Short Communication

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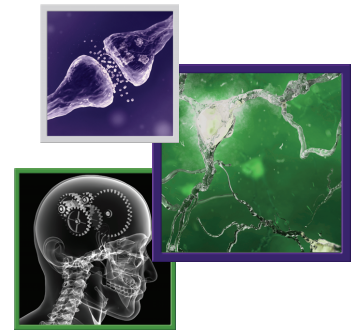
Neurodegenerative Disease Management



Satisfaction and practicality of a prefilled glatiramer acetate pen in relapsing–remitting multiple sclerosis patients

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Aim: Evaluation of practicality and patient satisfaction of a glatiramer acetate (GA) prefilled pen in patients with relapsing–remitting multiple sclerosis (RRMS). **Patients & methods:** A cross-sectional, multicenter, observational study evaluating patients' experiences with the GA-pen 3 months after its first use by means of self-reporting questionnaires. Primary end point was the proportion of patients who were satisfied with the pen. **Results:** 80 patients participated in the study. The majority (83.7%) was satisfied with the pen and 95% rated its application as easy or very easy. **Conclusion:** Most patients were satisfied with the GA-pen and rated its application as easy or very easy. Among the 12 device features, starting the injection without an injection button was considered the most appreciated feature. Improvements in pen functionality and design might allow patients to overcome many difficulties with self-injection, even those leading to nonadherence. But, this hypothesis awaits further validation by real-world follow-up studies.

Plain language summary: When patients with relapsing–remitting multiple sclerosis are treated with an injectable multiple sclerosis (MS) medication like glatiramer acetate (GA), doctors and patients have to think about the different methods of administration such as syringe or pen. This study aimed to assess the practicality and patient satisfaction with a prefilled pen containing GA in individuals with relapsing–remitting multiple sclerosis. The study involved 80 patients and used self-reporting questionnaires to evaluate their experiences with the GA pen. The results showed that most of the patients were satisfied with the GA pen and found the application of the pen to be easy or very easy. Starting the injection without the need for an additional button press was particularly well received by patients. These findings suggest that improvements in the functionality and design of the pen may help patients overcome challenges associated with self-injection.

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Keywords: adherence • disease-modifying therapy • glatiramer acetate • injection pen • multiple sclerosis • patient-reported outcome • RRMS • satisfaction

With a prevalence of more than 2.5 million people worldwide [1], multiple sclerosis (MS) affects the central nervous system (CNS) and leads to demyelinating and axonal damage in the cerebrum and spinal cord. Over the last two decades, the therapeutic armamentarium to treat mild to moderate forms of relapsing–remitting MS (RRMS) as well as highly active disease has been expanded considerably. The availability of many effective disease-modifying therapies (DMT) challenges decision-making for treating physicians in selecting the most appropriate therapy for each individual patient. With a growing understanding of the factors contributing to treatment adherence, patient preferences have gained increasing importance in the decision-making process, in addition to clinically relevant key factors such as efficacy and tolerability. In this context, route and frequency of administration have been shown

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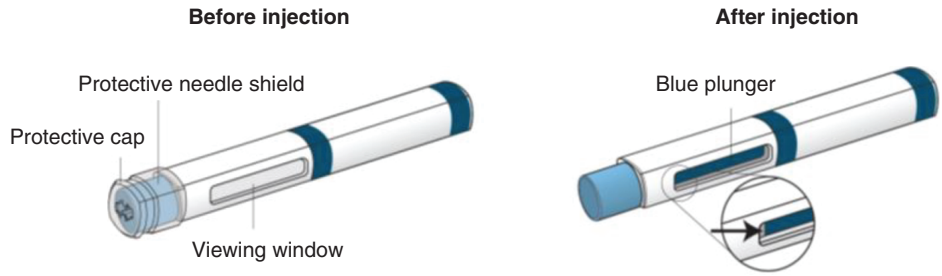

Figure 1. Single use glatiramer acetate prefilled autoinjector pen. During the injection process, the viewing window turns blue to indicate the injection progress. For details refer to the patient information leaflet [8].

to affect adherence, and anxiety due to self-injection may impair adherence and subsequently reduce positive long-term treatment responses [2,3].

Since 1996, glatiramer acetate (GA) in its subcutaneous 20 mg formulation is an established DMT for daily treatment of relapsing forms of MS with a well-recognized efficacy and safety profile [4,5]. Given the established association between frequency of administration and adherence [6], a formulation of 40 mg for a three-times weekly application was licenced in 2014 [7]. Both formulations were administered with a prefilled syringe. To address patient-relevant issues with self-injection, such as impaired manual dexterity and needle phobia, the administration device of the 40 mg formulation has been further modified. In 2019, a single-use prefilled autoinjector pen was licensed for subcutaneous self-injections of GA 40 mg thrice weekly (Figure 1). Compared with other autoinjector pens in the field of MS, the automated disposable injection device for prefilled syringes features a unique square, ergonomic design aimed to provide good grip and control. Instead of an injection button, the onset (start) of the injection is triggered by simply pushing the pen onto the skin. Audible clicks confirm the start and the end of the injection. In addition, a viewing window indicates the injection progress by changing color. To avoid accidental needle stick injuries, the needle is shielded before, during and after use. Although the pen was developed for self-injection at home, the first injection should be administered under the supervision of a healthcare professional, followed by monitoring the patient for another 30 min in case of adverse events. The prefilled pen can be stored in a refrigerator at 2–8°C. To avoid discomfort, it is advisable to allow 20 min for the refrigerated pen to warm up to room temperature before starting the injection. If no refrigerator is available, for instance when travelling, the prefilled pen can be stored between 15 and 25°C once for up to 1 month. The new GA 40 mg prefilled single-use injection pen was specifically designed to be user-friendly and to provide good acceptance for long-term use. The present noninterventional cross-sectional study was conducted to assess how MS patients value the features of the pen in a real-world setting in terms of practicality and overall treatment satisfaction.

Patients & methods

This cross-sectional, multicenter, open-label, observational Phase IV study was conducted in neurology practices associated with the NeuroTransData (NTD) network from July 2020 to June 2021. The NTD is a Germany-wide network of neurologists and psychiatrists founded in 2008. Members work in modern, highly effective and fully digitalised practices with a large patient pool throughout Germany. Currently, the NTD network includes 133 members from 66 practices taking care of more than 600,000 outpatients per year. The study design was reviewed and approved by the Ethics Committee of the Bavarian Medical Board (Bayerische Landesärztekammer, No. 20021), and is consistent with the ethical standards included in the Declaration of Helsinki of 1964 and its later amendments.

Patients aged ≥18 years with a confirmed diagnosis of RRMS according to the revised McDonald criteria of 2010 or 2017 [9,10] who started treatment with the single-use GA 40 mg prefilled injection pen were eligible to participate in the study. Patients could either initiate treatment with the GA pen *de novo* or switch from another mode of GA administration. Additional criteria for study participation were that therapy of RRMS with GA was indicated and that the decision about treating the patient with the GA pen was made independently from this study. GA pen treatment was only with branded GA (Copaxone®). All patients provided their written informed consent before entering the study. No diagnostic or therapeutic measures, exceeding the already pursued scope were required, and the treatment routine was not altered by this noninterventional, observational study.

Table 1. List of 12 questions (questionnaire 3) and corresponding device feature.

Question number	Question	Corresponding device feature
1	Few steps to prepare the pen for injection is useful	Minimal steps to prepare pen for injection
2	The hidden needle gives increased comfort	Hidden needle
3	It is useful to start the injection without an injection button	No injection button
4	It is easy to start the injection	Easy to start injection
5	The acoustic signal at the start and the end of the injection is useful	Confirmation sound
6	The injection process is quiet	Quit injection
7	The pen provides a good grip and control	The pen lies comfortable in hand while injecting
8	It is useful that the injection end is indicated visually through the viewing window turning blue	Colour injection guidance
9	It is easy to travel with my medication	Easy to travel with
10	The needle is shielded before and after use to avoid accidental needle stick injuries. It is a useful feature of the pen	Minimization of needle stick injuries
11	The pen gives the option of self-injection without the help of another person	Self-injection without primary help of family members
12	It is easy to dispose of the pen	Easy disposal

Please rate the answers on a scale from 0 (fully disagree) to 10 (fully agree).

Three months after their first use, patients rated their experiences with the self-administered pen via self-reporting questionnaires during routine visits. The three questionnaires were specifically designed for the study to collect information on a) satisfaction with the pen, b) ease of use and c) importance of the 12 different device functions (Supplementary Material). The primary end point was the proportion of patients who were satisfied with the pen, defined as a value of ≥6 on a visual analog scale (VAS) ranging from 0 (not satisfied at all) to 10 (very satisfied). Secondary end points were ease of use, rated on a 4-point Likert scale (very difficult, difficult, easy, very easy) and a ranking of device functions. Therefore, patients rated the 12 device features listed in Table 1 on a VAS ranging from 0 (fully disagree) to 10 (fully agree).

The collected data were analysed descriptively with epidemiological methods, using the SPSS (IBM Deutschland GmbH, Ehningen, Germany) for Windows programme package (Version 22.0). For continuous variables, statistical parameters including arithmetic mean, standard deviation and range were calculated. Frequency distributions for discrete variables were provided as percentage in relation to the total sample.

The primary hypothesis was that the proportions of patients who are satisfied and dissatisfied using the GA pen will be unequal, and that more patients will be satisfied with the GA pen. The null hypothesis was that 50% of patients will be satisfied using the GA pen. To reject the null hypothesis, using a two-sided test with 5% significance level and 80% power, 47 patients were required. To account for an expected dropout rate of 25%, a total of at least 63 patients were necessary. Sample size was calculated using a one-sample χ-squared test with normal approximation.

Results

In total, 80 patients with RRMS from 13 sites participated in the study. Of these, 72.5% (58/80) were treatment-naive (*de novo*) and 27.5% (22/80) had up to three prior therapies. At baseline, patients had a low disability score EDSS (Expanded Disability Status Scale), mean score was 1.3 (range 0–5.5). Median age was 41.8 years (range 19–81) and 70% (56/80) were female. 35% of patients were older than 65 years. All were of Caucasian origin. Mean (SD) disease duration from diagnosis was 6.8 (6.4) years.

Three months after the first use of the GA pen, the great majority of patients (83.7%, 67/80) indicated by a rating ≥6 on the VAS that they were satisfied with the pen (Figure 2). A total of 95% (76/80) of patients validated the application of the GA pen as easy or very easy (Figure 3). This is also reflected by the positive ratings of the 12 device features (Figure 4). Starting the injection without an injection button was considered a very useful feature and received the highest rating (9.3 ± 1.7). Furthermore, patients highly agreed that it was easy to start the injection and that the pen provides good grip and control. They appreciated the increased comfort provided by the hidden needle and considered it useful that very few steps were required to make the pen ready for injection. Patients also agreed that it was useful that the injection end is indicated visually through the viewing window turning blue and that the needle is shielded before and after use to avoid accidental needle stick injuries. Disposal of the pen was

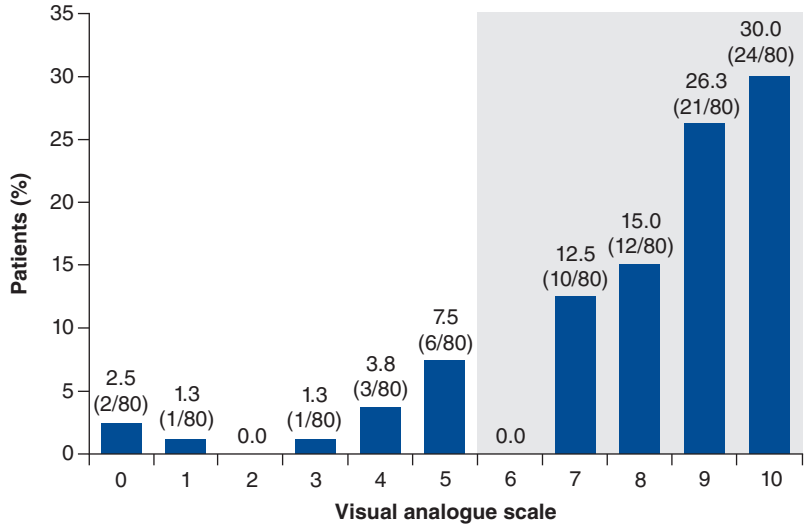

Figure 2. Rating of satisfaction on the visual analog scale ranging from 0 (not satisfied at all) to 10 (very satisfied). A value ≥6 (grey zone) indicated satisfaction with the pen.

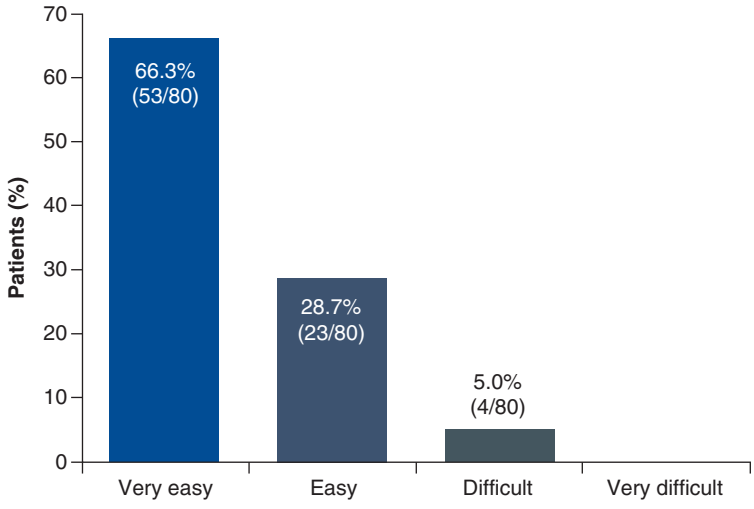

Figure 3. Ease of use, rated on a 4-point Likert scale.

considered easy and the acoustic signal at the onset and the end of the injection was rated useful. Self-injection was appreciated to be performed without the help of another person. The injection process was considered quiet, and the majority agreed that it is easy to travel with the medication.

Discussion

This study among 80 RRMS patients revealed a high rate of satisfaction with a single-use injection pen, as measured by a visual analog scale. The VAS was preferred to other validated tools assessing treatment or medication contentment such as the Treatment Satisfaction Questionnaire for Medication (TSQM) [11] or the Medication Satisfaction Questionnaire (MSQ) [12] because this study specifically aimed to assess patient's satisfaction with the application of a drug rather than satisfaction with the medication itself, which has been extensively studied before [13,14]. It turned out that most of the patients considered the application easy to manage and favorably rated any of the 12 selected features facilitating the application of the pen.

MS is a chronic disease requiring long-term treatment. Adherence to the prescribed regimen is a prerequisite for positive treatment response in terms of limiting the number of relapses, preventing new lesion formation, and delaying disability progression. Factors contributing to adherence in MS have been identified and reviewed over the past two decades [2,3,6], which led to a better understanding of patient's predilections. To boost adherence,

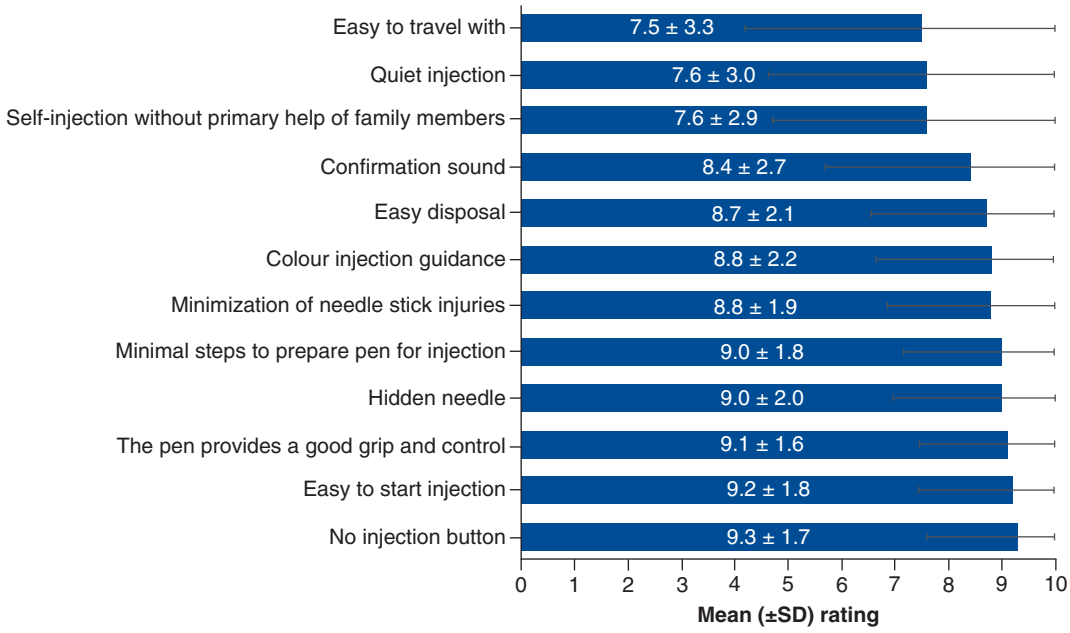

Figure 4. Ranking and mean rating of the device features on the visual analog scale.
SD: Standard deviation.

formulations and administration devices have been adapted to reduce barriers to injection therapy and to better meet the patient's needs and preferences.

Depending on which functional systems are affected, physical disability can make self-injection difficult [15]. Autoinjectors have proven beneficial for patients with poor manual dexterity [16]. Correspondingly, the features appreciated most by the patients of this study, like push-on-skin activation instead of a button, easy injection start, comfortable handling during the injection, and few preparation steps, address this issue, confirming that the GA pen investigated here provides good grip and control by optimized ergonomics. Additionally, the square shape prevents the pen from rolling away. Patients also agreed that the injection can be performed without primary help from others. Overall, the convenience of the administration procedure has been shown to substantially contribute to treatment adherence [17].

Some patients considered the process of regular self-injection burdensome. In particular, needle phobia has been identified to be a barrier to the self-administration of injectables. Up to 22% of the general population is known to experience needle phobia [18]. With the GA pen, the needle remains hidden at all times, which may help reduce anxiety. This feature, along with minimisation of needle stick injuries also achieved high levels of agreement among the patients.

The completion of the injection is indicated visually by a blue color filling the viewing window. In addition, an acoustic signal indicates the onset and end of the injection. The participants regarded both features as useful. In contrast, the ability to travel with the medication was considered of lower importance in comparison with the other features. Depending on their level of impairment, MS patients may be limited in their capacity to travel.

The efficacy and safety of GA administration have been investigated in earlier studies and therefore were not part of this investigation [4,5,7]. However, the use of autoinjector devices is generally known to reduce the incidence of injection site reactions compared with manual injection, thus adding to the patient's comfort [19].

Our results are in line with data from studies investigating the acceptance of autoinjector devices or pens for other injectables among MS patients [20–24]. For instance, an autoinjector pen for intramuscular IFN β-1a injections was also found to be associated with high levels of satisfaction and easy handling with little need for caregiver assistance [21]. Similarly, an electronic autoinjector obtained high degrees of patient satisfaction concerning to support of IFN β-1b treatment. In particular, the features of optical and acoustic signalling were considered very important [23].

The positive opinion of the patients concerning the features of the GA pen along with the attested easy application is reflected by the high rate of satisfied patients. Earlier studies have shown a meaningful impact of treatment

satisfaction on adherence and long-term persistence to therapy in general [2,17,25] and for GA in particular [13,14]. Combined with the favorable benefit/risk profile of GA, our results provide evidence that application of the GA pen might also increase adherence and, in consequence, lead to better long-term outcomes. Whether the GA pen has a beneficial long-term effect on adherence in clinical practice needs to be further investigated in real-world follow-up studies.

The study is limited by its noninterventional design, the reliance on patient questionnaires, and the absence of a direct comparator group. To limit confounders, patients had 3 months to familiarize themselves with the new application device before data were collected. This delay was intended to reduce potential bias in patients who switched from another therapy to GA (27.5%), thus having two adjustments affecting their judgement.

Conclusion

Adherence to treatment in multiple sclerosis is crucial to optimize the long-term treatment outcome of this chronic disease. Nonetheless, this issue remains a major challenge [26–28]. Improvements in pen functionality and design seem to allow patients to overcome some major difficulties with self-injection, including injectable MS medications. The current study shows that most patients were satisfied with the GA self-injection pen and rated its application as easy or very easy. Among the 12 device features, starting the injection without an injection button was considered the most appreciated feature and received the highest rating. Overall, all aspects of functionality and practicality received high positive ratings indicating the subjective relevance of such features for MS patients with injectable therapies. Improvements in pen functionality and design might help (allow) patients to overcome many difficulties with self-injection, even those that can lead to nonadherence to MS medications. But this hypothesis awaits further validation by real-world follow-up studies.

Summary points

- An automated disposable injection device for 40 mg glatiramer acetate (GA) prefilled syringes was developed to address patient-relevant issues with self-injection.
- In this German multicentre observational study relapsing–remitting multiple sclerosis (RRMS) patients rated their satisfaction with the GA self-injection pen.
- The single-use prefilled GA pen achieved a high rate (83.7%) of satisfied patients.
- A total of 95% of patients found the application easy or very easy.
- Among the 12 device features, starting the injection without an injection button was considered the most appreciated feature and received the highest rating.
- Patients also highly agreed that it was easy to start the injection and that the pen provides good grip and control.
- Treatment satisfaction is known to significantly impact patient adherence.
- Satisfaction with the GA pen may translate into improved treatment outcomes.
- Whether the use of GA pen has a beneficial effect on adherence in clinical practice needs to be investigated in further targeted long-term real-world studies.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/nmt-2022-0031

Author contributions

H Schreiber, J Hipp and F Roßnagel were responsible for study conception and design and drafting of the manuscript; H Schreiber, F Roßnagel and C Moritz were responsible for acquisition and interpretation of data; F Roßnagel and C Moritz were responsible for data analysis; all authors were responsible for revising the manuscript draft critically for important intellectual content; all authors provided final approval of the version to be published.

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Competing interests disclosure

H Schreiber: has received honoraria for advisory boards/consulting/lectures and research grants for clinical studies from Almirall, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Genzyme, Janssen, Merck, Novartis, Roche and Teva. J Hipp is an employee of TEVA. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

Teva GmbH provided medical writing support for drafting (in the development of) this article, which was conducted by P Jöstingmeyer (med: unit GmbH, Germany).

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval. In addition, informed consent has been obtained from the participants involved.

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