# REIMBURSEMENT PROCESS OF ORPHAN DRUGS IN THE CZECH REPUBLIC AFTER LEGISLATION CHANGE

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## Objectives

Specific reimbursement policy for Orphan medicinal products (OMPs) was adopted in January 2022 in the Czech Republic. The reimbursement policy is specified by Section 39da of the Act on Public Health Insurance. The aim of this study was to assess OMP reimbursement process after the legislation change with focus on administrative proceedings and pharmacoeconomic evaluations.

## Methods

Applications submitted and evaluated by the Czech HTA authority (State Institute for Drug Control) according to Section 39da of the Act on Public Health Insurance between 1 January 2022 and 23 May 2024 were identified. Applications with published decision report by the HTA authority were included in the analysis. Each decision report was reviewed, from which data relating to pharmacoeconomic analyses were extracted. Administrative proceedings were analysed in terms of timeliness and efficiency of the process. Descriptive statistics were used for data analysis. Costs were converted from Czech crowns (CZK) to Euros (EUR) using the cumulative exchange rate for 2024 (July-September) which was equal to 25.196 CZK/EUR.

## Results

15 administrative proceedings were identified in the specified period. Identified administrative proceedings are listed in **Table 1**. As shown in **Figure 1**, assessed OMPs in terms of reimbursement conditions most frequently focused on treatment of neurological diseases (n=5, 33.3%). Further, OMPs targeted hematologic disorders (n=3, 20.0%), solid tumours (n=2, 13.3%), cardiovascular diseases (n=2, 13.3%) as well as immune (n=1, 6.7%), pneumological (n=1, 6.7%), and musculoskeletal disorders (n=1, 6.7%). Compared to the therapeutic indications stated in summaries of product characteristics, approved reimbursement conditions were restrictive in vast majority of cases (12 out of 15, 80.0 %). OMPs targeted adult population (n=6), paediatric population (n=6), as well as both adults and children (n=3); see **Figure 2**. Mean time since EMA registration until the submission was 1,189 days and median time was 837 days. Mean time until the publication of first evaluation report and decision since the submission was 141 and 330 days, respectively, and median time equalled 136 and 301 days, respectively. At least one call for cooperation by HTA authority was issued in all proceedings, however, there were 2.4 calls for cooperation on average. Details regarding administrative proceeding processes are captured in **Table 2**.

**Table 1. Identified administrative proceedings and evaluated OMPs**

| Administrative proceeding identificator | Brand name | Active substance | Indication |
|---|---|---|---|
| SUKLS235088/2022 | KIMMTRAK | TEBENTAFUSP | Advanced uveal melanoma |
| SUKLS170986/2022 | ASPAVELI | PEGCETACOPLAN | Paroxysmal nocturnal haemoglobinuria |
| SUKLS132358/2022 | CRYSVITA | BUROSUMAB | X-linked hypophosphataemia |
| SUKLS166094/2023 | CABLIVI | CAPLACIZUMAB | Acquired thrombotic thrombocytopenic purpura |
| SUKLS88071/2022 | ONIVYDE PEGYLATED LIPOSOMAL | IRINOTECAN-SUCROSOFATE | Metastatic adenocarcinoma of the pancreas |
| SUKLS155130/2022 | KAFTRIO | IVACAFTOR | Cystic fibrosis |
| SUKLS211268/2022 | TAKHZYRO | LANADELUMAB | Hereditary angioedem |
| SUKLS269850/2022 | FINTEPLA | FENFLURAMINE-HYDROCHLORIDE | Dravet syndrome and Lennox-Gastaut syndrome |
| SUKLS6832/2022 | SPINRAZA | NUSINERSEN | Spinal muscular atrophy |
| SUKLS86076/2022 | TREPULMIX | TREPROSTINIL | Chronic thromboembolic pulmonary hypertension |
| SUKLS282064/2022 | EPIDYOLEX | CANNABIDIOL | Lennox-Gastaut syndrome or Dravet syndrome |
| SUKLS117667/2022 | VYNDAQEL | TAFAMIDIS | Transthyretin amyloidosis with polyneuropathy |
| SUKLS284354/2022 | ADCETRIS | BRENTUXIMAB VEDOTIN | Hodgkin lymphoma |
| SUKLS212173/2022 | EVRYSDI | RISDIPLAM | Spinal muscular atrophy |
| SUKLS180596/2022 | KOSELUGO | SELUMETINIB SULFATE | Symptomatic, inoperable plexiform neurofibromas |

**Figure 1. Number of administrative proceedings according to targeted disease category**

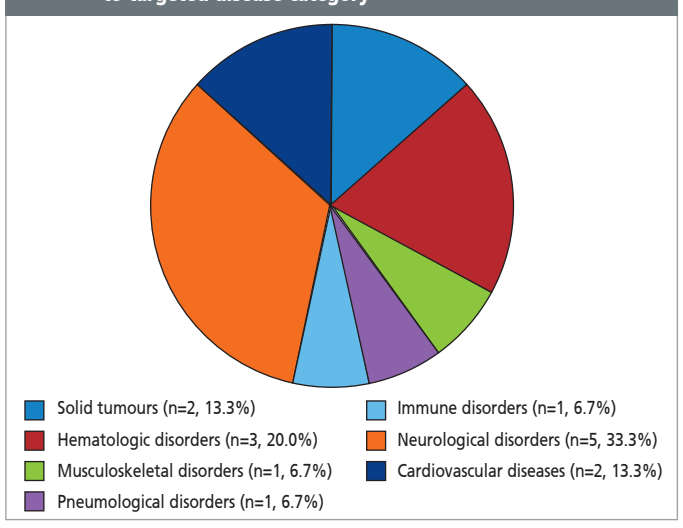
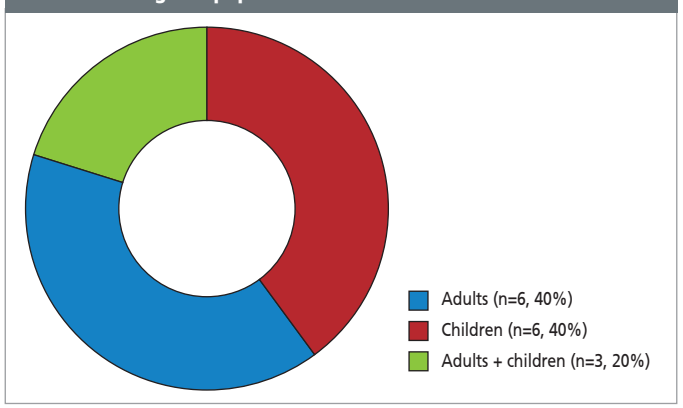



**Figure 2. Number of administrative proceedings according to targeted population**




In total, 30 cost-utility analyses (CUA) and 1 cost minimization analysis (CMA) were reported in the identified administrative proceedings and analysed, see **Table 3** for results. Best supportive care (BSC) was considered a comparator in majority of analyses (51.6%). The rest comprised of active therapy (48.4%). Lifetime horizon was adopted in 28 out of 31 analyses (90.3%), including CMA analysis, with mean applied lifetime horizon of 59.4 years. Other than lifetime horizons equalled 15 years (n=1) and 20 years (n=2). Considering all analyses (n=31), mean time horizon was 55.4 years.

Evaluated intervention generated more QALYs compared to comparator in all cost utility analyses (n=30). Mean patient increment of QALY was 3.07 with maximum of 9.10. Caregivers' QALY was reported in 9 analyses in total and was included in a base-case scenario in 6 analyses. Mean caregiver QALY increment equalled 2.15. The evaluated intervention compared to the comparator generated lower costs in 3 out of 30 cost-utility analyses. Considering positive incremental costs, the mean increment of costs was 1,121,542 EUR (n=27). Mean reported base-case ICER was 278,453 EUR/QALY (n=27). In total, 3 out of 30 cost-utility analyses were dominant, therefore ICERs were not reported. Cost minimization analysis was cost-saving.

When analysing the reported base-case ICERs (n=27) with regards to currently applied willingness to pay (WTP) threshold of 47,627 EUR/QALY (1,200,000 CZK/QALY), 2 out of 27 ICERs were lower than applied WTP. Furthermore, 9 reported base-case ICERs were lower than 3x WTP, 20 ICERs were lower than 10x WTP, and 7 ICERs were higher than

**Table 2. OMP administrative proceedings' process details**

| | N | Mean | Median | Minimum | Maximum |
|---|---|---|---|---|---|
| Time since EMA registration until submission (days) | 15 | 1,189.05 | 837.00 | 207.00 | 3,717.00 |
| Time since submission until 1st evaluation report (days) | 15 | 140.87 | 136.00 | 105.00 | 213.00 |
| Time since submission until decision (days) | 15 | 330.13 | 301.00 | 212.00 | 512.00 |
| Number of calls for cooperation | 15 | 2.40 | 2.00 | 1.00 | 5.00 |

**Table 3. Time horizon and cost-utility analyses results**

| | N | Mean | Median | Minimum | Maximum |
|---|---|---|---|---|---|
| Time horizon | | | | | |
| Lifetime horizon (years) | 28 | 59.39 | 57.50 | 3.00 | 100 |
| Overall time horizon (years) | 31 | 55.42 | 55.00 | 3.00 | 100.00 |
| Cost-utility analyses from payer perspective | | | | | |
| Patient increment of QALY | 30 | 3.07 | 1.83 | 0.12 | 9.10 |
| Caregiver increment of QALY | 9 | 2.15 | 0.62 | 0.28 | 13.26 |
| Increment of costs (EUR) | 27 | 1,121,542 | 394,853 | –1,650,955 | 4,682,342 |
| Base-case ICER (EUR/QALY) | 27 | 278,453 | 257,066 | 38,252 | 634,969 |
| Cost-utility analyses from societal perspective | | | | | |
| ICER (EUR/QALY) | 24 | 246,860 | 181,681 | 14,845 | 611,710 |
| % difference in ICER between payer perspective and societal perspective | 24 | –8.70% | –3.88% | –73.95% | 15.53% |

10x WTP. See **Figure 3** for number of analyses according to WTP range. However, the WTP is not routinely considered in case of evaluations according to Section 39da of the Act on Public Health Insurance, therefore, even OMP cost-effectiveness analyses with ICERs exceeding the applied WTP threshold would be considered for reimbursement.

Total of 25 cost-utility analyses from societal perspective were reported. One resulted in dominant ICER, otherwise, when considering societal perspective, mean ICER reduced to 246,860 EUR/QALY (n=24). Consideration of societal perspective led to a decrease of ICER in all cases. The ICER decreased on average by 8.7% when compared to base-case ICERs. Maximum ICER reduction was 74.0%.

Overall, 15 budget impact analyses (BIA) were presented, results can be seen in **Table 4**. Mean number of patients treated 5th year after intervention reimbursement was 127. Altogether, 1,908 patients have been assumed to be treated in the 5th year after reimbursement decision. The mean costs of the evaluated interventions in year 5 were 10,734,401 EUR, with the consideration of patient drop out from treatment in time. Considering the maximal patient potential, mean net BIA was 5,231,231 EUR. As can be seen in **Figure 4**, the biggest total expenses in terms of net BIA were generated by OMP treatment of cardiovascular patients, however the greatest patient population consisted of patients with

**Figure 3. Number of cost-effectiveness analyses according to applied WTP threshold range**

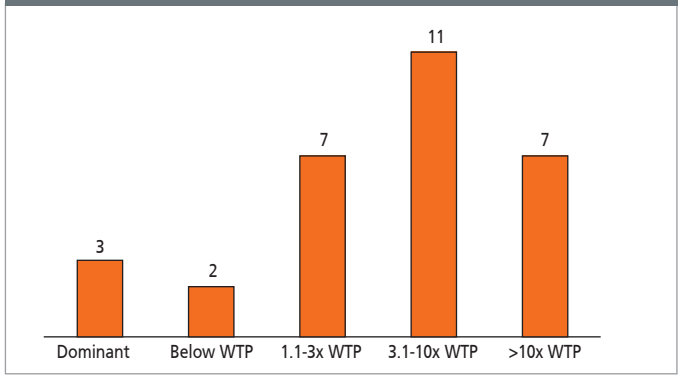



**Figure 4. 5th year net BIA according to number of patients treated**

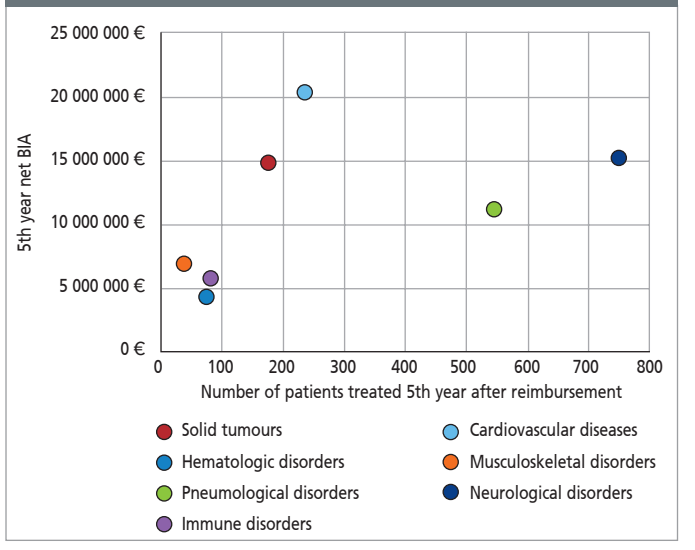



**Table 4. Budget impact analyses results**

| | N | Mean | Median | Minimum | Maximum |
|---|---|---|---|---|---|
| Budget impact analyses from payer perspective | | | | | |
| Number of patients treated in the 5th year after reimbursement decision | 15 | 127.20 | 82.00 | 15.00 | 545.00 |
| Evaluated intervention costs in the 5th year (EUR) | 15 | 10,734,401 | 2,929,691 | 322,435 | 62,652,156 |
| Net BIA in the 5th year (EUR) | 15 | 5,231,231 | 2,910,038 | –36,580 | 18,097,472 |
| Budget impact analyses from societal perspective | | | | | |
| Net BIA in the 5th year (EUR) | 9 | 5,907,162 | 4,409,430 | 581,930 | 17,464,997 |
| % difference in 5th year net BIA between payer perspective and societal perspective | 8* | –8.86% | –4.46% | –33.58% | 2.00% |

*One analysis was excluded from the calculation of percentual difference as change of netBIA is –7,738.23% in this case and is breaking the trend.

**Table 5. Other administrative proceedings' processes details**

| | N | Mean | Median |
|---|---|---|---|
| Permanent reimbursement process | | | |
| Time since submission until 1st evaluation report (days) | 470 | 71.60 | 52.00 |
| Time since submission until decision (days) | 470 | 115.56 | 80.00 |
| Number of calls for cooperation | 470 | 1.32 | 1.00 |
| Highly innovative drug program | | | |
| Time since submission until 1st evaluation report (days) | 38 | 76.35 | 49.00 |
| Time since submission until decision (days) | 38 | 120.75 | 75.00 |
| Number of calls for cooperation | 38 | 1.45 | 1.00 |

neurological disorders. BIA from societal perspective was reported in 9 cases with mean 5th year net BIA of 5,907,162 EUR. Including societal perspective led to mean 5th year net BIA change of -8.9%.

## Discussion

To put the OMP reimbursement process into broader context, presented results were compared to other types of reimbursement processes adopted in the Czech Republic: reimbursement of highly innovative drugs and permanent reimbursement. Considering the results of our analysis, it can be concluded that OMP reimbursement process is the most time-consuming type of reimbursement procedure in the Czech Republic (see **Table 2** and **Table 5**). Specifically, time since submission until publication of decision report was longer within the OMP reimbursement process compared to permanent reimbursement and reimbursement of highly innovative drugs by 215 and 209 days, respectively. Same trend can be seen in time since submission until first evaluation report parameter and the length of the OMP process may be also explained by the number of calls for cooperation.

Involvement of Ministry of Health in decision-making and inclusion of other participants such as Czech Medical Association and patient organisation into the OMP administrative proceeding, which are not involved in other reimbursement procedures, may also add to the length of the process. However, based on current trends, OMP reimbursement processes may shorten over time. For comparison, in our analysis, which predominantly included administrative proceedings initiated in 2022, median time since EMA registration until the initiation of OMP administrative proceedings in the Czech Republic was 837 days; for all OMP proceedings initiated in 2023 with published decision report, the median time was 375 days.

According to our analysis, ICER was on average almost six times higher than currently applied WTP, mainly due to the costs of orphan drugs. However, orphan drugs represent an efficacious and many times only option for treatment of rare diseases. At the same time, until recently used individual approval process is associated with huge administrative burden on healthcare providers as well as patients and is a source of uncertainty for patients. Specific procedure was highly needed to enable orphan drugs accessing the market in the Czech Republic as neither highly innovative drug program nor permanent reimbursement process were feasible for market access of orphan drugs

## Conclusions

**This analysis provides detailed insight into OMP reimbursement process over a more than two-year follow-up since the policy adoption. Policy change has allowed treatment of almost 2000 patients with OMPs over the defined time period. Treatment with OMPs generated considerable benefit in terms of patients' and caregivers' QoL, usually over a lifetime horizon. Applying societal perspective mostly led to reduced ICER and net BIA.**

**OMP administrative procedure provides early access to breakthrough medicines despite ICERs higher than applied WTP routinely used in the permanent process.**

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