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Questionnaire

**Payer perceptions and use of ITC in HTA/P&R decision-making**

# QUESTIONNAIRE

## Section 1: Study design and data sources for indirect treatment comparisons

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|  | **In this section the research seeks to understand the acceptability of different study designs (e.g., RCTs, RWE) and data sources for the implementation of indirect treatment comparisons and acceptance by HTA bodies/payers in your country for P&R/coverage decisions. Please review the background information before progressing to the following questions**  **Definitions:**   * **Indirect treatment comparison (ITC):** A comparison of two different healthcare interventions that have not been directly compared with each other in a head-to-head trial, using summary level data only from separate studies. * **Network Meta-Analysis (NMA):** A technique for comparison of three or more interventions simultaneously in a single analysis. * **Anchored meta-analysis:**  Anchored indirect comparison is considered when connected evidence with a common comparator is available (i.e., two healthcare interventions compared against the same standard of care). * **Unanchored meta-analysis:** Unanchored comparisons is only considered where single-arm studies are involved, or in the absence of a connected network of randomized evidence.   **Indirect comparison methods where patient-level data available for at least one treatment**   * **Matching-adjusted indirect comparison (MAIC):** A technique using individual patient data (IPD) from trials of one treatment to match baseline summary statistics reported from trials of another treatment, and in some instances summary level data are also used in anchored analysis, to compare treatment outcomes across balanced trial populations. * **Simulated treatment comparison (STC):** A technique that involves estimating a linear regression model for the relationship between population characteristics and outcomes in a trial, where IPD is available, and then using the model to estimate that outcome for the other trial population; in some instances, summary level data are also used in anchored analysis. * **Propensity Score Reweighing and Matching:** A statistical technique that attempts to estimate the effect of a healthcare intervention by matching patients, with IPD only, from different treatments on characteristics that predict treatment.   If you need a refresher on methods and best practices please read the following sources:   * + [Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1](https://urldefense.com/v3/__https:/www.valueinhealthjournal.com/action/showPdf?pii=S1098-3015*2811*2901404-5__;JSU!!Eu8ikxSnpXkBCg!dwHXgDtis2O72BChG17N873FxTH6ploKa8qEip0L_EO-MqBQQwXvrLrO7_vGyswdwndSyLOST3ScPl0m4hSyEoWtXEYQ3vN_UCC_sgC7rQ$)   + [Conducting Indirect-Treatment-Comparison and Network-Meta-Analysis Studies: Report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices—Part 2](https://urldefense.com/v3/__https:/www.valueinhealthjournal.com/action/showPdf?pii=S1098-3015*2811*2901328-3__;JSU!!Eu8ikxSnpXkBCg!dwHXgDtis2O72BChG17N873FxTH6ploKa8qEip0L_EO-MqBQQwXvrLrO7_vGyswdwndSyLOST3ScPl0m4hSyEoWtXEYQ3vN_UCDacUKRpA$)   + [Good Research Practices for Comparative Effectiveness Research: Analytic Methods to Improve Causal Inference from Nonrandomized Studies of Treatment Effects Using Secondary Data Sources: The ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report—Part III](https://urldefense.com/v3/__https:/www.valueinhealthjournal.com/article/S1098-3015(10)60310-5/pdf?_returnURL=https*3A*2F*2Flinkinghub.elsevier.com*2Fretrieve*2Fpii*2FS1098301510603105*3Fshowall*3Dtrue__;JSUlJSUlJSU!!Eu8ikxSnpXkBCg!dwHXgDtis2O72BChG17N873FxTH6ploKa8qEip0L_EO-MqBQQwXvrLrO7_vGyswdwndSyLOST3ScPl0m4hSyEoWtXEYQ3vN_UCC0WlL_Wg$)   + [EUnetHTA Methodology Guideline, Comparators & Comparisons: Direct and Indirect comparisons, adapted version 2.0 (2015).](https://urldefense.com/v3/__https:/www.eunethta.eu/wp-content/uploads/2018/03/Direct_comparators_comparisons.pdf__;!!Eu8ikxSnpXkBCg!dwHXgDtis2O72BChG17N873FxTH6ploKa8qEip0L_EO-MqBQQwXvrLrO7_vGyswdwndSyLOST3ScPl0m4hSyEoWtXEYQ3vN_UCBcBF4c4Q$) |

1. **Is indirect treatment comparison (ITC) accepted in your country/organization** to inform payer decisions? If yes/depends on case by case, are there **well-defined and prescribed criteria/requirements regarding the use of ITC** to assess the comparative effectiveness of a new therapy?   
   Is there **any relaxation in the criteria/requirements for acceptance of ITCs** (e.g., orphan conditions, high unmet need, low budget impact)?  
   Please provide your answer and rationale, along with indicative examples/case studies that demonstrate this.

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| Question | Response | (Optional) Conditions for acceptance of ITC | Rationale |
| **Is ITC accepted in your country/organization to inform payer decisions?** | Select one: Yes Depends on case-by-case No | **–** | Open text [mandatory] |
| **Are well-defined/prescribed criteria/requirements established in your country/organization for ITC?** | Select one: Yes Depends on case-by-case No | **–** | Open text [mandatory] |
| **Relaxation of criteria for acceptance of ITC?** | Select one: Yes Yes, conditionally No | Select all that apply: Orphan condition High unmet need Low budget impact Other (please explain in rationale box) Not applicable | Open text [mandatory] |

**Comment box**: Please provide indicative example(s) of therapies where relaxation of criteria for ITC was accepted in HTA/payer decision-making.

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| Open text [mandatory] |

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|  | *Please review the following definitions of study types and data sources before responding to the following question:*   * **Randomized controlled trial**: A prospective explanatory study that measures the effectiveness of a new intervention or treatment, with randomization between treatment groups reducing bias and providing a rigorous tool to examine cause-effect relationships between an intervention and outcome. * **Single arm trial**: In this design, a sample of individuals with the targeted medical condition is given the experimental therapy and then followed over time to observe their response. The design may be desirable when the available patient pool is limited and thus it is not optimal to randomize many participants to a control arm. * **Pragmatic trial:** A study that tests multiple interventions, but conducted in real-world clinical practice settings, without randomization for treatment assignment, with typical patients and by qualified clinicians, who may not, however, have a research background. They are designed to help chose between care options, as opposed to an RCT which is used to test causal research. * **Observational trial**: A prospective study consisting of only a single group of subjects included in the study design, in which all subjects received a single intervention and the outcomes are assessed over time, thus there are no data to show that people with the condition have improved compared to those who didn’t receive treatment. Single group studies do not include a direct, concurrent comparison group. Observational study designs in general suffer from a potential lack of exchangeability of exposed and unexposed subjects (i.e., the ‘counterfactual outcome’ is related to the outcome in the untreated group, which may differ from what would have occurred in the treated in the absence of treatment). * **External comparator arm**: An external comparator or control (sometimes called a synthetic control) is aggregated, real world data (RWD) from patients that are similar to the clinical trial population. Researchers can use an external comparator to understand how trial-like patients progress without exposure to the interventional product from the trial. |

1. **Data from which study types** (e.g., RCT, non-randomized studies, RWD) **would be accepted in different arms of ITC/relative effectiveness assessment by HTA body/payers** in your country? Please consider the credibility of the data source and rate on a scale from 1 to 7 (1=not accepted/low credibility; 7=high acceptance/credibility) and provide your rationale.   
   Would acceptance of these study types improve on a case-by-case basis under certain conditions, and which would these be (e.g., if unfeasible/unethical to undertake comparative study in rare/orphan conditions, for breakthrough therapies and conditions of high unmet medical need, where the evidence base is limited)?  
   Is there preference for data source being similar across treatment arms within an indirect comparison?

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| Data source accepted for ITC | Acceptance/credibility level  (1-7 scale; 1=not accepted, 7=highly accepted) | Rationale for top-3 most acceptable data types |
| **Placebo-controlled randomized controlled trials (RCTs)** | Select one: 1= not accepted/low credibility 2 3 4= moderate acceptance/credibility 5 6 7= high acceptance/credibility | Open text [please provide rationale for top-3 data sources] |
| **Active control RCTs** | Select one [1-7] |
| **Non-randomized trials** | Select one [1-7] |
| **Single-arm trials** | Select one [1-7] |
| **Pragmatic clinical trials** | Select one [1-7] |
| **Observational trials** | Select one [1-7] |
| **Real world data (RWD) studies for external comparator arm** | | |
| **RWD – electronic health records/medical charts** | Select one [1-7] | Open text [please provide rationale for top-3 RWD] |
| **RWD – patient registries** | Select one [1-7] |
| **RWD – natural history study/prospective observational** | Select one [1-7] |
| **RWD – administrative claims data** | Select one [1-7] |
| **Other (please describe in rationale box)** | Select one [1-7] (*optional*) | Open text [optional] |

**Comment box**: Is there preference for data source being similar across treatment arms within an indirect comparison? For example, RCT data for one treatment vs. Pragmatic trial data for the second treatment vs. RWD from patient registries for the third treatment OR is consistency across data sources desired within an indirect comparison?

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| Open text [mandatory] |

1. Regarding the **selection of relevant treatment comparators for ITC**, is this based on specific guidance (e.g., national guidelines) and which international/national/**[European]** EUnetHTA guidelines prescribe the selection of relevant treatment comparator in your country?   
   Are you aware if these documents follow the current methodological best-practices to conduct indirect-treatment comparisons (e.g., ISPOR)?

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| Question | Response | Rationale |
| **Is selection of relevant comparator therapies for ITC by HTA body/payers in your country based on specific guidance?** | Select one: Yes, national clinical guidelines Yes, global/regional clinical guidelines Yes, national methodological guidelines Yes, global/regional methodological guidelines Yes, based on practice patterns in country No Other (please describe in rationale) | Open text [mandatory] |
| **Which guidelines/best practice documents prescribe selection of relevant comparators in your country?** | Open text [Please list the name of the relevant rules that apply in your country/organization] | **–** |

**Comment box**: Are you aware if documents, used in your country to provide guidance for the selection of the relevant treatment comparator for ITC, follow the latest methodological best-practices (e.g., ISPOR)?

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| Open text [mandatory] |

1. On the selection of relevant treatment comparators for ITC, **would payers in your country consider the inclusion of studies with therapies that do not have a marketing authorization** (i.e., off-label use) **or that are not covered/reimbursed** in the target indication, although it is considered the standard of care (SoC) in clinical guidelines? Please provide your rationale and if accepted under what circumstances.

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| Question | Response | Rationale |
| **Would payers in your country accept/require an ITC that includes a comparator without a regulatory label or not reimbursed although it may be the clinical standard of care in the studied indication?** | Select one: Yes Yes, conditionally No | Open text [mandatory] |

1. What **endpoints/outcomes are relevant for the HTA body/payers** in your country to assess the magnitude of treatment effects with ITCs (e.g., efficacy, safety, PRO/HRQoL,)? Please rate on a scale from 1 to 7 (1=not relevant; 7=very relevant) and provide your rationale.  
   Note for safety outcomes: The PRO-CTCAE is a patient-reported outcome (PRO) measurement system developed to evaluate symptomatic toxicity in patients on cancer clinical trials. It was designed to be used as a companion to the Common Terminology Criteria for Adverse Events (CTCAE)

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| Outcomes assessed with ITC | Relevance for payer decision-making | Rationale |
| **Efficacy – time-to-event outcomes (e.g., survival)** | Select one: 1= not relevant 2 3 4= moderately relevant 5 6 7= highly relevant | Open text [please provide rationale for most relevant efficacy outcomes in ITC] |
| **Efficacy – response rates (e.g., ORR)** | Select one [1-7] |
| **Efficacy – surrogate endpoints (e.g., progression-free survival, based on biomarker)** | Select one [1-7] |
| **Safety – discontinuation rate** | Select one [1-7] | Open text [please provide rationale for most relevant safety outcomes in ITC] |
| **Safety – physician reported grade ≥3 AE rate** | Select one [1-7] |
| **Safety – patient reported AEs (e.g., PRO-CTCAE)** | Select one [1-7] |
| **Health-related quality of life (HRQoL)** | Select one [1-7] | Open text [mandatory] |

**Comment box**: Please comment whether results from primary vs. secondary endpoints (i.e., results are statistically significant or not) are equally relevant for ITC in your country.

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| Open text [mandatory] |

## Section 2: Methods and data analytics for indirect treatment comparisons

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|  | *In this section the research seeks to understand the acceptability of different methods and data analytics accepted by HTA bodies/payers in your country for the implementation of indirect treatment comparisons that inform P&R/coverage decisions. Please review the background information before progressing to the following questions* |
|  | *Please review the below definitions before answering the next question:*  **Definitions:**   * **Indirect comparison:** A comparison of two different healthcare interventions that have not been directly compared with each other in a head-to-head trial, using summary level data only from separate studies. * **Network Meta-Analysis (NMA):** A technique for comparison of three or more interventions simultaneously in a single analysis. * **Anchored meta-analysis:**  Anchored indirect comparison is considered when connected evidence with a common comparator is available (i.e., two healthcare interventions compared against the same standard of care). * **Unanchored meta-analysis:** Unanchored comparisons is only considered where single-arm studies are involved, or in the absence of a connected network of randomized evidence. * **Matching-adjusted indirect comparison (MAIC):** A technique using individual patient data (IPD) from trials of one treatment to match baseline summary statistics reported from trials of another treatment, and in some instances summary level data are also used in anchored analysis, to compare treatment outcomes across balanced trial populations. * **Simulated treatment comparison (STC):** A technique that involves estimating a linear regression model for the relationship between population characteristics and outcomes in a trial, where IPD is available, and then using the model to estimate that outcome for the other trial population; in some instances, summary level data are also used in anchored analysis. * **Propensity Score Matching and (re)Weighing (PSM/PSW):** A statistical technique that attempts to estimate the effect of a healthcare intervention by matching patients, with IPD only, from different treatments on characteristics that predict treatment. |

1. What is the **level of acceptance of different indirect comparison methods for HTA/payer decision-making** across therapy areas in your country/organization? Please provide your rationale and indicate under what circumstances each method would be more/less appropriate.

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| Indirect comparison type | Acceptance of method for HTA/payer decision-making | Rationale and circumstances where this type of indirect comparison is appropriate |
| **NMA** | Select one: Yes Yes under conditions No Not familiar with this method | Open text [mandatory] |
| **MAIC** | Select one: Yes Yes under conditions No Not familiar with this method | Open text [mandatory] |
| **STC** | Select one: Yes Yes under conditions No Not familiar with this method | Open text [mandatory] |
| **Other types (please describe in text box; e.g., Propensity Score Matching)** | Select one: Yes Yes under conditions No Not familiar with this method | Open text [mandatory] |

**Comment box**: Are you aware if any of these method(s) are recommended or not by the HTA body/payer assessors in your country?

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| Open text [mandatory] |

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|  | Please review the following definitions of study types before responding to the following question:   * **Anchored meta-analysis:**  Anchored indirect comparison is considered when connected evidence with a common comparator is available (i.e., two healthcare interventions compared against the same standard of care). * **Unanchored meta-analysis:** Unanchored comparisons is only considered where single-arm studies are involved, or in the absence of a connected network of randomized evidence. * **Matching-adjusted indirect comparison (MAIC):** A technique using individual patient data (IPD) from trials of one treatment to match baseline summary statistics reported from trials of another treatment, and in some instances summary level data are also used in anchored analysis, to compare treatment outcomes across balanced trial populations. * **Simulated treatment comparison (STC):** A technique that involves estimating a linear regression model for the relationship between population characteristics and outcomes in a trial, where IPD is available, and then using the model to estimate that outcome for the other trial population; in some instances summary level data are also used in anchored analysis. * **Propensity Score Matching and (re)Weighing (PSM/PSW):** A statistical technique that attempts to estimate the effect of a healthcare intervention by matching patients, with IPD only, from different treatments on characteristics that predict treatment. |

1. **In a scenario, when there is no common comparator, would you accept an unanchored ITC in your country/organization, why or why not**?

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| Open text [mandatory] |

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|  | *Please consider the following methodological guidelines before responding to the following question:*   * **ISPOR Good Practices Reports in ITC** (Report 1 [https://www.ispor.org/heor-resources/good-practices/article/interpreting-indirect-treatment-comparisons-and-network-meta-analysis-for-health-care-decision-making], Report 2 [https://www.ispor.org/heor-resources/good-practices/article/conducting-indirect-treatment-comparison-and-network-meta-analysis-studies], Report 3 [https://www.ispor.org/heor-resources/good-practices/article/indirect-treatment-comparison-network-meta-analysis-study-questionnaire-to-assess-study-relevance-and-credibility-to-inform-healthcare-decision-making]) * **[Europe only]** **EUnetHTA Guideline: Direct and Indirect Comparisons**, February 2013 (<https://www.eunethta.eu/wp-content/uploads/2013/01/Direct-and-indirect-comparisons.pdf>) * **[US only]** **AMCP format for formulary submissions version v4.1 and Institute for Clinical and Economic Review (ICER) Methods & Processes** (<https://www.amcp.org/sites/default/files/2019-03/AMCP-Format-V4.pdf>) * **[AU only]** **Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) v5.0** and Indirect Comparisons Working Group (ICWG) report ( <https://pbac.pbs.gov.au/content/information/files/pbac-guidelines-version-5.pdf>) * **[FR only]** **HAS Methodological Guidance**: Choices in methods for economic evaluation (6 Apr 2020) (<https://www.has-sante.fr/upload/docs/application/pdf/2020-11/methodological_guidance_2020_-choices_in_methods_for_economic_evaluation.pdf>) * **[DE only]** **Dossier for the Benefit Assessment pursuant to Section 35a of the German Social Code Book Five** – Module 4 and IQWiG General Methods v 6.0 ( <https://www.iqwig.de/methoden/general-methods_version-6-0.pdf>) * **[UK only]** **NICE health technology evaluations: the manual**; process and methods (31 Jan 2022) (https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741) and NICE Decision Support Unit (DSU) Technical Support Document 18: Methods for population-adjusted indirect comparisons in submissions to NICE [add hyperlink: <https://research-information.bris.ac.uk/ws/portalfiles/portal/94868463/Population_adjustment_TSD_FINAL.pdf>) |

1. Are there **specific methodological guidelines from agencies that undertake ITC that payers in your country would accept for coverage/HTA decision making** of a new therapy, and what is the gold standard for ITC? Please select both national and international guidance and best-practices from the dropdown list.  
   **[add on for FR/DE/UK]** Do the EUnetHTA methodological guidelines for ITC/relative effectiveness assessment align with your country’s HTA methods and what changes do you anticipate following implementation of the Joint Clinical Assessments (JCA) at the European level?

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| Question | List of guidelines (please select all that apply) | Rationale and please list methodological guidelines/best-practices adopted in your country |
| **What methodological guidelines/best-practices are followed/adhered to by HTA body/payers in your country for evidence assessment in ITC?** | Select all that apply: ISPOR Good Practices Reports in ITC (Reports 1-3)  EUnetHTA Guideline: Direct and Indirect Comparisons, February 2013  **[US]** AMCP format for formulary submissions version v4.1 and Institute for Clinical and Economic Review (ICER) Methods & Processes  **[AU]** Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) v5.0 and Indirect Comparisons Working Group (ICWG) report  **[FR]** HAS Methodological Guidance: Choices in methods for economic evaluation (6 Apr 2020)  **[DE]** Dossier for the Benefit Assessment pursuant to Section 35a of the German Social Code Book Five – Module 4 and IQWiG General Methods v 6.0  **[UK]** NICE health technology evaluations: the manual; process and methods (31 Jan 2022)  **[UK]** NICE Decision Support Unit (DSU) Technical Support Document 18: Methods for population-adjusted indirect comparisons in submissions to NICE Other (please report in rationale box) | Open text [mandatory] |

**Comment box**: Do the **EUnetHTA methodological guidelines for ITC/relative effectiveness assessment align with your country’s HTA** methods and what changes do you anticipate following implementation of the Joint Clinical Assessments (JCA) at the European level?

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| Open text [mandatory] |

1. Considering published guidelines and best practices in your country/organization for ITC (e.g., ***select all that apply per country*** *ISPOR Good Practices Reports in ITC, [****FR,DE,UK****] EUnetHTA Guideline: Direct and Indirect Report, [****US****] AMCP format for formulary submissions version v4.1 and Institute for Clinical and Economic Review (ICER) Methods & Processes, [****AU****] Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (PBAC) v5.0 and Indirect Comparisons Working Group (ICWG) report, [****FR****] HAS Methodological Guidance: Choices in methods for economic evaluation (6 Apr 2020), [****DE****] Dossier for the Benefit Assessment pursuant to Section 35a of the German Social Code Book Five – Module 4 and IQWiG General Methods v 6.0, [****UK****]* *NICE health technology evaluations: the manual; process and methods (31 Jan 2022) and NICE Decision Support Unit (DSU) Technical Support Document 18: Methods for population-adjusted indirect comparisons in submissions to NICE*) do you perceive that the currently accepted method(s)/statistical modelling approach(es) used by HTA body/payers in your country/organization:
2. sufficiently include key/state-of-the-art indirect comparison methods (e.g. MAIC or STC)?
3. provide detailed guidance on the use of observational or non-randomized trials?
4. clearly define when to employ qualitative versus quantitative summaries of data?
5. provide sufficient guidance to account for heterogeneity (e.g., meta-regression approach)?  
   Please provide your rationale for each sub-question.

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| Question | Response | Rationale |
| 1. **Do the accepted and used methods/approaches in your country sufficiently include key/state-of-the-art indirect comparison methods?** | Select one Yes No | Open text [mandatory: Please describe which methods you consider as state-of-the-art] |
| 1. **Do the accepted and used methods/approaches in your country provide detailed guidance on the use of observational or non-randomized trials?** | Select one Yes No | Open text [mandatory] |
| 1. **Do the accepted and used methods/approaches in your country provide sufficient guidance to account for heterogeneity?** | Select one Yes Yes, conditionally No | Open text [mandatory] |

## Section 3: Acceptability of indirect treatment comparison results

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|  | *In this section the research seeks to understand the acceptability of indirect treatment comparison results (e.g., consistency, transparency, and confidence intervals) and their acceptance by HTA bodies/payers in your country for P&R/coverage decisions. Please review the background information before progressing to the following questions* |

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|  | *Please consider the following methodological guidelines and definitions before responding to the following question:*   * Preferred Reporting Items for Systematic Reviews and Meta‐Analyses–Network Meta‐Analysis (**PRISMA**): an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses; PRISMA primarily focuses on the reporting of reviews evaluating the effects of interventions (Moher D, et al. PLoS Med. 2009 Jul 21;6(7):e1000097; add hyperlink: <http://www.prisma-statement.org/documents/PRISMA_2020_checklist.docx>) * The validity of an evidence base according to the ISPOR -AMCP-NPC Good Practice Task Force Report on ITC/NMA relevance and credibility [add hyperlink: <https://www.ispor.org/docs/default-source/resources/outcomes-research-guidelines-index/relevanceofnetworkmeta-analysisforhcdecisions4.pdf?sfvrsn=fc72e927_0>] is assessed based on **inclusion of all relevant RCT**, feasibility to **construct a network**, **exclusion of poor quality studies** bias that introduce bias, and **avoidance of systematic differences in treatment effect** modifiers (i.e., baseline patient or study characteristics that have an impact on the treatment effects) across the different treatment comparisons in the network. |

1. Please indicate the **prioritization of listed criteria** (i.e., critical, valuable, nice-to-have or not applicable; see definitions below) **to demonstrate ITC results of high quality/credibility that are impactful and relevant for payer decision-making in your country**. Please provide your rationale for the top-5 most critical/valuable criteria to ensure high quality and credible ITC results.  
   ***Definitions*:**

* **Critical**: criterion must be fulfilled for demonstration of high quality and credible ITC results; without this criterion, the ITC results are perceived to be of low quality and credibility
* **Valuable**: important but not vital criterion to demonstrate high quality and credibility of results
* **Nice-to-have**: a desirable but necessary criterion to demonstrate high quality and credibility of ITC results

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| Quality/credibility criterion | Prioritization for high quality/credibility of ITC results | Comment box: please provide your rationale on the top-5 most critical |
| **Evidence base and methods used for ITCs *(****See definitions above)* | Select one: Critical Valuable Nice-to-have Not applicable/do not know | Open text [mandatory] |
| **Quality of included studies** | Select one: [as above list] |
| **Adjustment of effect modifiers** | Select one: [as above list] |
| **Appropriate hazard ratio and confidence intervals** | Select one: [as above list] |
| **Consistency between direct and indirect evidence** | Select one: [as above list] |
| **Assessment of heterogeneity (e.g., in patient, trial or study characteristics)** | Select one: [as above list] |
| **Quality of reporting (e.g., adherence to PRISMA‐NMA)** | Select one: [as above list] |
| **Conflict of interest (e.g., sponsor of ITC)** | Select one: [as above list] |
| **Other (please report on comment box)** | Select one: [as above list] |

1. Is there any difference in the **impact of ITCs for payer decision-making depending on who sponsored or funded the analysis** (e.g., pharmaceutical companies vs. academia vs. HTA body)? Please rank the stakeholders in order of preference and provide your rationale.

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| Sponsor/funder of ITC | Please select if evidence provided from this sponsor is impactful for payer-decisions | How would you rank the agency in the impact it has on your decision making? (assign a unique rank order per row) | Rationale |
| **Pharmaceutical company/industry** | Select one: Yes Yes, conditionally No | Select one: Ranked 1st Ranked 2nd  Ranked 3rd | Open text [mandatory] |
| **Academic institution** | Select one: Yes No | Select one: Ranked 1st Ranked 2nd  Ranked 3rd | Open text [mandatory] |
| **HTA body** | Select one: Yes No | Select one: Ranked 1st Ranked 2nd  Ranked 3rd | Open text [mandatory] |

**Comment box**: If an ITC study is sponsored by a pharmaceutical company, but conducted and published from an academic institution, how would this change the impact of the study for payer decision-making?

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| Open text [mandatory] |

1. Please review the following **hypothetical reference cases in oncology** and indicate if ITC would be accepted for HTA/payer decision-making in your country:

* **Case 1**: Small molecule oral therapy studied with single-arm trial for small population size (orphan indication) that targets a specific biomarker (i.e., first in class with new mechanism of action). There are no clinical trials on the target indication, so an external comparator arm needs to be established.
* **Case 2**: A biologic therapy for cancer with high prevalence studied with an RCT and a comparator that is no longer the standard of care, with marginal clinical benefit but signals of improved efficacy in certain subgroups. Key comparators have been approved based on single arm trials, and manufacturer anticipates cross-trial differences between their product and comparator therapies.
* **Case 3**: A breakthrough cell & gene therapy (high-cost and potentially curative), studied in a single-arm open label trial for a narrow patient population in the last line setting (i.e., no treatment options only best supportive care [BSC]). There are available clinical trials of the historical standard of care in the target indication.

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| Hypothetical reference case | Acceptance of ITC for the comparative assessment of product | Data sources that will likely be accepted for ITC | Methods that will likely be accepted for ITC | Rationale for expected preference for study type(s)/method(s) |
| **Case 1:** Small molecule oral therapy studied with single-arm trial for small population (orphan indication) that targets a specific biomarker (i.e., first in class with new mechanism of action) | Select one: Yes Yes, conditionally No | Select all that apply: Non-randomized trials Single-arm trials Pragmatic clinical trials Observational trials RWD patient registries RWD EHR/chart review RWD natural history study RWD administrative claims data Other (please describe in rationale box) | Select all that apply: NMA MAIC STC Other (describe in rationale) | Open text [mandatory] |
| **Case 2:** A biologic therapy for cancer with high prevalence studied with an RCT and a comparator that is no longer the standard of care, with marginal clinical benefit but signals of improved efficacy in certain subgroups | Select one: Yes Yes, conditionally No | Select all that apply: RCTs Active control RCTs Non-randomized trials Single-arm trials Pragmatic clinical trials Observational trials RWD patient registries RWD EHR/chart review RWD natural history study RWD administrative claims data Other (please describe in rationale box) | Select all that apply: NMA  MAIC STC Other (describe in rationale) | Open text [mandatory] |
| **Case 3:** A breakthrough cell&gene therapy (high-cost and potentially curative), studied in a single-arm open label trial for a narrow patient population in the last line setting (i.e., no treatment options only BSC) | Select one: Yes Yes, conditionally No | Select all that apply:   Non-randomized trials Single-arm trials Pragmatic clinical trials Observational trials RWD patient registries RWD EHR/chart review RWD natural history study RWD administrative claims data Other (please describe in rationale box) | Select all that apply: NMA  MAIC STC Other (describe in rationale) | Open text [mandatory] |

1. Considering the **role of indirect comparison for payer decision-making**  (e.g., **[Ex-US]** reimbursement, pricing negotiation **/ [US]** coverage and placement in clinical pathway), please indicate on a scale from 1 to 7 (i.e., 1= not impactful at all and 7= very impactful) how impactful it can be for a positive **[Ex-US]** HTA/P&R **/ [US]** coverage and/or pathway placement outcome across therapy areas and specifically in oncology. Please provide your rationale.

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|  | Impact of indirect comparison for positive [Ex-US] HTA/P&R /[US] coverage | [US only] Impact of indirect comparison for positive pathway placement | Rationale |
| **Use of indirect comparison for payer-decision making in all therapy areas** | Select one: 1= not impactful 2 3 4= moderately impactful 5 6 7= highly impactful | Select one: 1= not impactful 2 3 4= moderately impactful 5 6 7= highly impactful | Open text [mandatory] |
| **Use of indirect comparison for payer-decision making in oncology** | Select one: 1= not impactful 2 3 4= moderately impactful 5 6 7= highly impactful | Select one: 1= not impactful 2 3 4= moderately impactful 5 6 7= highly impactful | Open text [mandatory] |

1. From your experience, please **provide example(s)/use case(s) where indirect comparison was accepted and positively impacted payer decision for an oncology therapy** in your country/organization (e.g., **[Ex-US]** reimbursement, pricing negotiation **/ [US]** coverage and placement in clinical pathway) (e.g., [DE-only] nivolumab in adjuvant melanoma and acceptance of adjusted indirect comparison for its re-assessment by the G-BA) and **example(s)/use case(s) where indirect comparison was not accepted and criticized**. Please indicate what was impacted by the ITC and the reasons for acceptance/rejection of the relevant evidence

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| --- | --- | --- | --- |
| Question | Examples/use cases (i.e., products and conditions) in your country/organization | Impact of indirect comparison on: (select all that apply) | Reasons for acceptance/rejection of indirect comparison |
| **Provide example(s)/use case(s) where an indirect comparison analysis had a positive impact on [Ex-US]** **reimbursement, pricing negotiation** **/ [US]** **coverage and placement in clinical pathway and was accepted by payers** | Open text [mandatory] | Select all that apply: HTA reimbursement pricing formulary coverage  **[US only]** clinical pathway Other (provide details in free-text box) | Open text [mandatory] |
| **Provide example(s)/use case(s) where an indirect comparison analysis was criticized and not accepted/rejected for payer decision-making** | Open text [mandatory] | **–** | Open text [mandatory] |

**END OF SURVEY**