## ANNEX I – Original version of the Survey (in Spanish)

Marque el tipo de institución que mejor se ajuste a la institución para la que usted trabaja:

* Agencia de evaluación de tecnologías sanitarias
* Agencia reguladora
* Entidad gubernamental (ya sea de un gobierno regional o del gobierno nacional)
* Institución académica o de investigación
* Consultora
* Industria
* Otro/a

Indique la franja de años de experiencia profesional que mejor se ajusten a su perfil (años haciendo el doctorado se contabilizarían como experiencia profesional):

* 1-3 años
* 3-5 años
* 5-8 años
* 8 años o más

Marque el tipo de perfil que mejor se ajuste a su puesto:

* Director, coordinador o responsable de área, unidad, departamento o equivalente
* Personal técnico, profesor o investigador
* Personal de gestión o similar
* Otro/a

Por favor, marque la opción que, en su opinión, sería más adecuada para medir cada una de las categorías indicadas para los medicamentos sobre los que se va a decidir su inclusión o no en el paquete básico de prestaciones del SNS:

1. GRAVEDAD, DURACIÓN Y SECUELAS DE LAS DISTINTAS PATOLOGÍAS PARA LAS QUE RESULTEN INDICADOS

Por favor, marque aquellas opciones que considere apropiadas y compatibles para medir gravedad, duración y secuelas de las distintas patologías para las que está indicado un nuevo medicamento sobre el que hay que tomar una decisión de inclusión en el paquete básico del SNS (en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):

* El AcutePhysiology And Chronic Health Evaluation (APACHE) II [1,2], que mide gravedad en pacientes en cuidados intensivos, u otros instrumentos similares específicos de áreas terapéuticas concretas (el que sea relevante para el medicamento sobre el cual se va a decidir su inclusión o no en el paquete básico de prestaciones del SNS), acompañado de una medida temporal de duración
* Los ‘años de vida ajustados por discapacidad’ (AVAD, o DALY por sus siglas en inglés) [3]
* El Año de Vida Ajustado por Calidad (AVAC) [4]
* Marcadores clínicos de gravedad y secuelas, o un número de unidades de medida clínica de eficacia específica a la patología que tenga significado clínico, añadiéndoles una medida temporal de duración (Ejemplos: los índices de letalidad y de morbi-mortalidad son medidas ampliamente aceptadas de la gravedad de una enfermedad; otros indicadores útiles son la frecuencia de eventos graves que cursan con hospitalización o visitas a urgencias).
* Otro – por favor indique sólo el instrumento de medida de gravedad, duración y secuelas de una enfermedad que le parezca más apropiado (sólo uno) (Texto libe)
1. NECESIDADES ESPECÍFICAS DE CIERTOS COLECTIVOS

Existen grupos poblacionales que, debido a sus características o a las de la enfermedad que padecen, son tenidos en cuenta de manera específica dentro de las decisiones de financiación de medicamentos en España. De los grupos poblacionales que listamos abajo, marque todos los que crea que merecen consideración especial en dichas decisiones en España (en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):

* Poblaciones con una afección para la que no existe una alternativa terapéutica satisfactoria, siguiendo la definición de la Comisión Europea de necesidad médica no cubierta [5] o también situaciones en las que existe laguna terapéutica en patología grave, lo que implica ausencia de alternativas eficaces de tratamiento, tal y como se define en el plan para la consolidación de los informes de posicionamiento terapéutico de los medicamentos en el sistema nacional de salud [6].
* Los medicamentos huérfanos [7], siguiendo la definición de la EMA[[1]](#footnote-1), o para enfermedades ultra-raras.
* La población pediátrica [9]
* Pacientes enfrentándose al final de sus vidas [10]
* Otro – por favor ponga sólo el grupo poblacional que le parezca más apropiado tener en cuenta (sólo uno) (Texto libe)
1. VALOR TERAPÉUTICO Y SOCIAL DEL MEDICAMENTO Y BENEFICIO CLÍNICO INCREMENTAL DEL MISMO TENIENDO EN CUENTA SU RELACIÓN COSTE-EFECTIVIDAD

El valor terapéutico de un medicamento y su coste-efectividad se puede medir de diversas maneras, y el valor social del mismo tiene maneras de medirse diferentes. Por tanto, le presentaremos primero alternativas para medir: (1) valor terapéutico; (2) coste-efectividad, y; (3) valor social.

1. Por favor, de los siguientes instrumentos para medir el valor terapéutico o beneficio clínico incremental de los medicamentos marque las opciones que le parezcan apropiadas (marque más de una opción si cree que múltiples parámetros podrían informar mejor la decisión que uno sólo – en caso de considerar que esta dimensión de valor no debería ser tenida en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):
* El Año de Vida Ajustado por Calidad (AVAC) [4].
* El impacto de la nueva estrategia en las variables clínicas específicas a la patología que se está tratando o alguna otra medida clínica de eficacia específica a la patología.
* Una medida de beneficio real de la nueva terapia basada en una combinación de criterios clínicos, que se acaban traduciendo en un índice (al estilo del sistema francés [11]).
* Otro – por favor pon sólo el instrumento de medida de valor terapéutico que te parezca más apropiado (sólo uno) (Texto libre)
1. Por favor, de los siguientes instrumentos para medir la relación coste-efectividad de los medicamentos marque las opciones que le parezcan apropiadas (en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):
* La ratio de Coste-Utilidad Incremental (RCUI, o ICUR por sus siglas en inglés) usando medidas de utilidad como el AVAC
* La ratio de Coste-Efectividad Incremental (RCEI, o ICER por sus siglas en inglés) usando medidas de efectividad clínica (una/s variable/s concreta/s de medida clínica de eficacia específica a la patología, que tenga significado clínico)
* Otro – por favor ponga sólo el instrumento que le parezca más apropiado para medir la relación de coste-efectividad de una nueva terapia (sólo uno) (Texto libe)

Para poder apoyar decisiones de financiación de medicamentos en una ratio de coste-efectividad y/o de coste-utilidad, es necesario tener una referencia de qué se considera uso eficiente de recursos en el sistema:

* ¿Cree que hace falta un umbral de coste-utilidad en España? Si / No
* Si cree que hace falta un umbral, marque la opción que le parezca más apropiada:
* Un umbral explícito (descrito y especificado en los manuales metodológicos que enmarcan la actividad de evaluación de tecnologías sanitarias en un país)
* Un umbral implícito (no oficialmente especificado, deducido de publicaciones en revistas especializadas y de informes publicados)
* ¿Cree que debe haber diferentes umbrales para diferentes grupos poblacionales / situaciones especiales? Si / No

(3) Los medicamentos, además de tener un valor terapéutico directo en salud para los pacientes para los que están indicados, aportan un beneficio para la sociedad en conjunto a varios niveles [12], que se puede medir (marque todas las opciones que le parezcan relevantes – en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):

* Los familiares y otros cuidadores informales de los pacientes ven mejorada su calidad de vida en paralelo a la mejora de las condiciones de vida de los pacientes a los que cuidan.
* Los pacientes (y sus cuidadores informales) además de beneficiarse de una mejora en salud a causa del uso del medicamento, en ocasiones pueden volver a trabajar antes o en condiciones más favorables a su productividad que sin la nueva terapia.
* La empresa farmacéutica que produce el nuevo medicamento es posible que genere un impacto económico considerable, en el empleo del país generando gran cantidad de empleo de calidad para personal cualificado y en otros aspectos de la economía (como por ejemplo la competitividad, el valor añadido que genera, etc.) [12]
* Otro – por favor ponga sólo una manera de medir el valor social del medicamento que no hayamos listado en las opciones anteriores (Texto libre)
1. RACIONALIZACIÓN DEL GASTO PÚBLICO DESTINADO A PRESTACIÓN FARMACÉUTICA E IMPACTO PRESUPUESTARIO EN EL SISTEMA NACIONAL DE SALUD

El análisis de impacto presupuestario es la medida estándar para reflejar el impacto que la incorporación de una nueva tecnología tiene en el presupuesto de un sistema sanitario, y existen guías metodológicas que describen cómo hacerlo adecuadamente [13]. Sin embargo, la legislación no entra a describir la manera en que mide el impacto presupuestario de nuevos medicamentos para apoyar sus decisiones de financiación. Por favor, marque sólo la casilla que describa mejor los costes que le parezcan relevantes para un análisis de impacto presupuestario. En caso de opinar que habría otra manera más adecuada de medir el impacto presupuestario o si considera que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre:

* El impacto presupuestario solo tiene que tener en cuenta los gastos en la terapia farmacéutica nueva y actual en un horizonte temporal de 3 a 5 años
* El impacto presupuestario debe tener en cuenta todos los costes sanitarios (administración de la terapia, efectos adversos, etc.) en un horizonte temporal de 3 a 5 años
* Otro – por favor ponga sólo el instrumento de medida de impacto presupuestario, diferente al ya mencionado arriba, que le parezca más apropiado (sólo uno) (Texto libre)
1. EXISTENCIA DE MEDICAMENTOS U OTRAS ALTERNATIVAS TERAPÉUTICAS PARA LAS MISMAS AFECCIONES A MENOR PRECIO O INFERIOR COSTE DE TRATAMIENTO

Mediante este criterio se tiene en cuenta si existe una alternativa terapéutica de eficacia similar o superior y a menor coste que el nuevo medicamento. Para medir esto, se pueden utilizar los conceptos de equivalencia terapéutica o los grupos ATC5 (La clasificación Anatómica, Terapéutica y Química (ATC) es un sistema de codificación de los medicamentos, según su efecto farmacológico, sus indicaciones terapéuticas y su estructura química. Se divide en cinco niveles: el primer nivel (ATC1) es el más general y el quinto nivel (ATC5) el más detallado – designa el principio activo específico o asociación farmacológica [14]). A alternativas equivalentes, nunca se paga más. Si conoce otra manera más apropiada de medir esto, propóngala más abajo (en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):

* Concepto de alternativa terapéutica equivalente
* Grupos ATC4
* Grupos ATC5
* Otro – por favor ponga sólo el instrumento, diferente a los mencionados arriba, que le parezca más apropiado (sólo uno) (Texto libe)
1. GRADO DE INNOVACIÓN DEL MEDICAMENTO

Para los propósitos de esta encuesta utilizaremos la definición de grado de innovación basada en las dimensiones de valor que componen el concepto identificadas en una investigación previa [15]). Esto es: salto cualitativo en su indicación (`step-change’), conveniencia (`convenience’), robustez de la evidencia (`strength of evidence base’) teniendo en cuenta el grado de incertidumbre asociado a la evidencia (entre otros factores), impacto en futura I+D (`impact on future R&D’).

Ahora, ¿con que tipo de instrumento cree que debería medirse el grado de innovación para apoyar la toma de decisiones de financiación de medicamentos en España tal y como describe la ley? Por favor, marque sólo el instrumento que, bajo su punto de vista, sea más apropiado (en caso de considerar que este parámetro no debería ser tenido en cuenta en las decisiones de financiación de los medicamentos en España, por favor marque la casilla ‘Otro’ y explique su posición en el casillero de texto libre):

* Un instrumento tipo ‘checklist’ (actualmente sólo conocemos el ‘checklist’ de INAHTA [16] que se aplica a la evaluación de tecnologías sanitarias en general – nosotros propondremos un ‘checklist’ específico para medir el grado de innovación, como parte de este proyecto).
* Como parte de un Análisis de Decisiones Multicriterio (MCDA por sus siglas en inglés), como uno de los dominios de valor medidos y capturados (como, por ejemplo, en el Advance Value Framework desarrollado y publicado por Angelis & Kanavos (2017) [17] o el ‘innovómetro’ propuesto por Zaragozá-García & Cuéllar (2017) [18], teniendo en cuenta que varios de los parámetros ya medidos en epígrafes anteriores serían contabilizados por duplicado si usásemos el ‘innovómetro’ ya que éste captura parámetros como el valor terapéutico por ejemplo).
* Otro – por favor pon sólo el instrumento de medida de grado de innovación, distinto a los mencionados arriba, que te parezca más apropiado (sólo uno) (Texto libe)

PONDERACIÓN DE CADA CRITERIO

Por favor, indique el peso (de 0 a 100) que usted crea que debería tener cada criterio en las decisiones de financiación de medicamentos en España. Por favor, tenga en cuenta que la suma de las puntuaciones otorgadas debe ser 100.

1. Gravedad, duración y secuelas de las distintas patologías para las que resulten indicados;
2. Necesidades específicas de ciertos colectivos;
3. Valor terapéutico y social del medicamento y beneficio clínico incremental del mismo teniendo en cuenta su relación coste-efectividad;
4. Racionalización del gasto público destinado a prestación farmacéutica e impacto presupuestario en el Sistema Nacional de Salud;
5. Existencia de medicamentos u otras alternativas terapéuticas para las mismas afecciones a menor precio o inferior coste de tratamiento;
6. Grado de innovación del medicamento.

IDONEIDAD DE LOS CRITERIOS LISTADOS EN LA LEY PARA APOYAR DECISIONES DE FINANCIACIÓN DE MEDICAMENTOS EN ESPAÑA

Por favor, responda sí o no a la siguiente pregunta:

¿Cree que los criterios listados en la ley para apoyar la toma de decisiones sobre financiación de medicamentos en España son los adecuados?

* Si
* No

¿Cree que habría que añadir algún criterio a los listados en la ley para apoyar la toma de decisiones sobre financiación de medicamentos en España de manera idónea?

* Si
* No

En la lista de criterios utilizados en España para apoyar este tipo de decisiones, observamos una diferencia respecto a otros marcos de apoyo a la toma de decisiones de nuestro entorno. Esto es, la consideración específica de la perspectiva de los pacientes. Por favor, responda sí o no a la siguiente pregunta:

¿Cree que habría que añadir la perspectiva de los pacientes como un criterio adicional a los listados en la ley para apoyar la toma de decisiones sobre financiación de medicamentos en España de manera idónea?

* Si
* No

## ANNEX II – Translated version of the Survey (into English)

Tick the type of institution that best fits the institution you work for:

* Health Technology Assessment Agency
* Regulatory Agency
* Governmental entity (either regional government or national government)
* Academic or research institution
* Consultant
* Industry
* Other

Please indicate the range of years of professional experience that best fits your profile (years of doctoral studies would count as professional experience):

* 1-3 years
* 3-5 years
* 5-8 years
* 8 years or more

Tick the type of profile that best suits your position:

* Director, coordinator or head of area, unit, department or equivalent
* Technical staff, teachers or researchers
* Management staff or similar
* Other

Please tick the option that, in your opinion, would be most appropriate to measure each of the categories indicated for the medicines for which a decision on their inclusion or non-inclusion in the basic package of benefits of the NHS is to be taken:

1. SEVERITY, DURATION AND SEQUELAE OF THE VARIOUS PATHOLOGIES FOR WHICH THEY ARE INDICATED

Please tick those options that you consider appropriate and compatible for measuring severity, duration and sequelae of the different pathologies for which a new medicine for which a decision on inclusion in the basic package of the NHS is indicated (in case you consider that this parameter should not be considered in the funding decisions for medicines in Spain, please tick the box 'Other' and explain your position in the free text box):

* The Acute Physiology And Chronic Health Evaluation (APACHE) II [1,2], which measures severity in intensive care patients, or other similar instruments specific to particular therapeutic areas (whichever is relevant to the medicine for which inclusion or non-inclusion in the basic NHS benefits package is to be decided), accompanied by a temporal measure of duration
* Disability-adjusted life years (DALYs) [3].
* Quality Adjusted Life Year (QALY) [4].
* Clinical markers of severity and sequelae, or a number of clinical units of measure of pathology-specific efficacy that have clinical significance, with the addition of a temporal measure of duration (Examples: case fatality and morbidity-mortality rates are widely accepted measures of disease severity; other useful indicators are the frequency of serious events leading to hospitalisation or emergency department visits).
* Other - please indicate only the instrument for measuring severity, duration and sequelae of
* a disease that seems most appropriate to you (only one) (Free Text)
1. SPECIFIC NEEDS OF CERTAIN GROUPS

There are population groups that, due to their characteristics or those of the disease they suffer from, are specifically taken into account in decisions on the financing of medicines in Spain. Of the population groups listed below, please tick all those that you believe deserve special consideration in such decisions in Spain (if you consider that this parameter should not be taken into account in decisions on the financing of medicines in Spain, please tick the 'Other' box and explain your position in the free text box):

* Populations with a condition for which there is no satisfactory therapeutic alternative, following the European Commission's definition of unmet medical need [5] or also situations where there is a therapeutic gap in serious pathology, implying an absence of effective treatment alternatives, as defined in the plan for the consolidation of therapeutic positioning reports of medicinal products in the national health system [6].
* Orphan medicine [7], as defined by the EMA [8], or for ultra-rare diseases.
* The paediatric population [9]
* Patients facing the end of their lives [10].
* Other - please put only the population group you think it is most appropriate to take into account (only one) (Free text)
1. THERAPEUTIC AND SOCIAL VALUE OF THE MEDICINE AND ITS INCREMENTAL CLINICAL BENEFIT, TAKING INTO ACCOUNT ITS COST-EFFECTIVENESS

The therapeutic value of a medicine and its cost-effectiveness can be measured in different ways, and the social value of a medicine has different ways of being measured. Therefore, we will first present alternatives for measuring: (1) therapeutic value; (2) cost-effectiveness, and; (3) social value.

1. Please tick the options that seem appropriate from the following instruments for measuring the therapeutic value or incremental clinical benefit of medicines (tick more than one option if you think that multiple parameters would better inform the decision than just one - if you consider that this value dimension should not be taken into account in funding decisions for medicines in Spain, please tick the 'Other' box and explain your position in the free text box):
* Quality Adjusted Life Year (QALY) [4].
* The impact of the new strategy on clinical variables specific to the pathology being treated or some other clinical measure of efficacy specific to the pathology.
* A measure of real benefit of the new therapy based on a combination of clinical criteria, eventually translated into an index (in the style of the French system [11]).
* Other - please put only the instrument of measurement of therapeutic value that seems most appropriate to you (only one) (Free text)
1. Please tick the appropriate options from the following instruments to measure the cost-effectiveness of medicines (in case you consider that this parameter should not be taken into account in funding decisions for medicines in Spain, please tick the box 'Other' and explain your position in the free text box):
* Incremental Cost to Utility Ratio (RCUI, or ICUR) using utility measures such as QALY
* The Incremental Cost-Effectiveness Ratio (ICER) using clinical effectiveness measures (a concrete, clinically meaningful, pathology-specific clinical effectiveness variable(s)).
* Other - please put only the instrument you think is most appropriate to measure the cost-effectiveness of a new therapy (only one) (Free text)

In order to support medicines financing decisions on a cost-effectiveness and/or cost-utility ratio, it is necessary to have a benchmark of what is considered efficient use of resources in the system:

* Do you think there is a need for a cost-utility threshold in Spain? Yes / No
* If you think a threshold is needed, please tick the option that seems most appropriate:
* An explicit threshold (described and specified in the methodological manuals that frame the health technology assessment activity in a country)
* An implicit threshold (not officially specified, deduced from publications in peer-reviewed journals and published reports).
* Do you think there should be different thresholds for different population groups / special situations? Yes / No
1. Medicines, in addition to having a direct therapeutic health value for the patients for whom they are indicated, bring a benefit to society as a whole at various levels [12], which can be measured (tick all options that seem relevant to you - in case you consider that this parameter should not be taken into account in funding decisions on medicines in Spain, please tick the box 'Other' and explain your position in the free text box):
* Family members and other informal caregivers of patients see their quality of life improve in parallel with the improvement of the living conditions of the patients they care for.
* Patients (and their informal caregivers) in addition to benefiting from improved health due to the use of the medicine, are sometimes able to return to work earlier or in conditions more favourable to their productivity than without the new therapy.
* The pharmaceutical company producing the new medicine is likely to have a considerable economic impact, on employment in the country by generating a large number of quality jobs for qualified personnel and on other aspects of the economy (e.g. competitiveness, value added, etc.) [12].
* Other - please put only one way of measuring the social value of the medicine that we have not listed in the above options (Free text)
1. RATIONALISATION OF PUBLIC EXPENDITURE ON PHARMACEUTICALS AND THE BUDGETARY IMPACT ON THE NATIONAL HEALTH SYSTEM

Budget impact analysis is the standard measure to reflect the impact that the introduction of a new technology has on the budget of a healthcare system, and methodological guidelines exist that describe how to do this adequately [13]. However, the legislation does not go into describing how it measures the budgetary impact of new medicines to support its funding decisions. Please tick only the box that best describes the costs that seem relevant for a budget impact analysis. In case you are of the opinion that there would be another more appropriate way to measure budget impact or if you consider that this parameter should not be taken into account in funding decisions for medicines in Spain, please tick the box 'Other' and explain your position in the free text box:

* The budgetary impact only has to take into account expenditure on new and current pharmaceutical therapy over a time horizon of 3 to 5 years.
* The budgetary impact should take into account all healthcare costs (administration of therapy, adverse effects, etc.) over a time horizon of 3-5 years.
* Other - please put only the budgetary impact measurement instrument, other than the one mentioned above, which seems most appropriate to you (only one) (Free text)
1. AVAILABILITY OF MEDICINES OR OTHER THERAPEUTIC ALTERNATIVES FOR THE SAME CONDITIONS AT A LOWER PRICE OR LOWER COST OF TREATMENT

This criterion takes into account whether there is a therapeutic alternative with similar or superior efficacy and at lower cost than the new medicine. To measure this, the concepts of therapeutic equivalence or ATC groups can be used5 (The Anatomical, Therapeutic and Chemical Classification (ATC) is a coding system for medicines according to their pharmacological effect, therapeutic indications and chemical structure. It is divided into five levels: the first level (ATC1) is the most general and the fifth level (ATC5) the most detailed - it designates the specific active substance or pharmacological association [14]). For equivalent alternatives, you never pay more. If you know of another more appropriate way to measure this, please propose it below (in case you consider that this parameter should not be taken into account in funding decisions for medicines in Spain, please tick the box 'Other' and explain your position in the free text box):

* Concept of equivalent therapeutic alternative
* ATC4 groups
* ATC5 groups
* Other - please put only the instrument, other than those mentioned above, that seems most appropriate to you (only one) (Free text)
1. DEGREE OF INNOVATION OF THE MEDICINAL PRODUCT

For the purposes of this survey we will use the definition of degree of innovation based on the value dimensions that make up the concept identified in previous research [15]). That is: qualitative leap in its indication (`step-change'), convenience (`convenience'), robustness of evidence (`strength of evidence base') taking into account the degree of uncertainty associated with the evidence (among other factors), impact on future R&D (`impact on future R&D').

Now, what kind of instrument do you think should be used to measure the degree of innovation to support the decision making on the financing of medicines in Spain as described in the law? Please tick only the instrument that, in your view, is most appropriate (in case you consider that this parameter should not be taken into account in funding decisions for medicines in Spain, please tick the box 'Other' and explain your position in the free text box):

* A checklist instrument (currently we are only aware of the INAHTA checklist [16] which applies to health technology assessment in general - we will propose a specific checklist to measure the degree of innovation as part of this project).
* As part of a Multi-Criteria Decision Analysis (MCDA), as one of the value domains measured and captured (as, for example, in the Advance Value Framework developed and published by Angelis & Kanavos (2017) [17] or the 'innovometer' proposed by Zaragozá-García & Cuéllar (2017) [18], taking into account that several of the parameters already measured in previous headings would be double-counted if we were to use the 'innovometer' as it captures parameters such as the therapeutic value domains measured in previous headings.
* Other - please put only the instrument for measuring the degree of innovation, other than those mentioned above, that seems most appropriate to you (only one) (Free Text)

WEIGHTING OF EACH CRITERION

Please indicate the weight (from 0 to 100) that you think each criterion should have in the funding decisions for medicines in Spain. Please note that the sum of the scores given should be 100.

1. Severity, duration and sequelae of the different pathologies for which they are indicated;
2. Specific needs of certain groups;
3. Therapeutic and social value of the medicinal product and incremental clinical benefit of the medicinal product taking into account its cost-effectiveness;
4. Rationalisation of public expenditure on pharmaceuticals and the budgetary impact on the

National Health System;

1. Availability of medicines or other therapeutic alternatives for the same conditions at a lower price or lower cost of treatment;
2. Degree of innovation of the medicinal product.

SUITABILITY OF THE CRITERIA LISTED IN THE LAW TO SUPPORT FUNDING DECISIONS FOR MEDICINES IN SPAIN

Please answer yes or no to the following question:

Do you think that the criteria listed in the law to support decision-making on the financing of medicines in Spain are adequate?

* Yes
* No

Do you think that any criteria should be added to those listed in the law to support decision-making on medicines funding in Spain in an appropriate manner?

* Yes
* No

In the list of criteria used in Spain to support this type of decision, we observe a difference with respect to other decision support frameworks in our environment. This is the specific consideration of the patients' perspective. Please answer yes or no to the following question:

Do you think that the patients' perspective should be added as an additional criterion to those listed in the law to support decision-making on medicines funding in Spain in an appropriate way?

* Yes
* No

## References for annex i and annex ii

1. Knaus, W. A., Draper, E. A., Wagner, D. P., & Zimmerman, J. E. (1985). APACHE II: a severity of disease classification system. *Critical care medicine*, *13*(10), 818–829.
2. Wagner, D. P., & Draper, E. A. (1984). Acute physiology and chronic health evaluation (APACHE II) and Medicare reimbursement. Health care financing review, Suppl(Suppl), 91–105.
3. Murray, C. J., & Acharya, A. K. (1997). Understanding DALYs (disability-adjusted life years). Journal of health economics, 16(6), 703–730. [https://doi.org/10.1016/s0167-6296(97)00004-0](https://doi.org/10.1016/s0167-6296%2897%2900004-0)
4. Whitehead, S. J., & Ali, S. (2010). Health outcomes in economic evaluation: the QALY and utilities. British medical bulletin, 96, 5–21. <https://doi.org/10.1093/bmb/ldq033>
5. Diario Oficial de la Unión Europea (2006). REGLAMENTO (CE) No 507/2006 DE LA COMISIÓN de 29 de Marzo de 2006 sobre la autorización condicional de comercialización de los medicamentos de uso humano que entran en el ámbito de aplicación del Reglamento (CE) no 726/2004 del Parlamento Europeo y del Consejo. Disponible en: <https://eur-lex.europa.eu/legal-content/ES/TXT/HTML/?uri=CELEX:32006R0507>
6. Ministerio de Sanidad del Gobierno de España (2020). Plan para la consolidación de los informes de posicionamiento terapéutico de los medicamentos en el Sistema Nacional de Salud. Available at: <https://www.sanidad.gob.es/gl/profesionales/farmacia/IPT/docs/20200708.Plan_de_accion_para_la_consolidacion_de_los_IPT.actCPF8Julio.pdf>
7. Melnikova I. (2012). Rare diseases and orphan drugs. Nature reviews. Drug discovery, 11(4), 267–268. <https://doi.org/10.1038/nrd3654>
8. EMA website (2023). Orphan designation: Overview. Available at: <https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview>
9. Spadoni C. (2018). Pediatric Drug Development: Challenges and Opportunities. Current therapeutic research, clinical and experimental, 90, 119–122. <https://doi.org/10.1016/j.curtheres.2018.12.001>
10. Linley, W. G., & Hughes, D. A. (2013). Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain. Health economics, 22(8), 948–964. <https://doi.org/10.1002/hec.2872>
11. Haute Autorité de Santé (2014). Pricing & Reimbursement of drugs and HTA policies in France. Available at: <https://www.has-sante.fr/upload/docs/application/pdf/2014-03/pricing_reimbursement_of_drugs_and_hta_policies_in_france.pdf>
12. Weber (2021). El valor del medicamento desde una perspectiva social 2021. Madrid, España: Fundación Weber. Available at: <https://weber.org.es/wp-content/uploads/2023/03/libro_digital_valor_medicamento_actualizacion_2020_final.pdf>
13. Puig-Junoy, J., Oliva-Moreno, J., Trapero-Bertrán, M., Abellán-Perpiñán, J. M., & Brosa-Riestra, M. (2014). Guía y recomendaciones para la realización y presentación de evaluaciones económicas y análisis de impacto presupuestario de medicamentos en el ámbito del CatSalut. Barcelona: Servei Català de la Salut (CatSalut). Available at: <https://catsalut.gencat.cat/web/.content/minisite/catsalut/proveidors_professionals/medicaments_farmacia/farmaeconomica/caeip/gaeip_publica_castellano_octubre2014_catsalut.pdf>
14. World Health Organization. (2009). The anatomical therapeutic chemical classification system with defined daily doses-ATC/DDD. Available at: <https://www.who.int/standards/classifications/other-classifications/the-anatomical-therapeutic-chemical-classification-system-with-defined-daily-doses>
15. Rejon-Parrilla, J. C., Espin, J., & Epstein, D. (2022). How innovation can be defined, evaluated and rewarded in health technology assessment. Health economics review, 12(1), 1. <https://doi.org/10.1186/s13561-021-00342-y>
16. Hailey D. (2003). Toward transparency in health technology assessment: a checklist for HTA reports. International journal of technology assessment in health care, 19(1), 1–7. <https://doi.org/10.1017/s0266462303000011>
17. Angelis, A., & Kanavos, P. (2017). Multiple Criteria Decision Analysis (MCDA) for evaluating new medicines in Health Technology Assessment and beyond: The Advance Value Framework. Social science & medicine (1982), 188, 137–156. <https://doi.org/10.1016/j.socscimed.2017.06.024>
18. Zaragozá-García F, Cuéllar-Rodríguez S. (2017). Valoración de la innovación terapéutica: importancia y medida. In: Innovación y regulación en biomedicina: obligados a entenderse (ed. Del Llano Señarís JE). Fundación Gaspar Casal; ISBN: 978-84-697-2531-3; pp 237-72. Available at: <https://fundaciongasparcasal.org/wp-content/uploads/2021/02/Innovacon-y-Regulacion-en-Biomedicina-Obligados-a-Entenderse.pdf>

## ANNEX III – Distribution of the survey

The groups, professional associations and institutions we used to reach the target respondents were: (1) the Spanish Association of Health Economics (AES), which is an association of professionals working in the field of health economics and HTA. Most members are academics.; (2) the Spanish Network of Health Technology Assessment Agencies (RedETS), which is a network of HTA bodies in Spain mainly focusing on HTA of medical devices; (3) the GENESIS group, which is a group created within the Spanish Society of Hospital pharmacist, entailing hospital pharmacists with an interest in HTA for hospital decision making purposes, created to coordinate and harmonise practices across Spanish hospitals, and to further develop the guidance supporting their evaluations; (4) the Spanish Agency of Medicines and Health Products (AEMPS), which is the national regulatory body which produces therapeutic positioning reports (a form of HTA) on new medicines; (5) Farmaindustria (the Spanish Pharmaceutical Industry Association), a trade body representing producers of patented medicines; (6) the Spanish chapter of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), which is a society including industry, academia and consulting firm; and (7) civil servants, technical analysts and advisors to the Spanish Ministry of Health on topics covering the economic evaluation of health interventions and HTA.

We distributed the survey to members of the AES community using their mailing list. To reach staff members of the RedETS, we asked the directors of the agencies to forward the email to the targeted staff in the Network. We used a member of the GENESIS group to make the survey available to hospital pharmacists. We distributed the survey to AEMPS staff via one of their directors. The members of the Spanish Chapter of ISPOR received the survey via one of the Board Members of their Chapter. One of the co-authors of the paper (DE) was holding a role as advisor to the Spanish Ministry of health whilst this research was being performed, and distributed the survey to the relevant civil servants. We distributed the survey to members of the Spanish Farmaindustria through one of the members of their Board.

## ANNEX IV – Respondents who chose multiple answers (N=90)

|  |  |  |  |
| --- | --- | --- | --- |
| **Criteria / Question** | **Number of options chosen by respondent** | **Number of respondents** | **% of respondents** |
| **Severity, duration and sequelae** | 1 | 35 | 39 |
| 2 | 21 | 23 |
| 3 | 24 | 27 |
| 4 | 8 | 9 |
| Other/none | 2 | 2 |
| **Groups with specific needs** | 1 | 15 | 17 |
| 2 | 20 | 22 |
| 3 | 35 | 39 |
| 4 | 15 | 17 |
| Other/none | 5 | 6 |
| **Therapeutic value** | 1 | 34 | 38 |
| 2 | 42 | 47 |
| 3 | 14 | 16 |
| Other/none | 0 | 0 |
| **Incremental Cost-effectiveness** | 1 | 46 | 51 |
| 2 | 42 | 47 |
| Other/none | 2 | 2 |
| **Social value** | 1 | 11 | 12 |
| 2 | 57 | 63 |
| 3 | 20 | 22 |
| Other/none | 2 | 2 |
| **Rationalization of public spending** | 1 | 81 | 90 |
| Other/none | 9 | 10 |
| **Availability of therapeutic alternatives** | 1 | 62 | 69 |
| 2 | 18 | 20 |
| 3 | 2 | 2 |
| Other/none | 8 | 9 |
| **Degree of innovation** | 1 | 81 | 90 |
| Other/none | 9 | 10 |

**Note:** we rounded up where decimals were .5 or higher and down when they were .49 or lower. This may have caused that, in some instances, total percentages were 101 or 99 instead of 100; questions about the threshold only had one possible answer, and the option to tick the ‘Other’ free text box was not offered, so we did not include those in this table.

## ANNEX V – LOGISTIC REGRESSIONS

Table A1. Measurement of severity, duration and sequelae

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | (1) | (2) | (3) | (4) |
|  | Acute Physiology | DALY | QALY | Clinical markers |
| HTA agencies | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Regulatory agencies  | -0.121(0.888) | -0.749(0.352) | -1.303(0.130) | 0.729(0.443) |
|  |  |  |  |  |
| Consulting firms | -0.507(0.698) | -0.407(0.684) | -0.771(0.565) | 1.188(0.351) |
|  |  |  |  |  |
| Government Institution | -0.0164(0.985) | -1.163(0.154) | -1.613(0.055) | -0.605(0.442) |
|  |  |  |  |  |
| Industry | -0.403(0.683) | -0.419(0.615) | **-2.125\*(0.022)** | 1.633(0.177) |
|  |  |  |  |  |
| Academic institution  | -0.242(0.778) | -1.270(0.112) | 0.248(0.800) | **-2.065\*(0.016)** |
|  |  |  |  |  |
| Other | -1.051(0.385) | -0.651(0.454) | -1.345(0.164) | -0.604(0.496) |
|  |  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| 3-5 years | 0.611(0.663) | 0.746(0.569) | -0.597(0.687) | -0.454(0.610) |
|  |  |  |  |  |
| 5-8 years | 0(.) | 0(.) | -0.512(0.750) | -0.248(0.809) |
|  |  |  |  |  |
| 8 years or more | 0.328(0.794) | -0.198(0.861) | -0.705(0.594) | 0(.) |
|  |  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Other | 0(.) | 0(.) | -0.925(0.570) | 0(.) |
|  |  |  |  |  |
| Technicians, professors, researchers | 0.519(0.402) | -0.614(0.250) | **-1.657\*\*(0.008)** | 0.512(0.366) |
|  |  |  |  |  |
| Constant | -1.613(0.232) | 0.893(0.454) | 3.268\*(0.025) | 0.604(0.369) |
| Observations | 83 | 83 | 90 | 84 |
| Pseudo *R*2 | 0.033 | 0.059 | 0.142 | 0.172 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A2. Necesities of certain specific patient groups

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | (1) | (2) | (3) | (4) |
|  | No therapeutic alternative | Orphan medicines | Pediatric population | End of life |
| HTA agencies | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Regulatory agencies  | 1.805(0.186) | -0.207(0.818) | 1.715(0.067) | -0.162(0.846) |
|  |  |  |  |  |
| Consulting firms | 0(.) | -0.867(0.439) | -0.639(0.545) | -1.248(0.242) |
|  |  |  |  |  |
| Government Institution | 0(.) | -1.029(0.220) | -0.751(0.372) | -1.847(0.057) |
|  |  |  |  |  |
| Industry | 0.330(0.742) | -0.0406(0.968) | 1.089(0.197) | 1.150(0.192) |
|  |  |  |  |  |
| Academic institution  | 1.072(0.312) | **-1.637\*(0.049)** | -0.493(0.536) | -1.004(0.251) |
|  |  |  |  |  |
| Other | 0(.) | -0.887(0.352) | 0.810(0.351) | -0.197(0.826) |
|  |  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| 3-5 years | -0.560(0.669) | -0.971(0.237) | 1.717(0.239) | -0.169(0.845) |
|  |  |  |  |  |
| 5-8 years | 0(.) | -0.679(0.516) | -0.890(0.605) | 0.830(0.427) |
|  |  |  |  |  |
| 8 years or more | 0(.) | 0(.) | 0.359(0.777) | 0(.) |
|  |  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Other | 0(.) | 0(.) | -0.0474(0.977) | -1.223(0.496) |
|  |  |  |  |  |
| Technicians, professors, researchers | -0.0806(0.920) | -0.441(0.422) | -0.301(0.586) | **-1.130\*(0.046)** |
|  |  |  |  |  |
| Constant | 0.729(0.359) | 1.784\*(0.017) | -0.637(0.627) | 0.331(0.617) |
| Observations | 44 | 84 | 90 | 86 |
| Pseudo *R*2 | 0.057 | 0.067 | 0.157 | 0.148 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A3. Clinical and social value

|  |  |  |  |
| --- | --- | --- | --- |
|  | (1) | (2) | (3) |
|  | V\_AVAC | V\_clin | V\_comb |
| HTA agencies | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Regulatory agencies  | -1.503(0.098) | 0.631(0.424) | 0.517(0.515) |
|  |  |  |  |
| Consulting firms | 0(.) | -0.432(0.658) | -0.634(0.522) |
|  |  |  |  |
| Government Institution | -0.908(0.360) | 0.380(0.602) | -0.494(0.529) |
|  |  |  |  |
| Industry | -1.171(0.231) | 0.496(0.545) | 0.351(0.673) |
|  |  |  |  |
| Academic institution  | -0.172(0.868) | -0.851(0.273) | -0.552(0.471) |
|  |  |  |  |
| Other | -0.409(0.722) | 0.140(0.868) | -0.339(0.693) |
|  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| 3-5 years | -1.058(0.203) | 0.756(0.586) | -0.153(0.903) |
|  |  |  |  |
| 5-8 years | 0.679(0.632) | 0.584(0.696) | 0(.) |
|  |  |  |  |
| 8 years or more | 0(.) | 1.207(0.332) | -0.303(0.785) |
|  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Other | -1.648(0.334) | 0(.) | 0(.) |
|  |  |  |  |
| Technicians, professors, researchers | -0.192(0.753) | -0.138(0.784) | -0.526(0.313) |
|  |  |  |  |
| Constant | 2.099\*(0.014) | -1.062(0.413) | 0.648(0.579) |
| Observations | 79 | 88 | 83 |
| Pseudo *R*2 | 0.084 | 0.051 | 0.035 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A4. Instruments to measure cost-effectiveness

|  |  |  |
| --- | --- | --- |
|  | (1) | (2) |
|  | C\_ICUR | C\_ICER |
| HTA agencies | 0(.) | 0(.) |
|  |  |  |
| Regulatory agencies  | **-3.052\*\*(0.004)** | 0.444(0.640) |
|  |  |  |
| Consulting firms | 0(.) | -1.281(0.209) |
|  |  |  |
| Government Institution | **-2.296\*(0.028)** | -0.702(0.367) |
|  |  |  |
| Industry | -1.508(0.186) | 0.485(0.621) |
|  |  |  |
| Academic institution  | -1.458(0.178) | -0.566(0.476) |
|  |  |  |
| Other | -0.0793(0.960) | -0.329(0.719) |
|  |  |  |
| 1-3 years | 0(.) | 0(.) |
|  |  |  |
| 3-5 years | -0.357(0.823) | 0.982(0.463) |
|  |  |  |
| 5-8 years | 1.705(0.396) | -1.289(0.399) |
|  |  |  |
| 8 years or more | 0.719(0.622) | 0.885(0.435) |
|  |  |  |
| Management/direction position | 0(.) | 0(.) |
|  |  |  |
| Other | -2.694(0.146) | 0(.) |
|  |  |  |
|  |  |  |
| Technicians, professors, researchers | -0.396(0.533) | 0.0649(0.906) |
|  |  |  |
| Constant | 2.275(0.143) | 0.108(0.927) |
| Observations | 83 | 88 |
| Pseudo *R*2 | 0.188 | 0.090 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A5. Thresholds

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | (1) | (2) | (3) | (4) |
|  | Threshold? | Explicit | Implicit | Exceptions |
| HTA agencies | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Regulatory agencies  | -1.944(0.125) | **-2.990\*\*(0.003)** | 2.234(0.068) | -0.129(0.900) |
|  |  |  |  |  |
| Consulting firms | 0(.) | -0.0675(0.962) | 0.460(0.768) | -0.0695(0.960) |
|  |  |  |  |  |
| Government Institution | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| Industry | -1.084(0.495) | -0.412(0.716) | 0.138(0.927) | 0(.) |
|  |  |  |  |  |
| Academic institution  | -0.638(0.673) | -1.486(0.122) | 1.769(0.143) | -1.429(0.104) |
|  |  |  |  |  |
| Other | -1.243(0.432) | -0.674(0.552) | 1.224(0.358) | -0.863(0.387) |
|  |  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
| 3-5 years | -0.859(0.410) | 0.175(0.857) | -0.808(0.511) | 1.508(0.377) |
|  |  |  |  |  |
| 5-8 years | 0(.) | -1.269(0.382) | 1.916(0.236) | -0.200(0.909) |
|  |  |  |  |  |
| 8 years or more | 0(.) | 0(.) | 0(.) | 0.519(0.711) |
|  |  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) | 0(.) |
|  |  |  |  |  |
|  |  |  |  |  |
| Technicians, professors, researchers | -0.839(0.382) | 0.156(0.809) | -0.552(0.422) | -0.649(0.354) |
|  |  |  |  |  |
| Constant | 3.763\*\*(0.008) | 1.859\*(0.039) | -2.252\*(0.046) | 1.342(0.341) |
| Observations | 61 | 71 | 71 | 63 |
| Pseudo *R*2 | 0.103 | 0.166 | 0.112 | 0.080 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A6. Social value

|  |  |  |  |
| --- | --- | --- | --- |
|  | (1) | (2) | (3) |
|  | Family impact | Patient impact | Industry impact |
| HTA agencies | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Regulatory agencies  | -2.356(0.084) | -0.351(0.809) | -0.452(0.637) |
|  |  |  |  |
| Consulting firms | 0(.) | 0(.) | 0.522(0.623) |
|  |  |  |  |
| Government Institution | **-3.159\*(0.015)** | 0(.) | -0.865(0.414) |
|  |  |  |  |
| Industry | -1.169(0.469) | 0(.) | 0.293(0.755) |
|  |  |  |  |
| Academic institution  | **-2.686\*(0.045)** | 0.458(0.761) | 0.401(0.644) |
|  |  |  |  |
| Other | -1.479(0.361) | 0(.) | 0(.) |
|  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| 3-5 years | -0.731(0.476) | -0.914(0.531) | **1.834\*(0.039)** |
|  |  |  |  |
| 5-8 years | -1.734(0.218) | 0(.) | 0(.) |
|  |  |  |  |
| 8 years or more | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
|  |  |  |  |
| Technicians, professors, researchers | -0.0000992(1.000) | 0.379(0.734) | **-1.603\*(0.021)** |
|  |  |  |  |
| Constant | 3.559\*\*(0.006) | 1.925(0.092) | -0.235(0.751) |
| Observations | 77 | 33 | 70 |
| Pseudo *R*2 | 0.164 | 0.044 | 0.145 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A7. Rationalization of public spending

|  |  |  |
| --- | --- | --- |
|  | (1) | (2) |
|  | P\_farm | P\_san |
| HTA agencies | 0(.) | 0(.) |
|  |  |  |
| Regulatory agencies  | 1.577(0.239) | **-2.477\*(0.025)** |
|  |  |  |
| Consulting firms | 0(.) | -3.147(0.084) |
|  |  |  |
| Government Institution | 0(.) | -0.808(0.576) |
|  |  |  |
| Industry | 0(.) | -1.064(0.465) |
|  |  |  |
| Academic institution  | 0(.) | -0.0481(0.972) |
|  |  |  |
| Other | 0(.) | -1.843(0.156) |
|  |  |  |
| 1-3 years | 0(.) | 0(.) |
|  |  |  |
| 3-5 years | 0.241(0.863) | -0.899(0.382) |
|  |  |  |
| 5-8 years | 0(.) | 0(.) |
|  |  |  |
| 8 years or more | 0(.) | 0(.) |
|  |  |  |
| Management/direction position | 0(.) | 0(.) |
|  |  |  |
|  |  |  |
| Technicians, professors, researchers | 0(.) | **-2.879\*(0.012)** |
|  |  |  |
| Constant | -2.564\*(0.026) | 4.939\*\*\*(0.001) |
| Observations | 20 | 79 |
| Pseudo *R*2 | 0.089 | 0.262 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A8. Availability of other medicines and therapeutic alternatives

|  |  |  |  |
| --- | --- | --- | --- |
|  | (1) | (2) | (3) |
|  | A\_equ | A\_atc4 | A\_atc5 |
| HTA agencies | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Regulatory agencies  | -0.208(0.802) | -0.301(0.812) | **-2.486\*(0.033)** |
|  |  |  |  |
| Consulting firms | -1.820(0.091) | 1.232(0.419) | -0.442(0.659) |
|  |  |  |  |
| Government Institution | -0.0603(0.943) | 0.436(0.686) | -0.552(0.457) |
|  |  |  |  |
| Industry | -1.163(0.171) | 0.484(0.685) | 0.0289(0.972) |
|  |  |  |  |
| Academic institution  | -0.181(0.819) | -0.398(0.754) | -0.431(0.570) |
|  |  |  |  |
| Other | 1.978(0.145) | -0.292(0.839) | 0(.) |
|  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| 3-5 years | 1.044(0.237) | -0.159(0.896) | 0.321(0.825) |
|  |  |  |  |
| 5-8 years | 2.046(0.190) | 0.851(0.458) | 1.766(0.241) |
|  |  |  |  |
| 8 years or more | 0(.) | 0(.) | 1.512(0.230) |
|  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Other | -2.334(0.210) | 2.503(0.189) | 0(.) |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| Technicians, professors, researchers | -0.592(0.293) | 1.410(0.114) | 0.383(0.501) |
|  |  |  |  |
| Constant | 0.903(0.184) | -3.024\*\*(0.005) | -1.358(0.301) |
| Observations | 86 | 86 | 79 |
| Pseudo *R*2 | 0.132 | 0.094 | 0.102 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A9. Innovation

|  |  |  |
| --- | --- | --- |
|  | (1) | (2) |
|  | I\_chec | I\_mcda |
| HTA agencies | 0(.) | 0(.) |
|  |  |  |
| Regulatory agencies  | -0.983(0.235) | 0.0191(0.980) |
|  |  |  |
| Consulting firms | 0.378(0.701) | -0.209(0.832) |
|  |  |  |
| Government Institution | 0.770(0.323) | -0.580(0.456) |
|  |  |  |
| Industry | 0.611(0.459) | -0.426(0.607) |
|  |  |  |
| Academic institution  | -0.140(0.851) | -0.605(0.439) |
|  |  |  |
| Other | -0.195(0.819) | -1.061(0.269) |
|  |  |  |
| 1-3 years | 0(.) | 0(.) |
|  |  |  |
| 3-5 years | -0.872(0.530) | 0.792(0.567) |
|  |  |  |
| 5-8 years | 0.240(0.883) | -0.316(0.846) |
|  |  |  |
| 8 years or more | -0.887(0.480) | 0.625(0.618) |
|  |  |  |
| Management/direction position | 0(.) | 0(.) |
|  |  |  |
|  |  |  |
| Technicians, professors, researchers | 0.138(0.788) | -0.266(0.612) |
|  |  |  |
| Constant | 0.796(0.537) | -0.704(0.587) |
| Observations | 88 | 88 |
| Pseudo *R*2 | 0.063 | 0.028 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

Table A10. Adequacy of criteria

|  |  |  |  |
| --- | --- | --- | --- |
|  | (1) | (2) | (3) |
|  | Criterios\_adec\_a | Criterios\_adicional | Criterio\_paciente |
| HTA agencies | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| Regulatory agencies  | -0.447(0.614) | 0.887(0.338) | -0.259(0.750) |
|  |  |  |  |
| Consulting firms | **-2.566\*(0.023)** | 0(.) | 0(.) |
|  |  |  |  |
| Government Institution | -1.160(0.179) | 0.968(0.251) | -0.201(0.806) |
|  |  |  |  |
| Industry | -1.649(0.070) | 0.374(0.671) | 1.335(0.264) |
|  |  |  |  |
| Academic institution  | **-2.669\*\*(0.004)** | 1.136(0.219) | -0.707(0.363) |
|  |  |  |  |
| Other | -2.252\*(0.020) | 0.136(0.879) | -0.201(0.824) |
|  |  |  |  |
| 1-3 years | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
| 3-5 years | -1.692(0.053) | -0.0797(0.956) | 0.0406(0.961) |
|  |  |  |  |
| 5-8 years | 0.420(0.733) | -1.765(0.248) | 0.651(0.587) |
|  |  |  |  |
| 8 years or more | 0(.) | -0.414(0.745) | 0(.) |
|  |  |  |  |
| Management/direction position | 0(.) | 0(.) | 0(.) |
|  |  |  |  |
|  |  |  |  |
| Technicians, professors, researchers | -0.209(0.704) | -0.127(0.824) | -0.461(0.400) |
|  |  |  |  |
| Constant | 1.650\*(0.029) | 1.029(0.436) | 1.108(0.102) |
| Observations | 84 | 81 | 77 |
| Pseudo *R*2 | 0.153 | 0.060 | 0.058 |

*p*-values in parentheses

\* *p* < 0.05, \*\* *p* < 0.01, \*\*\* *p* < 0.001

## ANNEX VI – All responses to all questions in the survey

|  |  |  |
| --- | --- | --- |
| **Criteria / Question** | **Measurement option** | **Respondents N (%) that picked it**  |
| **Severity, duration and sequelae** | Severity instrument | 19 (21%) |
| DALYs | 40 (44%) |
| QALYs | 61 (68%) |
| Clinical units | 61 (68%) |
| Other | 2 (2%) |
| **Groups with specific needs** | End of life | 32 (36%) |
| Paediatric population | 42 (47%) |
| Rare diseases | 64 (71%) |
| Unmet need | 82 (91%) |
| Other | 5 (6%) |
| **Therapeutic value** | Clinical units | 44 (49%) |
| Benefit index (French approach) | 44 (49%) |
| QALYs | 72 (80%) |
| Other | 0 (0%) |
| **Incremental Cost-effectiveness** | ICER | 60 (67%) |
| ICUR | 70 (78%) |
| Other | 4 (4%) |
| **Cost-Utility Threshold** **(yes / no)** | No | 6 (7%) |
| Yes | 84 (93%) |
| **Threshold (explicit / implicit)** | Implicit | 14 (16%) |
| Explicit | 70 (78%) |
| **Threshold (different in special situations: yes / no)** | No | 10 (11%) |
| Yes | 74 (82%) |
| **Social value** | Impact on economy | 25 (28%) |
| QoL informal carers | 73 (81%) |
| Productivity | 87 (97%) |
| Other | 4 (4%) |
| **Rationalization of public spending (budget impact)** | Pharmaceutical spending, 3-5 years horizon | 3 (3%) |
| Total expenditure, 3-5 years horizon | 78 (87%) |
| Other | 9 (10%) |
| **Availability of therapeutic alternatives** | ATC4 | 11 (12%) |
| ATC5 | 34 (38%) |
| Therapeutic equivalent | 59 (66%) |
| Other | 8 (9%) |
| **Degree of innovation** | MCDA | 32 (36%) |
| Checklist | 49 (54%) |
| Other | 9 (10%) |
| **Are we addressing all relevant criteria?** | Yes | 44% |
| No | 56% |
| **Should any criteria be added to the current list?** | No | 23% |
| Yes | 77% |
| **Do you think the perspective of patients should be an additional criterion?** | No | 26% |
| Yes | 74% |

**Note:** *The relative weights are presented on a different table, in the body of the paper. They are presented as means, based on a total of 88 correctly formulated responses (2 did not sum up to 100). It was a weighting exercise, not a matter of picking options. Hence, percentages are not relevant.*

1. Definición de la EMA de medicamento huérfano: <https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview> [↑](#footnote-ref-1)