No.8, Issue III. August 2015
Published: 17 August 2015

Actualities of Hungarian pharmaceutical financing market

Newsletter

HEALTHWARE CONSULTING LTD.

News, current issues

- **Legislations** come into force between 01/07/2015 and 01/08/2015**:** Act XI of 1991 (01.07.2015); Act LXXXIII of 1997 (01.07.2015, 22.07.2015,01.08.2015); Act CLIV of 1997 (01.07.2015,01.08.2015); Act XXV of 1998 (01.07.2015); Act II of 2000 (01.08.2015); Act XCV of 2005 (01.07.2015); Act XCVII of 2006 (01.07.2015); Act XCVIII of 2006 (01.07.2015); NM Decree No.9/1993. (16.07.2015); Gov.Decree No.284/1997. (22.07.2015); Gov.Decree No.43/1999. (03.07.2015,22.07.2015); Gov.Decree No.337/2008. (22.07.2015); Gov.Decree No.235/2009. (22.07.2015,01.07.2015); Gov.Decree No.323/2010. (22.07.2015); Gov.Decree No.16/2012. (22.07.2015)
- **NEWS:** *"Ten billions in healthcare IT development"* link
- **NEWS:** *"It is the way hospital waiting lists would be shortened"* link
- **NEWS:** *"Discounts would be given by pharmacies if they could"* link
- **NEWS:** *"BCG vaccine shortage problem will be solved"* link
- **NEWS:** *"Everybody should hand down the social security card"* link

Macro approach to financing healthcare and medicinal products

Balance of the Health Insurance Fund

Billion HUF

Health Security Fund	2014. I-XII.	2015 original appropriation	2015		
			I-VI. months	% of appropriation	% of last year
Total of Budgetary Expenditures	**1 907,1**	**1 910,8**	**959,8**	**100,5%**	**103,6%**
Curative preventive provisions	945,6	948,6	469,5	99,0%	103,7%
Medicine subsidies	302,3	298,1	158,6	106,4%	106,6%
Medicine subsidies (pharmacy)	286,4	224,4	152,3	135,7%	107,9%
Total of Budgetary Revenues	**1 907,1**	**1 910,8**	**964,3**	**100,9%**	**99,9%**
Social Security Contributions	896,3	1 198,5	608,2	101,5%	135,1%
Contribution of Pharmaceutical Manufacturers and Wholesalers	57,4	58,0	33,3	114,9%	113,6%
Balance	**0,0**	**0,0**	**4,4**		**0,0%**

The 2015 budget counts with 0,2% increase in the expenditure and in the revenues too, while the balance is nil. The central budget contribution is planned to be less with 35,1% than last year fulfilment, and this gap is filled with the 33,7% higher social security contribution (302 billion HUFs). The medicine subsidies plan are lower with 4,2 billion HUFs than last year expenses.
In the first six months of 2015 the Health Security Fund produced a 0,47% surplus. Medicine subsidies shows 6,4% surplus as a result of the medicines' higher turnover particularly that reimbursement based on special permission (+5,3 billion HUFs, which is 275% higher than subsidies in 2014H1).

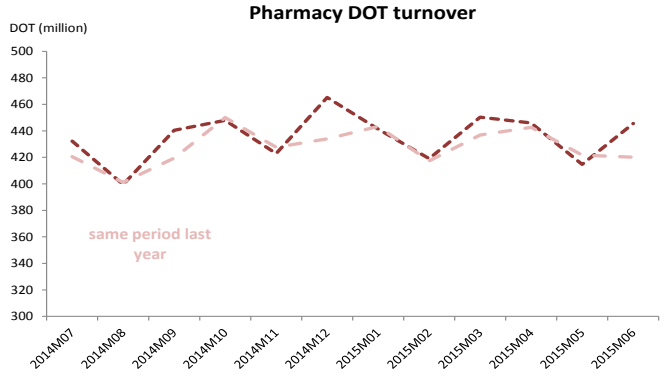
Changes to subsidised medicinal product categories

Changes in the public drug list	2015 Mar.	2015 Apr.	2015 May	2015 June	2015 July	2015 Aug.	2015
Number of new products	31	57	11	16	12	34	193
Number of new AI	5	2	1	2	2	4	21
Number of delisted products	36	44	51	30	16	16	229
Prices							
Decrease	7	166	3	0	42	5	248
Increase	0	3	0	0	5	0	11

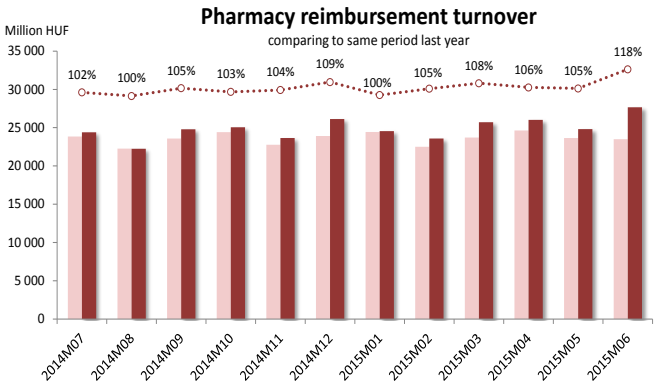
Changes in the public drug list	2015 Mar.	2015 Apr.	2015 May	2015 June	2015 July	2015 Aug.	2015
Reimbursement							
Decrease	6	393	1	0	71	4	523
Increase	1	69	0	0	6	0	89
Co-payment							
Decrease	14	255	5	0	47	7	371
Increase	1	280	0	0	34	0	339

Source: Healthware analysis based on OEP-PUPHA data

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



Source: Healthware analysis based on OEP's data



Source: Healthware analysis based on OEP's data

While the turnover of reimbursed medicines in pharmacies increased by 2,74% in 2014 (measured in DOT), the total medicine subsidy of Health Security Fund was higher by 2,21%. The subsidy of new INNs (got reimbursed status in 2014) was 1,26% of the yearly total, while its turnover was only 0,03% of the yearly DOT turnover.
Drug sales in the first six months of 2015 was 0,79% higher than the same period last year, while the average reimbursement per DOT increased with 3,81% compared to the previous month and was higher with 11,66% than the last year's average. The reimbursement turnover is 4,95% higher for this period compared to last year.

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Market data

Marketing authorisation information

2014	EMA	OGYI
New brands	70	182
New SKUs	359	1 879

2015 - Q2	EMA	OGYI
New brands	14	45
New SKUs	128	518

June 2015	EMA	OGYI
New brands	7	21
New SKUs	257	275

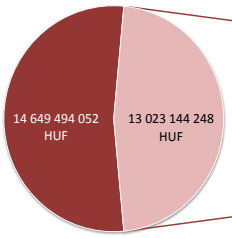
Source: Healthware analysis based on OGYI's and EMA's data

Average number of **medical sales reps**; 06/2015

All	1 809
Medicinal products	1 531
Medical aids	250
Both	28

Source: Healthware analysis based on OGYI's

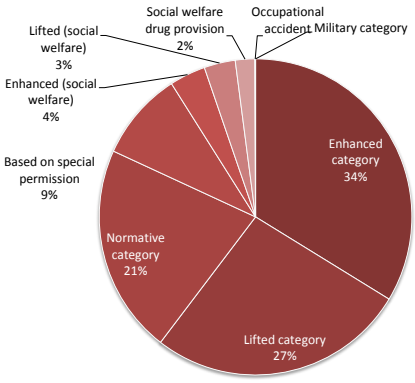
TOP10 **DISTRIBUTOR** by all reimbursement paid in June 2015



TOP 10 - DISTRIBUTOR	Reimbursement
Novartis Hungária Kft.	2 461 796 610 HUF
SANOFI-AVENTIS Zrt.	1 676 608 809 HUF
EGIS Gyógyszergyár Zrt.	1 315 419 981 HUF
Richter Gedeon Vegyészeti Gyár NyRt.	1 262 443 006 HUF
TEVA Gyógyszergyár Zrt.	1 198 225 353 HUF
AbbVie Kft.	1 188 726 235 HUF
Pfizer Kft.	1 096 519 407 HUF
Lilly Hungaria Kft.	975 126 513 HUF
Novo Nordisk Hungária Kft.	967 517 014 HUF
Sandoz Hungária Kereskedelmi Kft.	880 761 321 HUF

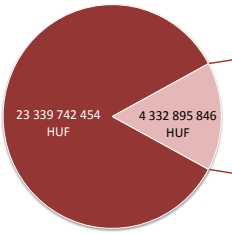
Source: Healthware analysis based on the sales turnover that pharmacies produced from POM

Drug reimbursement by **legal title**; 06/2015



Source: Healthware analysis based on the sales

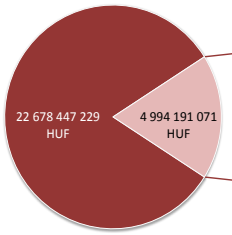
TOP10 **BRAND** by all reimbursement paid in June 2015



TOP 10 - BRAND	Distributor	Reimbursement
VIEKIRAX	AbbVie Kft.	932 032 576 HUF
CLEXANE	SANOFI-AVENTIS Zrt.	564 370 438 HUF
GLIVEC	Novartis Hungária Kft.	547 211 706 HUF
XEPLION	Janssen-Cilag Gyógyszerkereskedelmi Marketing S	437 972 905 HUF
SPIRIVA	Boehringer Ingelheim Pharma Gesellschaft m. b. H	406 195 684 HUF
LANTUS	SANOFI-AVENTIS Zrt.	354 853 907 HUF
HUMULIN	Lilly Hungaria Kft.	304 606 530 HUF
SUTENT	Pfizer Kft.	276 876 347 HUF
LEVEMIR	Novo Nordisk Hungária Kft.	259 196 959 HUF
TASIGNA	Novartis Hungária Kft.	249 578 794 HUF

Source: Healthware analysis based on the sales turnover that pharmacies produced from POM

TOP10 **ATC** by all reimbursement paid in June 2015



TOP 10 - ATC	International non-proprietary name (INN)	Reimbursement
J05AX67	ombitasvir, paritaprevir and ritonavir	932 032 576 HUF
V06D	other nutrients	571 252 816 HUF
B01AB05	enoxaparin	564 370 438 HUF
L01XE01	imatinib	547 211 706 HUF
N05AX13	paliperidone	516 160 753 HUF
C10AA07	rosuvastatin	418 672 876 HUF
R03BB04	tiotropium bromide	406 195 684 HUF
A10AB01	insulin (human)	361 037 886 HUF
A10AE04	insulin glargine	354 853 907 HUF
C09BA04	perindopril and diuretics	322 402 429 HUF

Source: Healthware analysis based on the sales turnover that pharmacies produced from POM

TOP10 **ATC** by number of patients in June 2015

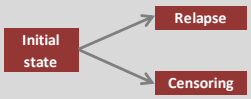
TOP 10 - ATC	International non-proprietary name (INN)	Patients
B01AC06	acetylsalicylic acid	358 350
C09BA04	perindopril and diuretics	294 553
C08CA01	amlodipine	274 914
C07AB12	nebivolol	248 276
C10AA05	atorvastatin	240 627
C10AA07	rosuvastatin	220 943
A02BC02	pantoprazole	204 070
M04AA01	allopurinol	203 882
C09AA04	perindopril	180 199
C09BB04	perindopril and amlodipin	167 498

Source: Healthware analysis based on the sales turnover that pharmacies produced from POM

Multi-state Models for Patient Pathway Analysis— Case study

Patient pathway is a time-ordered sequence of patients' states and conditions. To every state, patient's attributes are assigned, such as follow-up time, type of event, change in the patient's health condition, type of medical intervention and type and cost of therapy. There are several well-elaborated methods for statistical analysis of patient pathways. These are mostly implemented in some packages of R, which is a free, open-source statistical programming software.

The simplest patient pathway model analyses the hazard of a single event and the elapsed time until its occurrence. Even in this simple case there are actually two competing events i.e. the event of interest (e.g. relapse) and a censoring event of the patients' follow-up, since we cannot follow the patients' pathway until infinity.

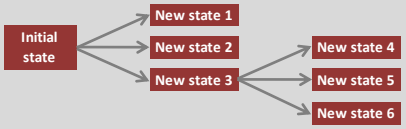


Censored follow-up time until a single event of interest can be modelled by standard methods such as Kaplan-Meier survival curves and Cox proportional hazard models [1].

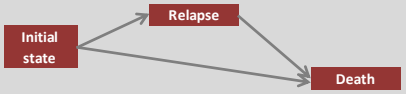
If we consider the problem closer then we realise, there is at least one more event – death – we should also take into account. These are competing events since if a patient dies then he or she cannot have a relapse anymore.

If there are multiple competing events and we are only interested in the risk or hazard of the event occurring first, then it is called competing risks model [1,2]. Competing risks models can be fitted by suitable Cox proportional hazard models [1]. This can be accomplished by using the "survival" and "mstate" packages of R.

It is not necessary to stop the follow-up at the first event or change in health condition. Modelling can be continued with the analysis of the time to the next event or events. We can imagine that every new state or condition is a starting point of a new competing risk. With a directed graph:



This kind of model for such a complex data is called a multi-state model. It is possible for example that first relapse competes with death and then – provided relapse has occurred first – we can analyse time to death and the hazard of death. Schematically:



In R the package "mstate" can be used for fitting multistate models.
Healthware Consulting Ltd. has been successfully applying Cox proportional hazard models to analyse patient pathways for years. We also have years of experience in fitting competing risk models in constructing patient pathway simulations. Patient pathway simulation can be suitably applied to the analysis of multi-state time-varying data. In the future we also plan to compile multi-state models based on the R package "mstate".
James Robins' IPTW method for assessing causality of therapeutic regimens connected to patient pathways [3] has been implemented several times at our company. There are examples in the literature of applying Robins' casual models in the analysis of multi-state patient pathways [4]. Robins' IPTW method can also be substituted with Bayesian models [5]. In the near future we plan to develop new models in this direction too.

[1] Therneau TM, Grambsch PM (2000): Modeling survival data. Extending the Cox Model. Springer.
[2] van Houwelingen HC, Putter H (2012): Dynamic Prediction in Clinical Survival Analysis. Taylor & Francis.
[3] Robins JM, Hernán MA, Brumback B (2000): Marginal Structural Models and Causal Inference in Epidemiology. Epidemiology 11: 550-560.
[4] Wahed AS, Thall PF (2013). Evaluating joint effects of induction-salvage treatment regimes on overall survival in acute leukaemia. Journal of the Royal Statistical Society: Series C (Applied Statistics), 62(1):67-83.
[5] Xu Y, Müller P, Wahed AS, Thall PF (2014): Bayesian Nonparametric Estimation for Dynamic Treatment Regimes with Sequential Transition Times. eprint arXiv:1405.2656.

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