HEALTHWARE

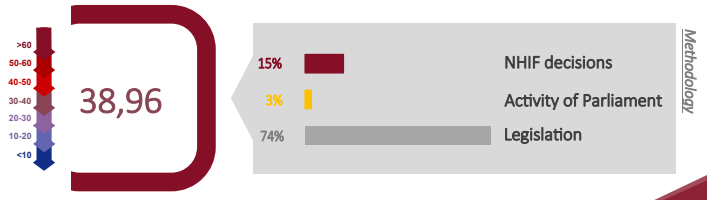
Actualities of Hungarian pharmaceutical financing market

Newsletter
No. 12 Issue IX. 2021
Published: 20/12/2021

News, current issues

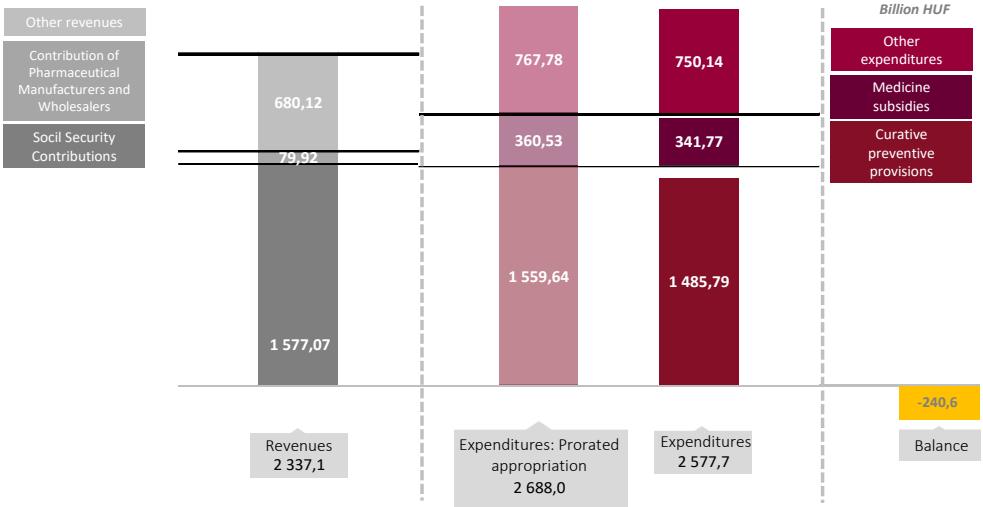
- News: You can no longer buy medicines online from January »
- News: V4 research: breakthroughs in cancer and rare diseases in the next decade »
- News: Medical aids: five professional organisations warn of shortages »

Decision-making index, October 2021



Macro approach to financing healthcare and medicinal products

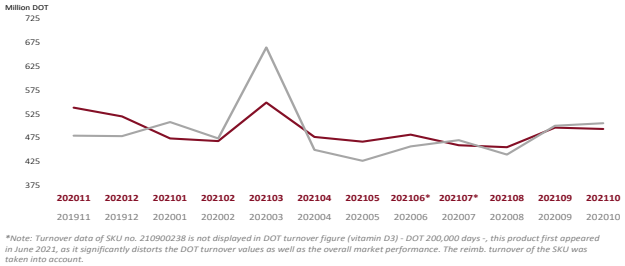
Balance of the Health Insurance Fund, October 2021



Source: Healthware analysis based on NHIFA data

Dynamics of the sales/circulation of prescription-only-medicine

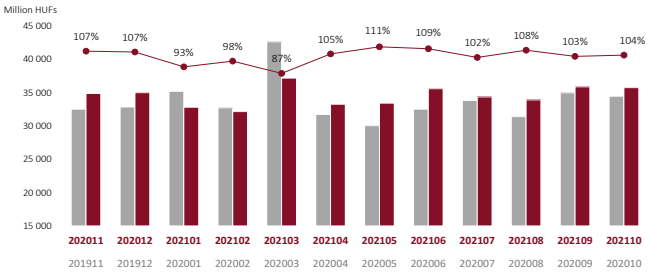
Pharmacy DOT turnover



**Note: Turnover data of SKU no. 210900238 is not displayed in DOT turnover figure (vitamin D3) - DOT 200,000 days -, this product first appeared in June 2021, as it significantly distorts the DOT turnover values as well as the overall market performance. The reimb. turnover of the SKU was taken into account.*

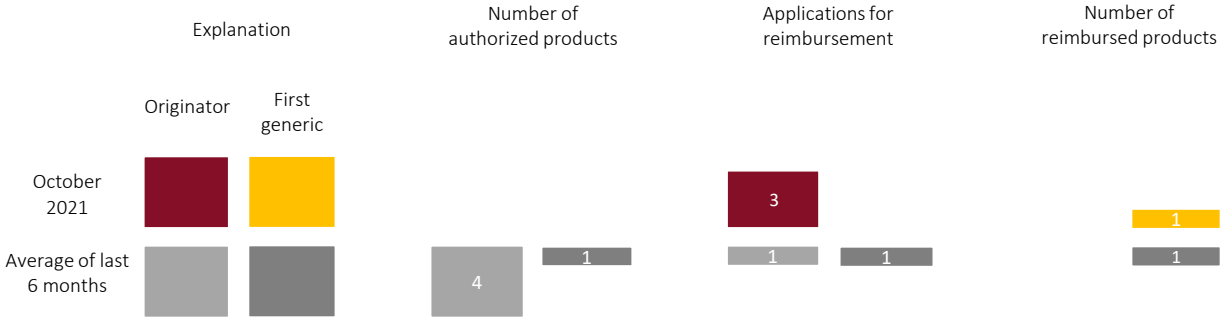
Source: Healthware analysis based on NHIFA data

Pharmacy reimbursement turnover



Source: Healthware analysis based on NHIFA data

Changes to subsidized medicinal product categories, October 2021



Source: Healthware analysis based on NHIFA data

Product offering

Survey of references, meta – analysis

We collect the available information, evidence in related articles, directives, studies, research.

As the first step of systematic research of the scientific literature we define the relevant keywords. Then we present the evidence charts, it is followed by organization and comparative analysis.

We are able to make an exact summary of the results with statistical methods, which is based on the systematic research of scientific literature that led to compiling the parameters of evidence charts.

More details: **link**

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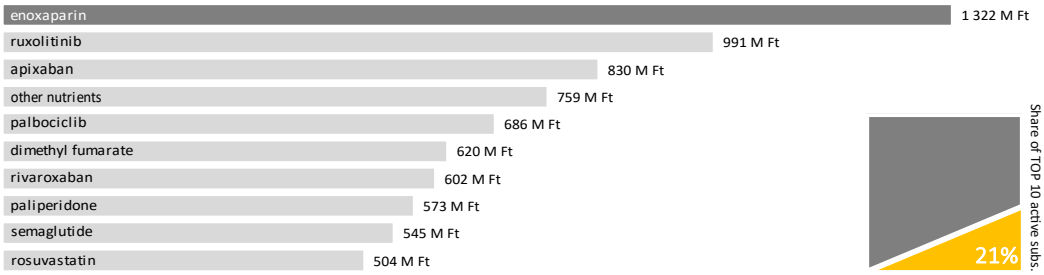
Market data

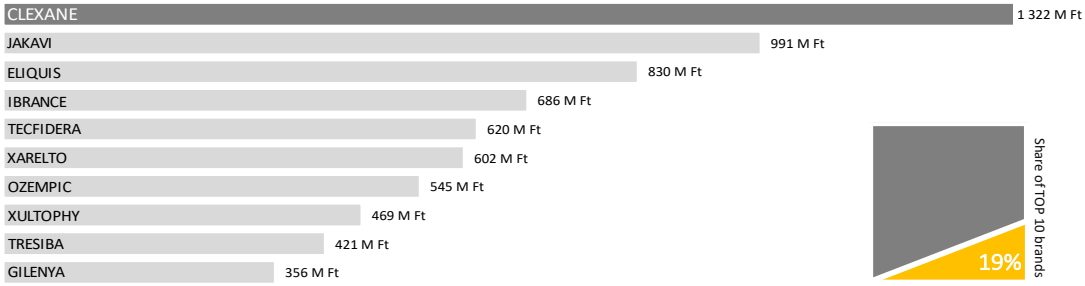
Toplists of reimbursement and number of patients, October 2021

TOP 10 ATCs by all reimbursement paid



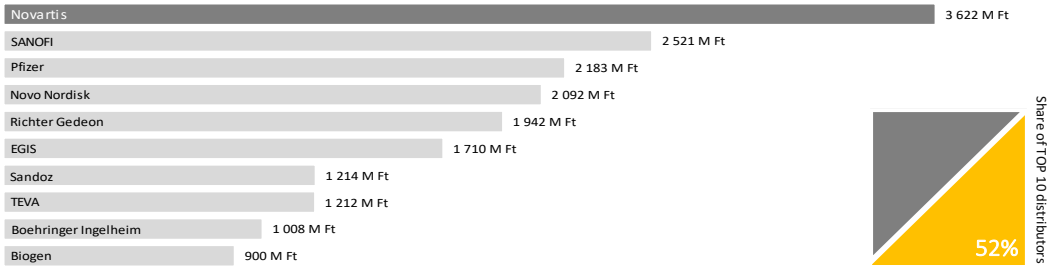
Source: Pharmacy turnover data, Healthware analysis

TOP 10 brands by all reimbursement paid



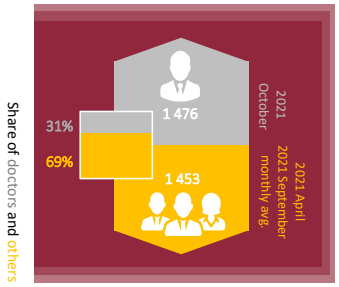
Source: Pharmacy turnover data, Healthware analysis

TOP 10 distributors by all reimbursement paid



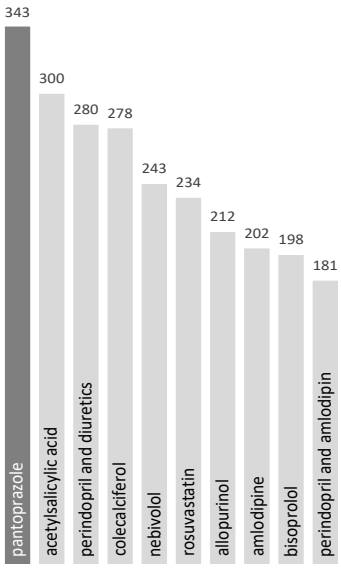
Source: Pharmacy turnover data, Healthware analysis

Average number of medical sales reps



Source: NHIFA data, Healthware analysis

TOP 10 active substances by number of patients (thousand patients)



Source: Pharmacy turnover data, Healthware analysis

Professional healthcare guideline on the methodology of health technology assessment — New threshold — Case study

The latest version of the professional healthcare guideline on the methodolgy of health technology assessment was published in November 2021. The previous directive was valid until 31.12.2020, but in the absence of a new directive, we have continued to prepare our health economic analyses in 2021 according to the recommendations of this directive, and OGYÉI-TÉF also evaluated the analyses on the basis of its recommendations. The new directive will apply from the date of its publication in the Health Gazette (19 November 2021).

The new Directive proposes new cost-effectiveness thresholds (Recommendation 7). Whereas the previous Directive set the threshold at three times GDP per capita, as recommended by the WHO - which was the same for all health technologies and all therapies - the new Directive recommends that different cost-effectiveness thresholds should be applied depending on the additional health gain, the size of which depends on whether the health technology is for rare or non-rare diseases.

1.IN CASE OF NON-RARE DISEASES:
the additional health gain indicator (Többlet-egészségnyereség mutató: TEM) is calculated using the following formula, then, depending on the value of the indicator, different thresholds can be applied to the technology.

$$\text{Additional health gain indicator} = \frac{\text{QALY}_{\text{examined technology}} - \text{QALY}_{\text{compar ator}}}{\text{QALY}_{\text{examined technology}}}$$

	Relative additional health gain		Cost-effectiveness threshold		
	TEM lower limit	TEM upper limit	(GDP per capita)	Thresh. HUF	Thresh. EUR*
Thresh. 1.	0	0,25	1,5	7 382 730 HUF	20 732 EUR
Thersh. 2.	0,25	0,6	2	9 843 640 HUF	27 643 EUR
Thresh. 3.	0,6	1	3	14 765 460 HUF	41 464 EUR

*Average 6 monthly exchange rate (EUR/HUF): 356,101 HUF

GDP per capita: 4 921 820 HUF (Source: KSH, October 2021)

Unfortunately, the limits in the table are wrongly defined (the upper limit of Threshold 1 is equal to the lower limit of Threshold 2 and the upper limit of Threshold 2 is equal to the lower limit of Threshold 3), i.e. if the TEM is 0,25 and 0,6, two limits can be applied in these cases. This would require interpretation and clarification by the OGYÉI-TÉF.

The recommendation is much stricter than the previous threshold of one limit value. Our experience has shown that it has been difficult to demonstrate cost-effectiveness at published prices for many innovative technologies, and we expect this to become even more difficult in the future.

2.IN CASE OF RARE DISEASES:
Cost-effectiveness threshold is calculated using the table below:

	ΔQALY	Percentile*	GDP Multipler**	Thresh. HUF	Tresh. EUR***
Thresh. 1.	0,5	0%	3	14 765 460 HUF	41 464 EUR
Thresh. 2.	1	2,56%	3,2	15 749 824 HUF	44 229 EUR
Thresh. 3.	5	23,08%	4,6	22 640 372 HUF	63 579 EUR
Thresh. 4.	10	48,72%	6,4	31 499 648 HUF	88 457 EUR
Thresh. 5.	15	74,36%	8,2	40 358 924 HUF	113 336 EUR
Thresh. 6.	20	100%	10	49 218 200 HUF	138 214 EUR

*Percentile: (ΔQALY[i]-min(ΔQALY)) /(max(ΔQALY)-min(ΔQALY))
**GDP Multipler: min(GDP multipler)+((max(GDP multipler)-min(GDP multipler))*Percentile)
***Average 6 monthly exchange rate (EUR/HUF): 356,101 HUF

GDP per capita: 4 921 820 HUF (Source: KSH, October 2021)

According to the Recommendation, the definition of 'orphan medicinal products (i.e. those designated by the licensing authority as suitable for the treatment of a rare disease)' is unclear and is sometimes referred to as a technology and sometimes as a medicinal product. It is not clear from the description whether this is only for products with EMA orphan status or whether it also applies to products with a registered orphan indication, which is the subject of the current submission. It is also not entirely clear from the table presented whether the

Orphan medicinal products are medicines for the treatment of rare diseases that meet the criteria for orphan medicinal products published by the EMA:

1) treatment of a life-threatening or chronically debilitating condition;
2) can treat less than 5/10 000 people in the EU;
3) estimated sales are unlikely to cover research and development costs;
4) there are no other satisfactory products vailabl in the rare disease market, or that offer significant clinical advantages over

EMA. Orphan deisgnation: Overview. https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview (13.12.2021.)

Professional healthcare guideline on the methodology of health technology assessment — New threshold — Case study

cost-effectiveness threshold is fixed within the ΔQALY thresholds or whether it varies within each threshold, calculated on the basis of the exact ΔQALY value.

The logic of classification for "rare" diseases differs from that for "non-rare" diseases. The methodology used for rare diseases clearly favours treatments with a long-term, lifelong effect and is more permissive for orphan drugs than for other drugs.

Instead of the qualitative stratification (relative additional health gain) used for "non-rare" diseases, the selection for "rare" diseases is based on a quantitative indicator that reflects a completely different logical approach, preferring long-term modelling. The preference for long-term modelling is of particular concern for rare diseases, where the available evidence is already limited. The uncertainties associated with lifetime analyses will be magnified here. If lifelong comparability is a priority for funding, it would have been desirable to include this aspect for 'non-rare' diseases.

CASE STUDY

The HTA summaries available on the OGYÉI website do not contain information on the total and incrementalQALY values to assess the cost-effectiveness of individual products already evaluated under the recommendations of the new Directive. Nevertheless, in order to get an idea of the expected impact of the new cost-effectiveness thresholds, we have taken a sample from our own analyses. We looked at our submissions in the field of oncology in 2021 and came to the following conclusions:

- under the old threshold, 1/3 of submissions contained cost-effective result.
- the current methodology is to assess results according to the first threshold for 1/3 and the second threshold for 2/3, but none of the new formulations would be cost-effective on this basis. None of the analyses examined showed that TEM fell below the third threshold.
- although the definition of orphan medicinal products in the Directive is not clear, it is our understanding that a product is an orphan medicinal product if it has EMA orphan status for the indication concerned. Such a product was not present in the sample examined, despite the fact that in some cases the indication concerned, based on its incidence, would meet the orphan category. Even if the cost-effectiveness of these products is assessed according to the threshold methodology for orphan drugs, they cannot be considered cost-effective.

SUMMARY

The most important point of the changes in the new directive is the change in the threshold, which we believe will have a significant impact on the assessments and the decision-making process itself from next year.

It is important to highlight that a significant number of new innovative products target a narrower range of patients (mostly without EMA orphan status), immuno-oncology products are increasingly present in a wider range of indications (sometimes in combination with other products), with higher price level than previous biological therapies. These products have already had problems in demonstrating cost-effectiveness in a significant proportion of cases, and we do not believe that the thresholds for orphan drugs will address these problems.

With these recommendations, the gap between professional and patient expectations, international pricing expectations from manufacturers and the increasing cost-effectiveness requirements from funders is widening. In addition to the weakening HUF and sporadic uptake that has been the trend for several years, the further narrowing of the threshold is expected to further complicate the market entry/access of innovative products.

NICHE COST-EFFECTIVENESS TRESHOLD

Currently, NICE uses a general cost-effectiveness threshold of GBP 20 000-30 000/QALY [1]. This cost-effectiveness threshold is used in the technology appraisal, but there are exceptions where justified.

One of these exceptions are end-of-life therapies. Although there is no clearly declared cost-effectiveness threshold for end-of-life therapies by NICE, the ICER assessment of the technology appraisals rejected by NICE suggests that the threshold for these therapies is GBP 50 000/QALY [2].

Another such exception is the Highly Specialised Technologies (HTS). For these technologies, the cost-effectiveness threshold is GBP 100 000/QALY [3]. To apply a threshold 5 times higher than the general threshold, the technology must meet the following criteria:

- *The target population for the licensed indication is so small that treatment is usually concentrated in just a few NHS centres*
- *The targeted group of patients is isolated for clinical reasons*
- *The disease causes chronic and severe disability*
- *The technology is expected to be used exclusively in the highly specialised service*
- *The cost of acquiring the technology is expected to be very high*
- *The technology is suitable for a lifetime of use*
- *The need for technology at national level is significant*

Such a distinct threshold group could also include orphan drugs, but there is currently no declared ICER threshold for this by NICE.

[1]Appleby et al. (2007). NICE's cost effectiveness threshold. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1952475/ (2021.12.13.)
[2]Griffiths (2016). Nice's Criteria for End-Of-Life Therapies: Is there a Fourth Hurdle to Overcome?. https://www.valueinhealthjournal.com/article/S1098-3015(16)32191-X/pdf#:~:text=NICE%20does%20not%20formally%20state,(ICERs)%20of%20rejected 20submissions. (2021.12.13.)
[3]NICE (2017). Interim Process and Methods of the Highly Specialised Technologies Programme. Updated to reflect 2017 changes. https://www.nice.org.uk/media/default/about/what-we-do/nice-guidance/nice-highly-specialised-technologies-guidance/hst-interim-methods-process-guide-may-17.pdf (2021.12.13.)