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# Lung Cancer Health Technology Assessment Trends in Argentina, Brazil, Colombia and Mexico

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## Introduction

Lung cancer is a major public health issue in Latin America due to its high prevalence, being the leading cause of cancer-related deaths in some countries within the region, such as Argentina and Brazil[1,2], and the projected increase in lung cancer fatalities is poised to double by 2030 (3). Lung cancer can be categorized into two primary types: Non-Small Cell Lung Cancer (NSCLC), which accounts for approximately 80% of new cases, and Small Cell Lung Cancer, which comprises roughly 20% of cases[4]

Despite innovative oncology medicines becoming available, Latin American countries have not been able to adopt them widely, timely, and equally for all patients, leading to significant differences in health outcomes[2]. Some of these challenges have been reflected in how health technology assessment (HTA) processes inform decision-making in Latin America: HTA and decisions on the same or similar oncology drugs may vary among HTA bodies; factors influencing such variation have not been fully explored. Furthermore, even with HTA agencies issuing positive recommendations for novel therapies, those might not translate into timely access for patients, This also represents a challenge for medicines producers, who lack predictability on how the evidence submitted will translate into HTA and reimbursement outcomes[5]

## Objectives

This study aims to identify trends in evaluation frameworks and decision-making in NSCLC across HTA agencies in Argentina, Brazil, Colombia, and Mexico to understand where opportunities lie for HTA to fully support equitable patient access to innovation in lung cancer in Latin America, including:

- Mapping of similarities and differences in evaluation frameworks and decision-making criteria across agencies
- Identification of key organizations influencing HTA decisions and policy-making across selected HTA agencies, (eg., patients, medical societies, etc)
- Mapping of evolving HTA paradigms, including innovative methods being incorporated in the HTA processes
- Identification external factors influencing HTA outcomes, reimbursement decisions and budget allocation in NSCLC

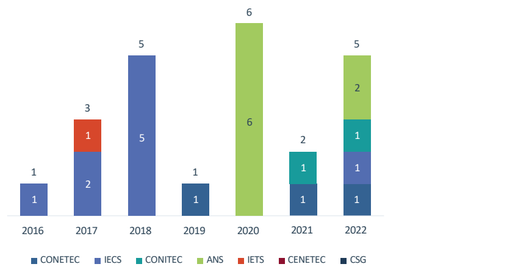
## Methods

Pragmatic literature review to identify HTA reports published from January 01, 2016, to November 01, 2022, assessing any NSCLC technologies by at least one of the key HTA bodies in Latin America.

The literature review was conducted in the following databases: Biblioteca Virtual en Salud, PubMed, Lilacs, EMBASE, and supplemented by a manual search to retrieve HTA reports and reimbursement data directly from the agencies' websites.

## Results

### Figure 1. Published Reports (2016 – 2022) Across HTA Agencies




In relation to the source of reports, 12 were from Argentina (3 CONETEC; 9 IECS); 10 from Brazil (CONITEC 2, ANS 8), and a single IETS report assessing the budget impact of 21 chemotherapies in multiple cancers (including lung) was retrieved from Colombia, and although technically not considered an HTA report, is relevant for the discussion and was therefore included. No published HTA reports were identified from Mexico.

5 technologies received a positive recommendation (all in Brazil), while 7 were issued a negative recommendation (5 in Brazil, 2 in Argentina). Additionally, 3 technologies had their coverage conditioned to meeting certain criteria such as price renegotiation (all by CONETEC), while 8 technologies received no recommendation due to a lack of data available to inform a decision.

The transparency of reimbursement decisions remains a challenge. This is evident from the scarcity of publicly accessible reports detailing the medications covered and the disparities between non-binding HTA recommendations and the drugs listed on formularies.

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### Figure 2 | HTA Outcomes for Targeted Lung Cancer Therapies* by HTA Agency

| TARGET BIOMARKER | THERAPY | CONETEC (ARG) | IECS (ARG) | CONITEC (BRA) | ANS (BRA) | IETS (COL) | CENETEC (MEX) | CSG (MEX) |
|---|---|---|---|---|---|---|---|---|
| PD-1/PD-L1 | Atezolizumab | | No recommendation provided | | N/A (mandatory coverage) | | | |
| | Durvalumab | Contingent on price negotiation | | | N/A (mandatory coverage) | | | |
| | Nivolumab | Contingent on price negotiation | No recommendation provided | | N/A (mandatory coverage) | | | |
| | Pembrolizumab | Contingent on price negotiation | No recommendation provided (2x) | | N/A (mandatory coverage) | | | |
| ALK | Alectinib | | | | | | | |
| | Brigatinib | | | | | | | |
| | Ceritinib | | No recommendation provided | | | | | |
| | Lorlatinib | | | | | | | |
| ALK/ROS-1 | Crizotinib | | | | | | | |
| EGFR/EGFR T790M | Osimertinib | | No recommendation provided | | Exon 19/21; EGFR T790M | | | |
| NTRK | Larotrectinib | | | | | | | |
| Others | Afatinib | | | | | | | |
| | Nintedanib | | No recommendation provided | | 2L (after chemotherapy) | | | |

Positive Recommendation | Conditional Recommendation | No recommendation provided | Negative Recommendation | Not Assessed/Not publicly available | No Regulatory Approval

*This analysis was focused on the **13 targeted therapies** (20 total reports), therefore the other 3 studies (**SBRT, PET-CT, and BI for various CTs**) were **not considered***

### Figure 3 | HTA Agencies Alignment with ISPOR's Best Practices in HTA

| | | | | |
|---|---|---|---|---|
| ARG | CONETEC | Clear and defined structure, objectives, and prioritization process | Clear assessment framework | Clear context of results, including stakeholder perception/other HTAs | Recommendations on how to fund the new technologies (non-binding) |
| ARG | IECS | Process, while structured, is driven by submissions of a small network | Does not conduct a BIA/CEA | Clear context of results, with limited external stakeholder involvement | No regular re-assessment, undefined recommendations (non-binding) |
| BRA | Conitec | Clear and defined structure, objectives and process | Clear assessment framework | Clear context of results, including stakeholder perception/other HTAs | Provides coverage recommendations (binding), with possible reassessment |
| BRA | ANS | Clear and defined structure, objectives and HTA process | Clear assessment framework; not published in peer-reviewed journals | Clear context of results, with limited external stakeholder involvement | Provides coverage recommendations (binding), with possible reassessment |
| COL | IETS | No publicly available HTA publications<br>Budget impact analysis for 21 chemotherapies | | | |
| MEX | Cenetec | No publicly available HTA publications<br>Clinical practice guideline to guide treatment prescription | | | |
| MEX | CSG | No publicly available HTA publications* | | | |

Level of Alignment with ISPOR's Best Practices in HTA: LOW ■■■■■ HIGH

Reports published were evaluated utilizing ISPOR's report on good practices in HTA[6], and Argentina and Brazil demonstrated similarity across some domains of the checklist, which are described in **Figure 3**:

- In Brazil, CONITEC has a structured HTA process[7], with an established role of HTA in the country. The assessment framework is well-defined and consistent throughout reports while also allowing for the participation of external stakeholders (eg., medical societies, manufacturers, etc) in the evaluation process. ANS follows a similar evaluation process to CONITEC, with binding decisions applicable to the private sector
- In Argentina, while CONETEC also demonstrated similar robustness in terms of HTA processes with its value framework[8], the main difference compared to CONITEC lies in the implementation of HTA recommendations: CONITEC's outcomes are binding, while CONETEC's are not and only provide guidance for authorities' decision-making
- In Colombia[9] and Mexico[10], although the relevant local agencies have published HTA guidelines, it was not possible to evaluate the level of adherence of the respective agencies to ISPOR's best practices framework given the lack of publicly available reports on lung cancer
- HTA reports were generally published several years after the initial regulatory approval of each technology (28-63 months), and submissions were mostly driven by manufacturers.

### Figure 4 | Key Decision Drivers for Lung Cancer HTA Across Assessed Agencies

**Positive Decision Drivers**

**Unmet Needs & Therapeutic Benefit:** technologies focused on disease spaces with large unmet needs and/or clinical benefit are key drivers for incorporation, especially if there is public awareness

**Quality of Evidence:** evidence provided (e.g., clinical and economic, trial design, comparator selection) are strong value drivers for HTA agencies in their decision-making

**Economic Analyses:** cost-effectiveness and cost-utility are key drivers in HTA for some countries; with CONITEC establishing official CE thresholds, cost analyses are likely to become even more important to decision-making

**External Stakeholders Influence:** limited impact in decision-making currently; as stakeholders gain more relevance in discussions, however, influence on final decisions is likely to increase

**Negative Decision Drivers**

X **Budget Impact:** even if robust evidence is provided, the budget impact is the biggest hurdle to incorporation in analyzed HTAs, especially when considering the economic scenario/challenges within the region

X **Risk of Bias:** study limitations included in HTA submissions (GRADE*) are common value detractors, and while not as impactful as budget impact, are also key negative drivers

HTA outcomes in Latin America are highly driven by economic variables, and budget impact is often the key element in regional studies for decision-making, typically leading to negative decisions. On the other hand, the main positive driver is the therapeutic benefit provided by the evaluated technology and how it addresses current unmet needs.

Other relevant drivers (positive or negative) for decision-making among regional HTA agencies are presented in **Figure 4**.

## Discussion & Conclusion

### Discussion

- Between 2016 and 2022, HTA processes in Latin America presented significant disparities in terms of number of publicly available reports, time of assessment, key recommendation drivers, stakeholder involvement and impact on decision making for each HTA agency
- Only in Brazil HTA recommendations provided by agencies are binding, with CONITEC and ANS recommendations being applicable to the public and private sectors, respectively. In Argentina, though CONETEC and IECS recommendations are non-binding, NSCLC is included among the priority diseases in the Sistema Único de Reintegros por Gestión de Enfermedades (SURGE)[11], providing coverage to the overall population on a disease-based scheme via social security
- Data transparency is a key area of focus of the assessed HTA bodies, which aim to have clearer decision-making processes for the overall population, including allowing for external participation of stakeholders, such as patient advocacy groups (PAGs), medical societies, manufacturers, and others. Coordinating efforts to follow international best practices should also be incentivized, as these would also lead to more informed and balanced HTA decisions

### Conclusion

- Limited publicly available HTA reports on lung cancer have been identified in Argentina and Brazil, with mostly (78%) negative or no recommendation provided.
- Mexico and Colombia did not publish their assessments.
- Agencies in scope showcase a significant disparity in terms of the number of publicly available reports, time of assessment, key drivers of recommendations, stakeholder involvement and impact on decision making.
- Sharing information, involving stakeholders, and making documents publicly available can improve transparency, align data expectations, and allow for feasible submissions.

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