

# Use of single arms studies for Health Technology Assessment in Portugal

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## BACKGROUND AND OBJECTIVES

### BACKGROUND

- **Randomized controlled trials (RCTs) are considered the gold standard** to determine the efficacy of a new therapy or to evaluate its comparative effectiveness against standard of care. [1]
- However, regulators acknowledge situations where a RCT may not be operationally or ethically feasible, such as in rare disease patient populations. In such cases, data from **single arm trials**, namely phase I/II clinical trials, **complemented by external control arms are sometimes accepted** as evidence by both Regulatory and Health Technology Assessment (HTA) bodies. [1-2]
- This study aims to explore trends in HTA evaluations that use this type of evidence in Portugal and compare it to other European countries.

### OBJECTIVES

- Analyze **trends** in the number of medicinal products with phase I/II clinical trial data used in HTA processes in Portugal.
- Describe the **overall differences** between Portugal and other European countries in regards to overlapping medicinal products HTA decisions.

## METHODS

- **HTA reports publicly available** at the **Portuguese Health Authority database**[3] were reviewed covering **January 2017 to April 2022**.
- The Platform **“NAVLIN Price & Access Data by EVERSANA®”**[4] was used to extract data on **overlapping medicinal products** with available information on HTA processes in **other European countries**.
- To complement the analyzes a **literature review** was also made regarding information on other European countries HTA decisions.
- Existing Portuguese HTA processes with phase I/II clinical trial data as the highest level of clinical evidence for which a final recommendation was issued were documented.
- HTA published decisions for the same medicinal products and indications in other European countries were identified and documented when available.
- Descriptive analysis was applied for each entry in order to extract number of decisions, therapeutic area, time until decision and the clinical trial phase.
- A comparative analysis was made in order to evaluate the average time until the decision between overlapping medicinal products/indications.

## CONCLUSIONS

- There was a **growing trend** in Portugal for HTA **submissions using phase I/II clinical trial data** as the highest level of clinical evidence from 2018 to 2021.
- All **oncology indications** analyzed received **positive reimbursement** approvals, even with the quality of the evidence being deemed as mostly low to very low. This could be due to a **significant unmet need** in cancer indications.
- Overall, for the same medicinal products/indications evaluated, Portugal tends to present **longer times of evaluation** but appears to **have more positive decisions than some other countries**.

## MAIN LIMITATIONS

- The primary data source was the public information in websites of HTA agencies. In some cases HTA decisions were not available.
- Time to reimbursement decision assumes time from the date of the Marketing Authorization until the reimbursement decision date.
- The number of processes analyzed was scarce. The inclusion of more HTA evaluations over time may vary the results obtained.

## REFERENCES

[1] Hariton E, Locascio JJ. Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials. BJOG. 2018 Dec;125(13):1716.  
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[12] List of the decisions on the reimbursement processes." ZIN's website, 1 Apr. 2022, <https://english.zorginstituutnederland.nl/about-us/tasks-of-the-national-health-care-institute/assessment-of-outpatient-medicines-for-the-benefit-of-the-medicine-reimbursement-system-gvs>  
[13] List of the decisions on the reimbursement processes." SBU's website, 1 Apr. 2022, [www.sbu.se/en/publications2/](http://www.sbu.se/en/publications2/)

## RESULTS & DISCUSSION

- During the period evaluated, the first HTA decision in Portugal for a medicinal product with phase I/II clinical trial data was in 2018. Over time, there has been an increase in the number of such processes (Figure 1). [3]
- Of the **9 existing HTA processes, only 1 was not reimbursed** (ophthalmology) and the remaining 8, indicated for oncology diseases, had a positive reimbursement decision (Figure 2). Of these 8 decisions, 3 indications were in Lung Cancer, 3 in Lymphoma, 1 in Leukaemia and 1 in Skin Cancer. [3]
- **All decisions** that received a recommendation to Reimburse (8 out of 9) were classified by the HTA Body as having **“Non-quantifiable additional benefit”** and the quality of the evidence was either “Low” (6 out of 8) or “Very Low” (2 out of 8) with only 1 indication having evidence classified as “Moderate” (Figure 3). [3]

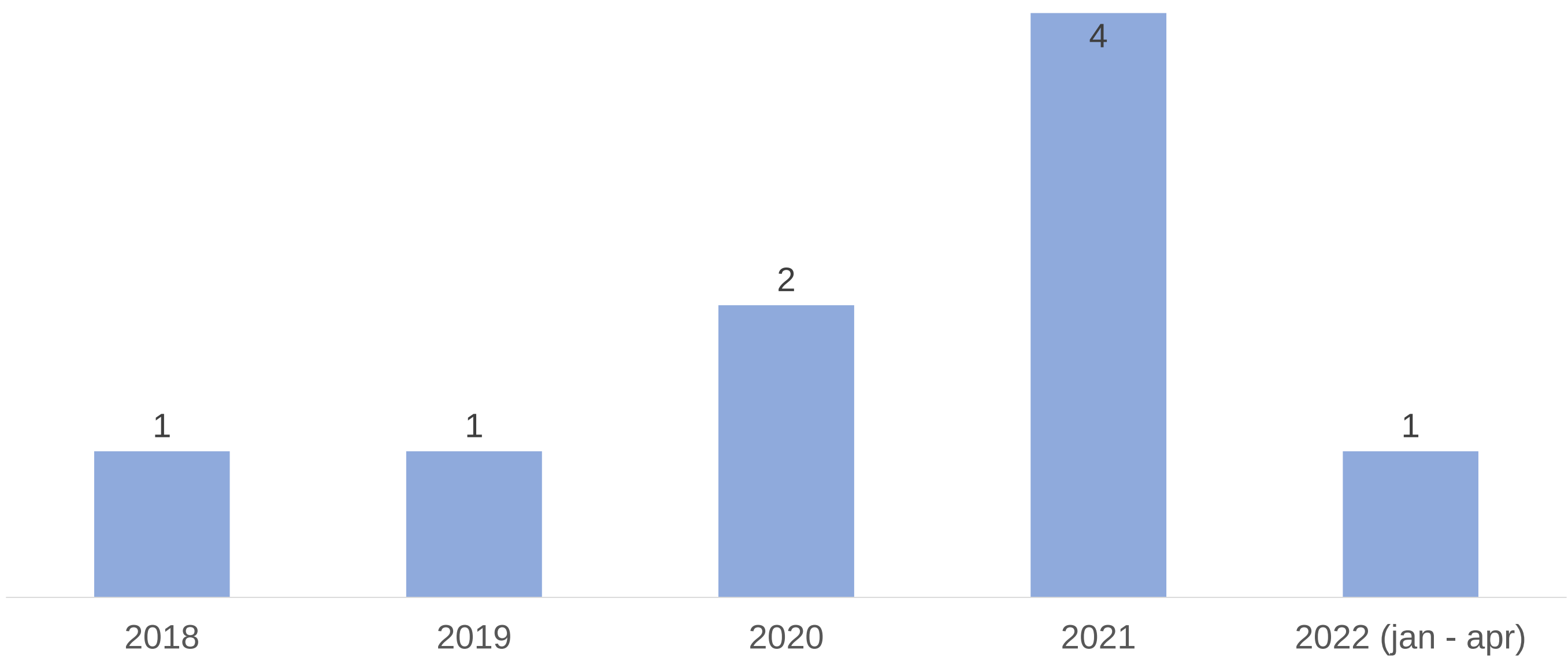
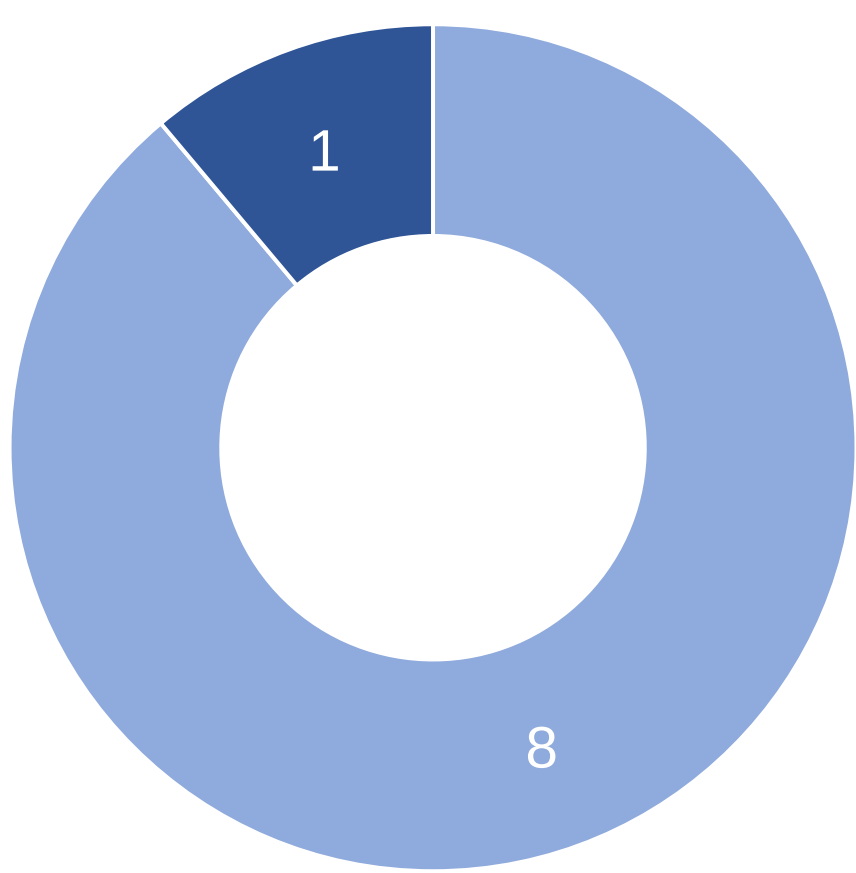


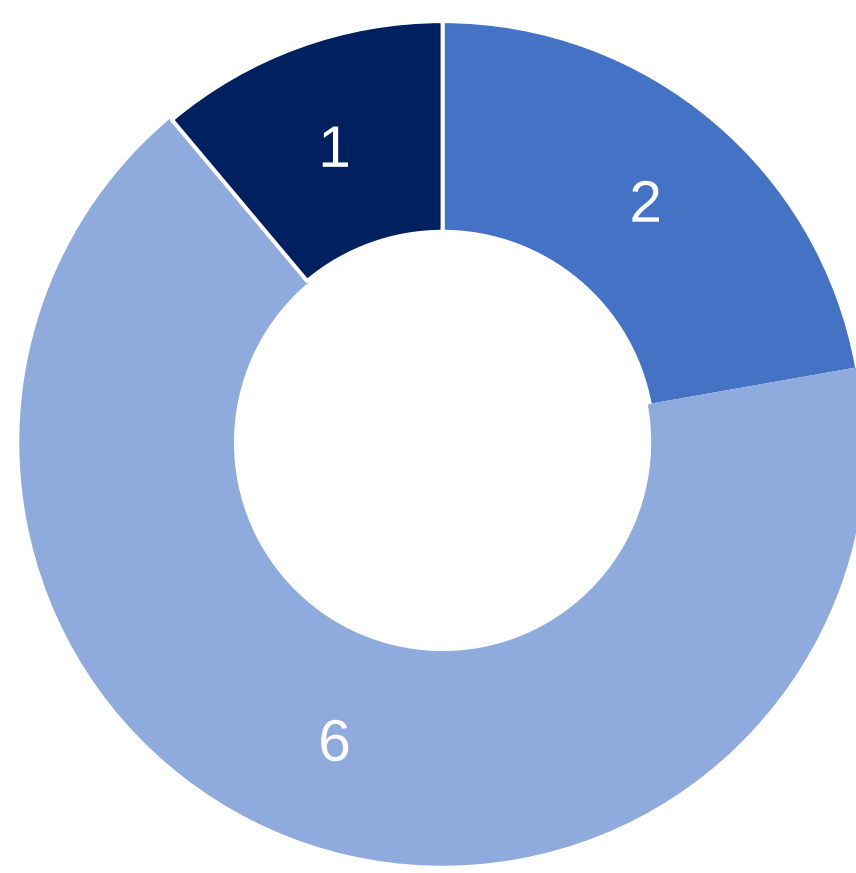
Figure 1. Number of HTA decisions for medicinal products presenting phase I/II clinical trials data in Portugal: 2018 – 2022 [3]

- Among the 9 decisions, 1 indication presented data from a phase 1 clinical trial, 6 presented data from a phase 2 clinical trial and 3 presented data from a phase 1/2 clinical trial. [3]
- The **average time until decision** for the **positive reimbursement** decisions (8 out of 9) was **33 months** (8 indications), ranging from 23 to 67 months. [3]
- The **average number of patients** involved in each trial was **133** (9 indications), with a population ranging from 68 to 210 patients included. [3]



■ Oncology ■ Ophthalmology

Figure 2. Portuguese HTA decisions by therapeutic area [3]



■ Very Low ■ Low ■ Moderate

Figure 3. Level of the quality of the evidence deemed by the Portuguese HTA agency [3]

- By **comparing** the HTA processes in Portugal with the **same medicinal products/indications** in **9 other European countries** - Germany, United Kingdom, France, Italy, Poland, Netherlands, Sweden, Poland and Spain - Portugal appears to **always have a longer time to reimbursement approval** aside from Poland (Table 1). [3-13]

Table 1. Comparison of the average time until positive reimbursement decisions for overlapping medicinal products & indications between Portugal and other European countries. [3-12]

| Country (number of overlapping processes) | Average time until positive reimbursement decision, months | Average time until positive reimbursement decision in Portugal, months |
|-------------------------------------------|------------------------------------------------------------|------------------------------------------------------------------------|
| United Kingdom (n=8)                      | 12                                                         | 33                                                                     |
| France (n=8)                              | 17                                                         | 33                                                                     |
| Germany (n=6)                             | 16                                                         | 31                                                                     |
| Italy (n=6)                               | 23                                                         | 31                                                                     |
| Scotland (n=6)                            | 11                                                         | 37                                                                     |
| Spain (n=4)                               | 13                                                         | 32                                                                     |
| Poland (n=2)                              | 40                                                         | 30                                                                     |
| Netherlands (n=2)                         | 4                                                          | 34                                                                     |
| Sweden (n=2)                              | 9                                                          | 30                                                                     |

- **3 therapeutic indications** had a **negative reimbursement decision in other countries but a positive decision in Portugal**. The countries where those indications were not reimbursed are the Netherlands (3 out of 3) , Poland (2 out of 3), Scotland (1 out of 3) and Sweden (1 out of 3). [3-12]
- The **reimbursement process in ophthalmology** that received a negative reimbursement decision in Portugal was reimbursed in Germany, France, Spain, Scotland, Poland and the Netherlands with an average time until positive reimbursement decision of 45 months, versus 42 months for a negative decision in Portugal. [3-12]