Negative HTA Recommendations for Medicines in Neurology Therapeutic Areas – Fourfold Higher Odds in Poland Compared with the United Kingdom

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CONCLUSION

- Poland remains a challenging market for access to innovative neurology medicines, with a fourfold higher odds of HTA rejection compared to the UK.
- There is an increasing trend of positive HTA recommendations for products suggesting risk-sharing agreements (RSA). RSAs may positively influence recommendation by the Polish HTA body (*Agencja Oceny Technologii Medycznych i Taryfikacji*; AOTMiT) for innovative medicines in neurology.

INTRODUCTION

- Neurological disorders remain the leading cause of disability-adjusted life years (DALYs of 276 million) and the second leading cause of deaths (9.0 million) globally[1].
- Technology appraisals (TA) by health technology assessment (HTA) bodies continue to pose a hurdle to broad access of innovative medicines in Europe, including Poland.
- Risk-sharing agreements (RSA) are a potential means of increasing chances of medicines acceptance and reimbursement.

1. Feigin VL, et al. *Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology.* doi:10.1016/s1474-4422(18)30499-x

OBJECTIVES

- The aim of this study was to compare TA outcomes of the Polish HTA body (*Agencja Oceny Technologii Medycznych i Taryfikacji*; AOTMiT) and UK reimbursement bodies (National Institute for Health and Care Excellence; NICE, Scottish Medicines Consortium; SMC) for medicines in neurology (F01-G99 of the ICD-10-CM Codes) and analyze RSA trends in Poland.

METHODS

- Published outcomes of TAs carried out by AOTMiT between 2015 and 2018 were reviewed and matched to the TAs carried out by NICE/SMC.
  - NICE TAs were considered as a primary source of information for the UK. In case NICE TA for a product of interest was unavailable, SMC TA was considered (if available).
- Fisher's exact test for a 2x2 contingency table was carried out to calculate odds ratio (OR) for a negative HTA outcome.
- Recommendations on including RSA in positive HTA decisions by AOTMiT were analyzed in two periods (2018 vs. 2015-2017).

TABLE 1: HTA OUTCOME BY AOTMiT AND NICE/SMC (2015 – 2018 YEAR)

	PRODUCT/INN	INDICATION (ICD-10-CM)	HTA OUTCOME	
			AOTMiT	NICE/SMC
2018 YEAR	SPINRAZA	Spinal Muscular Atrophy (compassionate use)		n/a
	FUMADERM	Multiple Sclerosis (MS)		MEA
	OCREVUS	Primary progressive MS	RSA	MEA
	GILENYA	2L / Rapidly evolving severe relapsing remitting MS		n/a
	LEMTRADA	2L MS	RSA	
	Quinidine Sulfate	Drug-resistant epilepsy caused by KCNT1 mutations		n/a
	FIRDAPSE	Lambert-Eaton myasthenic syndrome	RSA	
	OCREVUS	2L MS	RSA	MEA
	FERRIPROX	Neurodegeneration with brain iron accumulation		n/a
	NUEDEXTA	Amyotrophic Lateral Sclerosis		n/a
	MAVENCLAD	2L / Rapidly evolving severe relapsing remitting MS	Unclear	
	AUSTEDO	Huntington's disease		n/a
	GAMMALON	Autism, Motor and sensory aphasia		n/a
	INTUNIV	Attention Deficit Hyperactivity Disorder (ADHD)		
	LATUDA	Schizophrenia		
	XYREM	Narcolepsy with cataplexy		
2017 YEAR	SPINRAZA	Spinal Muscular Atrophy	RSA	MEA
	PETNIDAN/ZARONTIN	Drug-resistant epilepsy		n/a
	ORAP	Chronic Tourette syndrome		n/a
	ORAP	Chronic Leigh syndrome		n/a
	DYSTARDIS	Moderate to severe late dyskinesia		n/a
	MEXITIL	Multiple, including Becker muscular dystrophy		n/a
	SYNACTHEN	Multiple, including drug-resistant epilepsy		n/a
	DACEPTON	Advanced Parkinson's disease (PD)	RSA	n/a
	GILENYA	2L / Rapidly evolving severe relapsing remitting MS	Unclear	MEA
	CALCORT	Duchenne muscular dystrophy (DMD)		n/a
	BRIVIACT	Partial onset seizures	RSA	

KEY: NEGATIVE HTA OUTCOME | POSITIVE HTA OUTCOME | MEA = managed entry agreement; n/a = not analyzed

RESULTS

- A total of 77 HTA submissions were identified (48 from AOTMiT and 29 from NICE/SMC) **(Table 1).**
- The rejection rate was 39.6 % by AOTMiT and 13.8% by NICE/SMC.
- The OR for a negative HTA recommendation was 4.46 (95% CI 1.34 to 14.84, p=0.015) between AOTMiT and NICE/SMC **(Table 2).**
- RSA were recommended in 90% of positive TAs by AOTMiT in 2018 compared with 33% in positive TAs in 2015 – 2017 year.
- The odds for recommending RSA by AOTMiT increased 2.4 times in 2018 when compared with 2015 to 2017-year timeframe (95%CI 0.47 to 12.61, not significant) **(Table 3).**

LIMITATIONS

- ORs for a negative HTA recommendation and for recommending RSA by AOTMiT lack precision, which might be improved upon analyzing a larger sample of HTA submissions in a timeframe beyond 2015 to 2018.
- TA outcomes by NICE/SMC were unavailable for approximately 40% of analyzed submissions by AOTMiT, a substantial proportion of missing observations that may affected the OR for a negative HTA recommendation and the estimate precision.

TABLE 1: *continued.*

	PRODUCT/INN	INDICATION (ICD-10-CM)	HTA OUTCOME	
			AOTMiT	NICE/SMC
2016 YEAR	DUODOPA	Movement disorders in PD	RSA	MEA
	TRANSLARNA	Nonsense mutation DMD		MEA
	DIACOMIT	Severe myoclonic epilepsy (Dravet syndrome)		
	TALOXA	Multiple, including drug-resistant epilepsy		n/a
	TYSABRI	2L / Rapidly evolving severe relapsing remitting MS		
	TIXTELLER	Hepatic encephalopathy		
2015 YEAR	HITOFF	Idiopathic PD		
	BETAFERON	Secondary progressive MS		
	OXEPILAX	Epilepsy (re-assessment; new price)		n/a
	OXEPILAX	Epilepsy (re-assessment; current price)	RSA	n/a
	XEPLION	Schizophrenia		
	LYRICA	Peripheral and central neuropathic pain		
	LEMTRADA	MS		n/a
	PLEGRIDY	Relapsing remitting MS		
	BRINTELLIX	Major depressive disorders		
	AUBAGIO	MS		MEA
	ABILIFY MAINTENA	Schizophrenia		
	REBIF	MS in children < 12 years old		MEA
	AVONEX	MS in children < 12 years old		MEA
	COPAXONE	MS in children < 12 years old		MEA
	EXTAVIA	MS in children < 12 years old		MEA

TABLE 2: OR FOR A NEGATIVE HTA RECOMMENDATION BY AOTMiT

		HTA AGENCY	
		AOTMiT	NICE/SMC
HTA OUTCOME	NEGATIVE	20	4
	POSITIVE	28	25
Odds Ratio		4.4643	
95% CI		1.3427 to 14.8426	
Significance		P = 0.0147	

TABLE 3: OR FOR RECOMMENDING RSA BY AOTMiT

		TIMEFRAME	
		2018	2015-2017
RSA	YES	4	5
	NO	5	15
Odds Ratio		2.4000	
95% CI		0.4567 to 12.6130	
Significance		P = 0.3011	

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