CBAF312A2006 Study Results Abstract for Public Disclosure

Title

Survey among healthcare professionals (neurologists treating patients with MS and MS specialist nurses) and MS patients/caregivers in selected European countries plus Canada to evaluate the knowledge required for the safe use of Mayzent (siponimod).

Date

24-Oct-2025

NIS Type

NIS with Primary Data Collection

Keywords

Mayzent, Healthcare Professionals (HCPs), patients/caregivers, educational materials, multiple sclerosis, survey

Rationale and background

To enhance understanding of the effective and safe use of Mayzent (siponimod), HCPs and patients/caregivers are provided educational information on the specific areas of interest as agreed with EMA in the Mayzent EU RMP v2.1, dated 29-Oct-2020.

As per guidelines on GVP Module XVI rev 03 dated Jul 2024, evaluating the effectiveness of additional risk minimization measures proposed in the RMP is necessary to establish whether an intervention has been effective, and if not, why and which corrective actions are necessary.

This survey is a required additional pharmacovigilance activity that is included in the current Mayzent EU RMP v7.2. and includes Canada as an additional participating country at the request of the Canadian Health Authority.

Research question and objectives

The objective of this survey amongst HCPs and patients/caregivers in selected European countries, plus Canada, is to evaluate whether HCPs and patients/caregivers receive the educational materials and to evaluate whether the HCP and patients/caregiver educational materials are clearly presented and convey knowledge that support the effective use of Mayzent (siponimod) at initiation and throughout treatment.

The effectiveness of the educational materials was assessed using pre-specified criteria. The following criteria were applied:

- Effective receipt of educational materials: Receipt was considered effective if at least 70% of respondents reported receiving the educational materials.
- Effectiveness in increasing understanding: Each individual question was considered satisfactorily addressed if at least 70% of respondents answered the question correctly.

Primarily, the educational materials' content focuses on developing an understanding of the need for CYP2C9 genotyping prior to treatment initiation, managing bradyarrhythmias on treatment initiation, including the receipt and proper usage of the titration starter pack, and educating both HCP and patients

on need for treatment adherence. They also describe the management of infections, macular oedema, skin malignancies and pregnancy considerations.

Study design

The study included two distinct questionnaires designed to assess 1) HCPs (neurologists treating patients with MS and MS specialist nurses) knowledge in relation to their role in counselling and on-going management of patients who are receiving Mayzent treatment and 2) knowledge of patients who are receiving Mayzent or their caregivers in relation to their treatment.

Survey questions for HCPs and patients/caregivers were included to cover the important, identified or potential, risks of Mayzent.

Each questionnaire included an initial set of screening questions to confirm eligibility. Following this the HCP questionnaire comprised a total of 30 questions (two focused on receipt of educational materials resulting in 28 questions evaluating knowledge). The patient/caregiver questionnaire included a total of 19 questions (one focused on receipt of educational materials resulting in 18 questions evaluating knowledge).

Subjects and Setting

The study was conducted across two populations:

1. HCPs who prescribe, monitor and oversee the management / or provide in person medical supervision of patients on Mayzent (siponimod). These included treating physicians as well as MS specialist nurses
2. Patients/Caregivers of patients who are taking Mayzent (siponimod) to treat their MS and according to the prescription of their neurologists

The survey was administered in six European markets that represent distribution and prevalence of MS and where Mayzent (siponimod) was available and reimbursed for at least six months (Germany, Netherlands, Spain, Croatia, Sweden and Denmark), and Canada.

Study size

A total sample of N=220 completed surveys from HCPs (161 neurologists treating patients with MS and 59 MS specialist nurses) and N=118 completed surveys from patients/caregivers were evaluated.

Variables and data sources

Data sources included:

- For HCPs: eligibility materials administered through recruitment screener document, self-administered online survey questionnaire
- For Patients/caregivers: eligibility materials administered through the recruitment screener document, self-administered online survey questionnaire

Statistical methods

The analysis is descriptive in nature. For continuous variables, counts, means (with standard deviations), medians and ranges are provided. For categorical variables, frequencies and percentages (with 95% confidence intervals) are provided.

Results

HCPs were asked about receipt of two specific educational materials: the prescriber's checklist and the patient reminder card. HCPs in Netherlands were not asked about the patient reminder card as this is not in use in this market. A total of 85% (n=186/220) of HCPs recall receiving the prescriber's checklist and 75% (n=146/195) had received the patient reminder cards.

A total of 56% of patients/caregivers recalled receiving educational materials for Mayzent, with 16% unsure.

Comparisons have been made between HCPs or patients/caregivers who recall receiving the educational materials and those who do not, to evaluate the impact of the educational materials on knowledge. Those who recall receiving the materials show significantly higher levels of knowledge across some topics, highlighting the positive impact of educational materials on HCP and patient/caregiver understanding of key information relating to treatment with Mayzent.

The proportion of correct responses from HCPs and patient/caregivers across the remaining questions included in the surveys shows the level of knowledge required for the use of Mayzent. Among HCPs, 75% (21/28) of the survey questions had 50% or more correct responses. This included 12/28 questions that had 70% or more correct responses and these were all questions that required a single correct response. Furthermore, 7/28 questions demonstrated a strong level of knowledge, with 90% or more of HCPs responding correctly. Topics HCPs demonstrated good knowledge of include the need to determine CYP2C9 genotype, requirement for an ECG prior to initiation, risk of additive immune effects, timeframe to check liver transaminases, need to counsel patients on taking daily dose, first dose monitoring, counsel patients to report signs of infection, caution against sunlight, need to check VZV antibody status and the timeframe to delay treatment following VZV vaccination, actions needed if a patient has a serious infection, and the correct approach if a patient becomes pregnant.

There were 9/28 questions with 50–69% correct responses (4 with multiple correct responses, and 5 with a single correct response). There were also 7/28 questions with less than 50% correct responses (4 with multiple correct responses and 3 with a single correct response). Topics where knowledge was below 50% include the correct maintenance dose for patients with a genotype of CYP2C9*1*3 or CYP2C9*2*3, appropriate timing for skin examinations, specific details of the titration schedule, knowledge of all patient types where Mayzent is not recommended, patients requiring an ophthalmologic examination, and the length of time Mayzent remains in the blood following treatment discontinuation.

Of the 8 questions for HCPs with multiple correct responses that failed to reach the 70% threshold for success, 6 of these had one or more separate correct responses that were selected by 70% or more, indicating HCPs have good knowledge of these topics but failed to meet the criteria for success defined as selecting all correct responses.

In the patient/caregiver survey, 7/18 questions had 70% or more correct responses (3 with multiple correct responses (where selecting one of these was considered correct) and 4 with a single correct response), with only one question achieving 90% or higher. Topics patients/caregivers showed good knowledge of include the need to avoid pregnancy (>90%), need for an ECG prior to initiation, need for dose titration, symptoms of infection or liver impairment, skin conditions to report to their doctor, and the need to avoid exposure to sunlight.

5/18 questions had 50–69% correct responses (1 with multiple correct responses, and 4 with a single correct response). There were 6/18 questions with less than 50% correct responses (3 with multiple correct responses, and 3 with a single correct response). Topics where knowledge was below 50% include blood tests required prior to initiation, need for eye examinations, reasons for extended monitoring at first dose, timing of skin examination, duration of titration, and number of days can skip maintenance dose.

Of the 5 questions for patients/caregivers with multiple correct responses that failed to reach the 70% threshold for success, none of these had any separate correct responses that were selected by 70% of more.

Discussion

It should be noted that overall success has been measured based on clinically meaningful results, and not always by the strictest criteria, i.e. taking the proportion of respondents who selected all correct responses and no incorrect responses, or selecting an exact response which is aligned with the educational materials. The proportion of HCPs and patients/caregivers selecting some but not all the correct responses, or selecting a clinically more conservative response, is often higher, indicating good knowledge based on clinical experience and judgement. There were 8 questions for HCPs and 7 questions for patients/caregivers that had multiple correct responses – these represent a more robust

test of knowledge than a single response question and are more difficult for HCPs or patients/caregivers to be classified as fully correct due to the need to select all the correct responses.

HCPs demonstrated appropriate knowledge for most of the important identified or potential risks of Mayzent; however, areas where HCP knowledge appeared to be incomplete with regard to key topics included the following:

- Knowledge of the recommended maintenance dosing for patients with a genotype of CYP2C9*1*3 or CYP2C9*2*3 (H-Q4)
- Understanding of all patient types where Mayzent is not recommended (H-Q16). This question had 8 correct responses, and knowledge of these was varied with 4 correct responses selected by 50% or fewer HCPs and the other 4 selected by more than 65%
- Awareness of patient types where ophthalmologic examination is required prior to initiation (H-Q20). This question had 3 correct responses, of which each were selected by between 50% and 60% of HCPs; however, less than 50% selected all three correct responses
- Length of time female patients need to use effective contraception following discontinuation of Mayzent treatment (H-Q28). The correct answer of 10 days was selected by 40% of respondents; 57% chose 10 days or more while 39% responded that they did not know/were not sure of the correct answer.

Some areas where patients/caregivers show low levels of knowledge relate to patient eligibility and steps prior to initiation, where risk of low awareness among patients/caregivers is mitigated by the involvement of an HCP, who will be responsible for ensuring appropriate tests and checks are performed prior to initiation.

Areas where there are low levels of knowledge among patients/caregivers regarding key risks included the following:

- Awareness of all symptoms of macular oedema (P-Q12)
- Awareness of all symptoms of brain infection (P-Q13)
- Awareness of all symptoms of impaired liver function (P-Q14)
- Number of days they can interrupt Mayzent treatment before they need to reinitiate treatment with an up-titration schedule (P-Q19)
- Awareness of the number of days after stopping Mayzent that effective birth control is required (P-Q18)

Patients/caregivers have awareness of some symptoms to report and, based on the criteria of selecting at least one correct response, these questions achieve the 70% threshold for success. However, the proportion of patients/caregivers with awareness of all symptoms is low.

Although knowledge in some areas did not meet the designated threshold, it was unclear if the respondents were completing the survey from recall/memory or were using the educational materials while responding. The necessary information is available to HCPs and patients/caregivers in the label and patient information pack insert, in addition to being clearly explained in the educational materials. This is supported by the evidence that knowledge is higher among HCPs and patients/caregivers who recall receiving the educational materials, which demonstrates that the materials are effective at communicating the important safety information for Mayzent.

Conclusion

The survey results confirm that an acceptable number of HCPs involved in the prescribing and management of patients receiving Mayzent recall receiving the educational materials (Prescribers checklist). A lower proportion of patients/caregivers recall receiving the educational materials from their prescribers.

Patients/caregivers who were in receipt of the educational materials were more informed on some topics than those who did not recall receiving the materials, indicating that the materials were effective at communicating key messages. It is the responsibility of HCPs to distribute the materials to their patients. Ensuring that patients/caregivers receive the materials will have a positive impact on knowledge levels.

In summary, this robust assessment demonstrated overall appropriate understanding of the use of Mayzent, especially by HCPs. Several study limitations were acknowledged in relation to sampling considerations, response rate, survey question design, and reference to the educational materials.

The necessary information is available to HCPs and patients/caregivers in the label and patient information pack insert, in addition to being clearly explained in the educational materials. The educational materials have been thoroughly reviewed and are considered adequate to support the safe and effective use of Mayzent. With the completion of this study, the RMP commitment is fulfilled.

List of abbreviations

ECG	Electrocardiogram
EMA	European Medicines Agency
HCPs	Healthcare professionals including neurologists treating patients with MS and MS specialist nurses
MS	Multiple Sclerosis
RMP	Risk Management Plan
VZV	Varicella-zoster virus