Real-world dosing and adherence in patients with multiple sclerosis treated with nabiximols in Germany

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Background

- Approximately 2.8 million people worldwide and over 250,000 in Germany alone are affected by multiple sclerosis (MS), a chronic inflammatory demyelinating disorder of the central nervous system[1]
- Spasticity is an involuntary increase in muscle tone and is reported in up to 84% of patients with MS.[2–4] Pain, spasms, bladder and bowel dysfunction, mobility impairment, and fatigue are associated with MS-related spasticity (MSS) and can have a negative impact on quality of life[4–6]
- Failure to respond and unsatisfactory responses to current first-line anti-spasticity medications (ASMs), baclofen and tizanidine, have been reported in patients with MS[7–8]
- Nabiximols is approved for symptom improvement in adult patients with moderate to severe MS-related spasticity who have responded inadequately to other ASMs and who demonstrated clinically significant improvement in spasticity-related symptoms during an initial trial of therapy[a] in >25 countries outside of the US
- There is a need to assess real-world treatment patterns, dosage, and adherence to nabiximols in patients with MS

Objective

- To describe real-world dosage and adherence to nabiximols and describe treatment patterns among patients with MS using a claims database in Germany

Methods

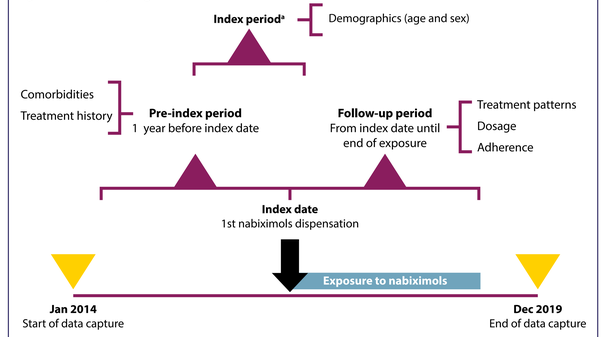
- This retrospective, non-interventional cohort study of patients with MS in Germany used anonymized secondary data extracted from the Institute for Applied Health Research Berlin (InGef) administrative claims database
- Inclusion criteria included an MS diagnosis 1 year before or on the index date (defined as the first nabiximols dispensation), ≥1 nabiximols dispensation on or after 01 January 2015, and observable information in the database for 1 year before the index date. Patients with a nabiximols dispensation before 01 January 2015 were excluded
- Data were captured between January 2014 and December 2019 (**Figure 1**)
- Patient characteristics and treatment patterns before and after nabiximols treatment (e.g., switching, ASM history) were summarized using descriptive statistics
- Nabiximols dosage was calculated from the number of nabiximols bottles dispensed per patient over the treatment period. The number of sprays was estimated assuming that 1 bottle equaled 90 sprays (1 spray = 10 mL)
- Adherence to nabiximols was described using proportion of days covered (PDC), calculated as the sum of days covered divided by the treatment period
- As a sensitivity analysis, patients whose estimated dose was >2 standard deviations from the mean were excluded

Table 1. Baseline patient characteristics

Variable	InGef (N = 837)
Age (years), mean (SD)	51.5 (11.2)
Sex, n (%)	
Female	508 (61)
Male	329 (39)
MS subtype, n (%)	
RRMS	217 (26)
SPMS	334 (40)
PPMS	286 (34)
Comorbidities, n (%)	
Depression and anxiety	548 (65)
Bladder and bowel dysfunction	464 (55)
Pain	448 (54)
Mobility impairment	435 (52)
Hypertensive disease	260 (31)
Peripheral vascular disease	197 (24)

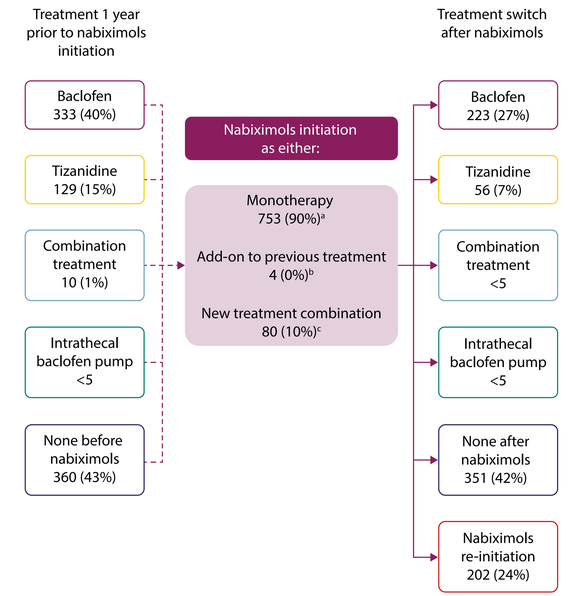
MS, multiple sclerosis; PPMS, primary progressive MS; RRMS, relapsing-remitting MS; SD, standard deviation; SPMS, secondary progressive MS.

Figure 1. Study design



[a]Considers the 3 months prior to and 1 month after the index date. The index period was extended to 6 months prior to and 1 month after to allow for more covariates needed for matching in a separate sub-analysis.

Figure 2. Treatment patterns before and after receiving nabiximols



[a]No other ASM initiated within 30 days of nabiximols initiation. [b]Other ASM initiated prior to nabiximols and not discontinued later than 30 days after initiating nabiximols. [c]Other ASM initiated within 30 days of nabiximols initiation. ASM, anti-spasticity medication.

- 43% of patients had no documented ASM 1 year before nabiximols initiation
- Baclofen was the most common ASM (40%) before nabiximols initiation
- 90% of patients initiated nabiximols as monotherapy
- Following nabiximols treatment, 42% of patients did not switch to another ASM
- The most common ASM after discontinuing nabiximols was baclofen (27%)

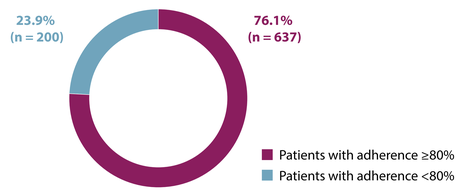
Table 2. Nabiximols dosage

Dosage*	Bottles per year (N = 837)	Sprays per day (N = 837)
Mean (SD)	27.5 (18.9)	6.8 (4.7)
Median (Q1, Q3)	29.6 (24.0, 29.6)	7.3 (5.9, 7.3)
Min, max	13.6, 547.4	3.4, 135.0

Max, maximum; min, minimum; Q, quartile; SD, standard deviation.
*Doses of greater than 12 sprays per day are not recommended per the European summary of product characteristics.[9]

- Mean (SD) dosage was 27.5 (18.9) nabiximols bottles per patient per year
- During a treatment episode, sprays per day ranged from 3.4 to 135.0 in patients with MS
- Median and quartiles indicate that 50% of patients receive between 24 and 29 nabiximols bottles per year
- Results from the sensitivity analysis excluding outliers (n = 2) were consistent with results from the primary analysis

Figure 3. Nabiximols adherence estimated as the PDC for the treatment period[a]



[a]A treatment period was defined as the time from the initial nabiximols dispensation until the end of the supply of nabiximols. Consecutive nabiximols dispensations were merged into one treatment period. A 60-day grace period was allowed. PDC, proportion of days covered.

- Mean and median adherence were 90% and 100%, respectively, suggesting that overall, patients had access to sufficient nabiximols medication over the full duration of the treatment period
- Results from the sensitivity analysis excluding outliers (n = 2) were consistent with results from the primary analysis

Results

- The mean age of the cohort (N = 837) was 51.5 years, and 61% of patients were women. Most patients (74%) had progressive MS (**Table 1**)

Limitations

- Although MS diagnoses were coded for each patient extracted from the database, it cannot be ascertained that all MS patients treated with nabiximols had spasticity, or if they received nabiximols for the treatment of MS-related spasticity as per the European summary of product characteristics (SmPC)
- There were limited clinical variables available in this German claims database
- Further real-world evidence covering other countries, healthcare systems, and treatment guidelines is needed to improve generalizability of these results

Conclusions

- In this German claims study of patients with MS, nabiximols adherence was high; the dosage was consistent with previous real-world studies,[10–14] and lower than reported in nabiximols pivotal trials among patients with MSS[15–16]

References: 1. Atlas of MS. MS International Federation. Available at https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms. Accessed February 22, 2023; 2. Hugos CL, et al. *Curr Neurol Neurosci Rep* 2019;19:79; 3. Rizzo MA, et al. *Mult Scler* 2004;10:589–595; 4. Milinis K, et al. *Mult Scler Relat Disord* 2016;5:34–39; 5. Bethoux F, et al. *Patient* 2016;9:537–546; 6. Henze T, et al. *Der Nervenarzt* 2013;84:214–222; 7. Medical Advisory Secretariat. *Ont Health Technol Assess Ser* 2005;5:1–93; 8. Arroyo González, R. *Expert Rev Neurother* 2018;18:785–791; 9. SATIVEX (nabiximols) [summary of product characteristics]. Dublin, Ireland: Jazz Pharmaceuticals; April 2022; 10. Pozzilli C. *Expert Rev Neurother* 2013;13(12Suppl):49–54; 11. Flachenecker P, et al. *Eur Neurol* 2014;71:173–181; 12. Oreja-Guevara C, et al. *Clin Exp Pharmacol* 2015;5:184; 13. Patti F, et al. *J Neurol Neurosurg Psychiatry* 2016;87:944–951; 14. Maccarrone M, et al. *Expert Rev Clin Pharmacol* 2017;10:443–455; 15. Novotna A, et al. *Eur J Neurol* 2011;18:1122–1131; 16. Markovà J, at al. *Int J Neurosci* 2018;129:119–128.

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