date	ATC	Condition
Cenobamate	28/07/22	N	Epilepsy
Dapagliflozin	24/02/22	A	Chronic heart failure
Trastuzumab deruxtecan	07/07/22	L	Breast cancer
Exuparvovec	10/04/23	L	L-aromatic decarboxylase deficiency
Anti-CD19 transduced autologous CD3+ cells	29/06/22	L	Mantle cell lymphoma
Risdiplam	07/03/22	M	Spinal muscular atrophy
Roxadustat	24/11/22	B	Anemia associated with chronic kidney disease
Tralokinumab	05/07/22	D	Atopic dermatitis
Somapacitan	28/03/22	H	Growth hormone deficiency
Lorlatinib	27/11/22	L	Lung cancer
Pegcetacoplan	21/03/23	L	Paroxysmal nocturnal hemoglobinuria
Tebentafusp	10/04/23	L	Uveal melanoma
Talazoparib	11/11/21	L	Breast cancer
Imipenem/cilastatin/relebactam	11/07/22	J	Hospital-acquired pneumonia
Nivolumab	28/03/22	L	Squamous cell carcinoma of the esophagus
Atezolizumab	29/06/22	L	Lung cancer
Tucatinib	29/06/22	L	Breast cancer

1 IPT in 2021 (from June until December)
 13 IPTs in 2022 (all year)
 3 IPTs in 2023 (from January to June)

RESULTS – 17 IPTs with EE section

Drug	Latest version date	ATC	Condition	Includes de novo EE
Cenobamate	28/07/22	N	Epilepsy	No
Dapagliflozin	24/02/22	A	Chronic heart failure	No
Trastuzumab deruxtecan	07/07/22	L	Breast cancer	No
Exuparvovec	10/04/23	L	L-aromatic decarboxylase deficiency	No
Anti-CD19 transduced autologous CD3+ cells	29/06/22	L	Mantle cell lymphoma	No
Risdiplam	07/03/22	M	Spinal muscular atrophy	No
Roxadustat	24/11/22	B	Anemia associated with chronic kidney disease	Yes
Tralokinumab	05/07/22	D	Atopic dermatitis	Yes
Somapacitan	28/03/22	H	Growth hormone deficiency	Yes
Lorlatinib	27/11/22	L	Lung cancer	Yes
Pegcetacoplan	21/03/23	L	Paroxysmal nocturnal hemoglobinuria	Yes
Tebentafusp	10/04/23	L	Uveal melanoma	Yes
Talazoparib	11/11/21	L	Breast cancer	Yes
Imipenem/cilastatin/relebactam	11/07/22	J	Hospital-acquired pneumonia	Yes
Nivolumab	28/03/22	L	Squamous cell carcinoma of the esophagus	Yes
Atezolizumab	29/06/22	L	Lung cancer	Yes
Tucatinib	29/06/22	L	Breast cancer	Yes

RESULTS – 17 IPTs with EE section

Drug	Latest version date	ATC	Condition	Includes de novo EE	Reason for not conducting de novo EE
Cenobamate	28/07/22	N	Epilepsy	No	Used previous EE
Dapagliflozin	24/02/22	A	Chronic heart failure	No	Used previous EE
Trastuzumab deruxtecan	07/07/22	L	Breast cancer	No	Not direct comparison
Exuparvovec	10/04/23	L	L-aromatic decarboxylase deficiency	No	Not direct comparison
Anti-CD19 transduced autologous CD3+ cells	29/06/22	L	Mantle cell lymphoma	No	Not direct comparison
Risdiplam	07/03/22	M	Spinal muscular atrophy	No	Not direct comparison
Roxadustat	24/11/22	B	Anemia associated with chronic kidney disease	Yes	NA
Tralokinumab	05/07/22	D	Atopic dermatitis	Yes	NA
Somapacitan	28/03/22	H	Growth hormone deficiency	Yes	NA
Lorlatinib	27/11/22	L	Lung cancer	Yes	NA
Pegcetacoplan	21/03/23	L	Paroxysmal nocturnal hemoglobinuria	Yes	NA
Tebentafusp	10/04/23	L	Uveal melanoma	Yes	NA
Talazoparib	11/11/21	L	Breast cancer	Yes	NA
Imipenem/cilastatin/relebactam	11/07/22	J	Hospital-acquired pneumonia	Yes	NA
Nivolumab	28/03/22	L	Squamous cell carcinoma of the esophagus	Yes	NA
Atezolizumab	29/06/22	L	Lung cancer	Yes	NA
Tucatinib	29/06/22	L	Breast cancer	Yes	NA

RESULTS – 17 IPTs with EE section

Drug	Latest version date	ATC	Condition	Includes de novo EE	Reason for not conducting de novo EE	Reviews previous EE studies
Cenobamate	28/07/22	N	Epilepsy	No	Used previous EE	Yes
Dapagliflozin	24/02/22	A	Chronic heart failure	No	Used previous EE	Yes
Trastuzumab deruxtecan	07/07/22	L	Breast cancer	No	Not direct comparison	NS
Exuparvovec	10/04/23	L	L-aromatic decarboxylase deficiency	No	Not direct comparison	Yes
Anti-CD19 transduced autologous CD3+ cells	29/06/22	L	Mantle cell lymphoma	No	Not direct comparison	Yes
Risdiplam	07/03/22	M	Spinal muscular atrophy	No	Not direct comparison	Yes
Roxadustat	24/11/22	B	Anemia associated with chronic kidney disease	Yes	NA	Yes
Tralokinumab	05/07/22	D	Atopic dermatitis	Yes	NA	Yes
Somapacitan	28/03/22	H	Growth hormone deficiency	Yes	NA	Yes
Lorlatinib	27/11/22	L	Lung cancer	Yes	NA	Yes
Pegcetacoplan	21/03/23	L	Paroxysmal nocturnal hemoglobinuria	Yes	NA	Yes
Tebentafusp	10/04/23	L	Uveal melanoma	Yes	NA	Yes
Talazoparib	11/11/21	L	Breast cancer	Yes	NA	Yes
Imipenem/cilastatin/relebactam	11/07/22	J	Hospital-acquired pneumonia	Yes	NA	NS
Nivolumab	28/03/22	L	Squamous cell carcinoma of the esophagus	Yes	NA	Yes
Atezolizumab	29/06/22	L	Lung cancer	Yes	NA	NS
Tucatinib	29/06/22	L	Breast cancer	Yes	NA	Yes

RESULTS – 11 IPTs with EE

Drug	Type of EE	
Roxadustat	CMA	Justified in two of them by the assumption that the alternatives were clinically equivalent
Tralokinumab	CMA	
Somapacitan	CMA	
Lorlatinib	CEA	Overall survival, progression-free survival and/or the percentage of patients responding to treatment as effectiveness measures
Pegcetacoplan	CEA	
Tebentafusp	CEA	
Talazoparib	CUA	Use QALY as effectiveness measure
Imipenem/cilastatin/relebactam	CUA	
Nivolumab	CUA	
Atezolizumab	CUA	
Tucatinib	CUA	

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective
Roxadustat	CMA	Healthcare system
Tralokinumab	CMA	NS
Somapacitan	CMA	NS
Lorlatinib	CEA	NS
Pegcetacoplan	CEA	Healthcare system
Tebentafusp	CEA	NS
Talazoparib	CUA	Healthcare system
Imipenem/cilastatin/relebactam	CUA	NS
Nivolumab	CUA	Healthcare system
Atezolizumab	CUA	Healthcare system
Tucatinib	CUA	Healthcare system

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective	Types of costs included
Roxadustat	CMA	Healthcare system	Drug costs
Tralokinumab	CMA	NS	Drug costs
Somapacitan	CMA	NS	Drug costs
Lorlatinib	CEA	NS	Drug and AE costs
Pegcetacoplan	CEA	Healthcare system	Drug costs
Tebentafusp	CEA	NS	Drug costs
Talazoparib	CUA	Healthcare system	Drug, diagnostics, AE, health visits and other clinical procedures costs
Imipenem/cilastatin/relebactam	CUA	NS	Drug, hospitalization, and complication costs
Nivolumab	CUA	Healthcare system	Drug, AE, and other treatment costs
Atezolizumab	CUA	Healthcare system	Drug, AE, and other treatment costs
Tucatinib	CUA	Healthcare system	Drug, AE, and other treatment costs

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective	Types of costs included	Time horizon	Discount rate
Roxadustat	CMA	Healthcare system	Drug costs	1 year	NA
Tralokinumab	CMA	NS	Drug costs	NS	NA
Somapacitan	CMA	NS	Drug costs	NS	NA
Lorlatinib	CEA	NS	Drug and AE costs	1 year	NA
Pegcetacoplan	CEA	Healthcare system	Drug costs	4 months	NA
Tebentafusp	CEA	NS	Drug costs	NS	NA
Talazoparib	CUA	Healthcare system	Drug, diagnostics, AE, health visits and other clinical procedures costs	43 months	NS
Imipenem/cilastatin/relebactam	CUA	NS	Drug, hospitalization, and complication costs	28 days, 1 year, 30 years	NS
Nivolumab	CUA	Healthcare system	Drug, AE, and other treatment costs	34, 70 months	3%
Atezolizumab	CUA	Healthcare system	Drug, AE, and other treatment costs	38, 80 months	3%
Tucatinib	CUA	Healthcare system	Drug, AE, and other treatment costs	33, 72 months	3%

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective	Types of costs included	Time horizon	Discount rate	Model-based	Type of modelling	Handling of uncertainty
Roxadustat	CMA	Healthcare system	Drug costs	1 year	NA	No	NA	Deterministic SA
Tralokinumab	CMA	NS	Drug costs	NS	NA	No	NA	No
Somapacitan	CMA	NS	Drug costs	NS	NA	No	NA	No
Lorlatinib	CEA	NS	Drug and AE costs	1 year	NA	No	NA	No
Pegcetacoplan	CEA	Healthcare system	Drug costs	4 months	NA	No	NA	No
Tebentafusp	CEA	NS	Drug costs	NS	NA	No	NA	No
Talazoparib	CUA	Healthcare system	Drug, diagnostics, AE, health visits and other clinical procedures costs	43 months	NS	Yes	Partition survival analysis	Deterministic SA
Imipenem/cilastatin/relebactam	CUA	NS	Drug, hospitalization, and complication costs	28 days, 1 year, 30 years	NS	Yes	Decision tree + Markov	Deterministic SA
Nivolumab	CUA	Healthcare system	Drug, AE, and other treatment costs	34, 70 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA
Atezolizumab	CUA	Healthcare system	Drug, AE, and other treatment costs	38, 80 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA
Tucatinib	CUA	Healthcare system	Drug, AE, and other treatment costs	33, 72 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective	Types of costs included	Time horizon	Discount rate	Model-based	Type of modelling	Handling of uncertainty	CET
Roxadustat	CMA	Healthcare system	Drug costs	1 year	NA	No	NA	Deterministic SA	NA
Tralokinumab	CMA	NS	Drug costs	NS	NA	No	NA	No	NA
Somapacitan	CMA	NS	Drug costs	NS	NA	No	NA	No	NA
Lorlatinib	CEA	NS	Drug and AE costs	1 year	NA	No	NA	No	NA
Pegcetacoplan	CEA	Healthcare system	Drug costs	4 months	NA	No	NA	No	NA
Tebentafusp	CEA	NS	Drug costs	NS	NA	No	NA	No	NA
Talazoparib	CUA	Healthcare system	Drug, diagnostics, AE, health visits and other clinical procedures costs	43 months	NS	Yes	Partition survival analysis	Deterministic SA	NS
Imipenem/cilastatin/relebactam	CUA	NS	Drug, hospitalization, and complication costs	28 days, 1 year, 30 years	NS	Yes	Decision tree + Markov	Deterministic SA	NS
Nivolumab	CUA	Healthcare system	Drug, AE, and other treatment costs	34, 70 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	25.000; 30.000; 60.000€
Atezolizumab	CUA	Healthcare system	Drug, AE, and other treatment costs	38, 80 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	30.000; 40.000€
Tucatinib	CUA	Healthcare system	Drug, AE, and other treatment costs	33, 72 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	25.000; 30.000; 60.000€

RESULTS – 11 IPTs with EE

Drug	Type of EE	Perspective	Types of costs included	Time horizon	Discount rate	Model-based	Type of modelling	Handling of uncertainty	CET	ICER	Funding
Roxadustat	CMA	Healthcare system	Drug costs	1 year	NA	No	NA	Deterministic SA	NA	NA	Non-requested
Tralokinumab	CMA	NS	Drug costs	NS	NA	No	NA	No	NA	NA	Restricted funding
Somapacitan	CMA	NS	Drug costs	NS	NA	No	NA	No	NA	NA	Non-identified
Lorlatinib	CEA	NS	Drug and AE costs	1 year	NA	No	NA	No	NA	Dominant	Non-identified
Pegcetacoplan	CEA	Healthcare system	Drug costs	4 months	NA	No	NA	No	NA	>6,000€ per responding patient	Restricted funding
Tebentafusp	CEA	NS	Drug costs	NS	NA	No	NA	No	NA	>500,000€ per LYG	Non-requested
Talazoparib	CUA	Healthcare system	Drug, diagnostics, AE, health visits and other clinical procedures costs	43 months	NS	Yes	Partition survival analysis	Deterministic SA	NS	>180,000€/QALY	Not funded
Imipenem/cilastatin/relebactam	CUA	NS	Drug, hospitalization, and complication costs	28 days, 1 year, 30 years	NS	Yes	Decision tree + Markov	Deterministic SA	NS	>400,000€/QALY (28 days)	Not funded
Nivolumab	CUA	Healthcare system	Drug, AE, and other treatment costs	34, 70 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	25.000; 30.000; 60.000€	>500.000€/QALY	Under evaluation
Atezolizumab	CUA	Healthcare system	Drug, AE, and other treatment costs	38, 80 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	30.000; 40.000€	>50,000€/QALY	Funded
Tucatinib	CUA	Healthcare system	Drug, AE, and other treatment costs	33, 72 months	3%	Yes	Partition survival analysis	Deterministic, probabilistic SA	25.000; 30.000; 60.000€	>200,000€/QALY	Funded

DISCUSSION

Good news

- ✓ First time, MoH has started to implement efficiency evaluation in IPTs
- ✓ Gradually (by “nodo”)
- ✓ Some examples of evaluations of high methodological quality, similar to what would be expected from other agencies with more experience

Not-so good news

- Slow and non-increasing pace for incorporating EE in IPTs
- Wide heterogeneity
 - In search methods
 - In reasons to conduct or not a de novo EE/chose type
 - In criteria to decide if cost-effective
- Differences across IPTs not always due to differences in evidence

DISCUSSION

- Currently, there is not specific EE guidelines → reference to GENESIS methods guide but insufficient for the IPT context
 - Need specific and detailed guidelines
- “According to available evidence” → when and how to conduct EE if evidence is poor?
 - Need explicit criteria to ensure homogeneity in decisions to perform or not an EE and to chose type
- Do we have the capacity to conduct an EE in each (relevant) IPT?
 - Alternative: economic evaluations might be provided by companies, which are then subject to the judgement of professionals working for the evaluating agencies and/or external experts appointed by these agencies

DISCUSSION

- Economic evaluations carried out to date have had a major influence on financing and pricing decisions?
- Based on very limited evidence → It does not look so
- Tricky question:
 - IPT is not the only source of information
 - Cost-effectiveness is one of the criteria to be considered
 - Requested prices by the pharmaceutical companies might be different to those used in IPT
 - If unfavorable decision, company can resubmit with additional information, if any, or a lower price proposal

¡MUCHAS GRACIAS!