

Preferences and Perspectives of Specialist Multiple Sclerosis Nurses and Patients with Multiple Sclerosis Regarding the New RebiSmart[®] 3.0 Autoinjector versus Other Assistive Devices

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Purpose: RebiSmart[®] is an electromechanical multidose autoinjector developed for administering subcutaneous interferon beta-1a in patients with multiple sclerosis (pwMS). This online survey aimed to understand MS nurses' and pwMS preferences and perceptions regarding the features of an upgraded version of the RebiSmart device (RebiSmart 3.0) compared to other assistive devices used for multiple sclerosis (MS) therapy.

Patients and Methods: Eligible MS nurses and pwMS from Germany, Italy, and the United Kingdom completed a double-blind, 30-minute online self-administered questionnaire, including a 10-minute video describing the features of RebiSmart 3.0 and its use in administering interferon beta-1a.

Results: In total, 102 participants (MS nurses, n=52; patients, n=50) completed the survey. Overall, 70% respondents found the RebiSmart 3.0 device "very"/"extremely" appealing, 53% were "very"/"extremely" interested in learning more, and 71% stated they would be "very"/"extremely" comfortable using (pwMS) or educating (MS nurses) on it. Among current or recent RebiSmart 2.0 users (vs RebiSmart 2.0 nonusers), 67% (vs 52%) rated RebiSmart 3.0 "very" or "extremely" appealing, 52% (vs 43%) were "very" or "extremely" interested in learning more about the device, and 67% (vs 48%) stated they would be "very" or "extremely" comfortable using the RebiSmart 3.0 device. Respondents ranked customizable injection process (including injection speed, hold time, depth and rotation guide), self-injection process, and hidden needle as the most important self-assistive device features. RebiSmart 3.0 was rated higher than other self-injecting devices on all tested features. Overall, with respect to the top three features, 89% of the MS nurses and 73% of PwMS rated RebiSmart 3.0 "very good" or "excellent". After reviewing the video, 52% respondents had no questions, 67% nurses recommended providing more information on the customizable injection process feature of RebiSmart 3.0 to patients, and 88% nurses considered patient demonstration materials to be the most helpful type of information for them when initiating and educating pwMS on self-assistive devices.

Conclusion: The overall reactions of MS nurses and pwMS to the RebiSmart 3.0 device features were positive. The incremental advances over previous versions of the device as well as in comparison with other currently available assistive devices were welcomed. The MS nurses identified key needs for patient education on the use of the device and the suitable approaches (training videos and educational leaflets) to support MS nurses and pwMS.

Keywords: subcutaneous interferon beta-1a, customizable injection, hidden needle, neurodegenerative disorder, nurse and patient device assessment, online survey

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating, and neurodegenerative disease of the central nervous system that commonly affects young adults.¹ Although there is no definite cure for MS, several disease-modifying therapies (DMTs) approved for treating MS reduce the relapse frequency and delay disease progression.^{1,2} Similar to

other chronic diseases, MS requires long-term treatment regimens, and nonadherence or suboptimal adherence to treatment remains a key challenge in managing MS.³ Several strategies have been implemented to improve the management of MS, such as identifying novel treatments, adopting patient support programs, and modifying drug delivery systems.^{4–6} The development of innovative autoinjection assistive devices is one such strategy for optimizing adherence, which ensures that patients with MS (pwMS) can receive maximum therapeutic benefits from their medication.^{4–6} Currently, several autoinjectors are available for the administration of MS treatments, each featuring unique designs, handling and distinct features. Betaconnect[®] is an electronic autoinjector designed for the administration of Betaseron[®]/Betaferon[®] (interferon beta-1b), whereas ExtaviPro[™] is as a mechanical autoinjector used for the administration of Extavia[®] (interferon beta-1b).^{7,8} Additionally, Avonex[®] and Plegridy[®] pens are available as prefilled single-dose autoinjectors intended for administration of Avonex[®] (interferon beta-1a) and Plegridy[®] (peginterferon beta-1a), respectively.^{9,10}

The RebiSmart[®] autoinjector device (Ares Trading S.A., Eysins, Switzerland [an affiliate of Merck KGaA]), is the first electromechanical multidose assistive device developed for administering subcutaneous interferon beta-1a ([sc IFN β -1a]; Rebif, Merck Europe, B.V., Amsterdam).^{11,12} Sc IFN β -1a is a well-established, first-line DMT used for treating relapsing MS.^{13–15} Sc IFN β -1a is typically self-administered at a recommended dose of 44 μ g three times a week.^{13,14,16} The RebiSmart device has been shown to improve patients' adherence to sc IFN β -1a therapy, which may lead to better clinical outcomes.^{17,18} The device has evolved to meet the changing needs of pwMS, as part of a comprehensive and continuous evaluation to determine whether the device is optimized to deliver maximum patient benefit that sc IFN β -1a therapy can provide. A recent formative usability study identified several strengths and opportunities for improvement in the existing RebiSmart device and formed the basis for an upgraded version of the device, RebiSmart 3.0.^{19,20}

The evolution of MS therapy has significantly impacted the role of MS nurses, deepening their involvement in the diagnosis, management, and support of pwMS.²¹ Because specialized MS nurses are well versed with the progression of MS and are acutely aware of the needs of their patients and patient care partners, they play a critical role in educating pwMS and their care partners about the disease and treatment options. MS nurses' opinions about the treatment devices used by patients may influence the patients' decision-making.²¹ Thus, it is imperative to understand MS nurses' perspectives as well as identify and address potential education gaps in training pwMS on the use of self-injection assistive devices.

From the patients' perspective, the choice of DMT greatly depends on personal preference and pwMS are required to evaluate the risk–benefit trade-offs of a treatment in terms of different features or attributes.²² As the number of DMTs and devices for administering these DMTs are expected to expand, it is relevant to study patients' understanding and attitudes toward new developments (DMTs and devices) and determine the device features that would be desirable.

Here, we report the results of a multinational online survey of MS nurses and pwMS that aimed to understand their perspectives on an upgraded version of the RebiSmart device (RebiSmart 3.0) compared with other assistive devices used for administering injectable MS therapies as well as identify potential educational gaps.

Patients and Methods

Survey Design and Participants

MS nurses and pwMS from an online panel of respondents based in Germany, Italy, and the United Kingdom (UK) were invited to participate in the study fielded from April through May 2022. The participants were asked to respond to a double-blind 30-minute online survey that included a self-administered questionnaire to determine study eligibility, a 10-minute video (with blinded device name, referred as Device Q during the survey) describing the features of the new RebiSmart 3.0 device and its use for administering sc IFN β -1a ([Supplementary Video](#)), followed by discrete choice questionnaire designed to meet the study objectives. The questionnaire was designed to collect information on the respondents' initial reactions to the features of the new RebiSmart 3.0 device and its uses, identify potential RebiSmart 3.0 characteristics that have a clear benefit compared with other assistive self-injection devices, and identify perceived educational gaps to be addressed to ensure smooth transition to RebiSmart 3.0 from current self-assistive devices, including RebiSmart version 2.0.

Eligibility to participate in the study was based on responses to a set of screening questions to ensure that participants had sufficient knowledge and experience with the use of assistive devices for injecting therapies to treat MS. Specialist MS nurses who had spent most of their worktime assisting pwMS, had initiated or educated pwMS on self-administered injectable treatments, and had at least 3 years of experience in initiating, educating, or managing pwMS on self-administered injectable treatments were eligible to participate in the study. PwMS who had experience with self-administered injectable treatment without support from their care partner, including current or recent users of RebiSmart 2.0 or other assistive devices, were also included in the study. We defined current RebiSmart 2.0 users as those who had used RebiSmart 2.0 for at least 1–2 years, recent RebiSmart 2.0 users as those who had used the device for at least 1 year but recently discontinued usage within the past 9 months, and current/recent users of self-administered injectable treatments other than RebiSmart 2.0 as those who had used such devices for at least 6 months and were currently using the devices or had recently discontinued them. PwMS who were likely to speak with their treating physician about the possibility of switching treatments in the next 6 months were excluded.

The survey included an exhaustive list of the features of assistive devices generated through a review of RebiSmart 2.0 and 3.0 user guides/product videos, a literature review of previous publications on assistive devices, and pilot interviews ($n = 3$) conducted in the UK to test or confirm features of any assistive device that are considered important to pwMS or MS nurses' satisfaction. Participants were asked to select the one feature they thought was most important and the one feature that they thought was least important to their satisfaction (for MS nurses, their patients' satisfaction) while using a self-injecting device to receive the MS treatment.

After watching the blinded demonstration video of the RebiSmart 3.0 device, all respondents were asked to rate their receptivity to the device (for example, appeal of the device, interest in learning more about the device, and comfort using the device) on a scale of 1–5, with 1 being “not at all” appealing/interested/comfortable and 5 being “extremely” appealing/interested/comfortable. Respondents were also asked to rate (scale of 1–5 with 1 being “poor” and 5 being “excellent”) how well they expected RebiSmart 3.0 to perform across each of the above-mentioned device features. To identify perceived educational gaps regarding the device features, respondents were asked questions such as “What sources do you use to stay up to date on MS treatments and associated devices?”, “Which of the following features of RebiSmart 3.0 do you have questions or concerns about that you would like more information on?”, and “From which sources would you want to learn more about RebiSmart 3.0?” MS nurses were asked to rank the top three features of RebiSmart 3.0 that manufacturers should provide additional materials or education on for pwMS who may use this device.

The survey questionnaire (select) is provided in the [Table S1](#).

The survey was organized and conducted through an independent external market research company (HawkPartners LLC, USA) according to international quality standards.

Statistical Analysis

Maximum difference analysis was used to determine the relative ranking of the device features in order of importance to user satisfaction for pwMS or perceived user satisfaction from MS nurses' viewpoint. Implementation of the Maximum difference analysis was chosen for this study in order to achieve clearer differentiation among the selected device attribute features and eliminates straight-lining and scale usage effects which can complicate traditional self-stated rating scale analysis.^{23,24} The responses were then analyzed using hierarchical Bayesian techniques to obtain the relative attribute motivation scores at the individual respondent level.

The survey results were quantified using anchored maximum difference analysis.²⁵ The respondents were presented with a randomly selected subset of features outside the maximum difference exercise and asked which of these assistive device attributes are most important to their satisfaction with any assistive device for self-administering an MS therapy. This additional information would help determine, for each individual, a performance level above which they would be satisfied, thereby setting a threshold for success. The action-based threshold (anchor) can highlight discrete messages with the power to appeal. Any message with a score above 100 was considered “significantly more or important”.

General Data Protection Regulation (GDPR) guidelines were followed, and all nurses and patients provided signed informed consent, which they were free to withdraw at any time without needing to state their reasons.

Results

Participants' Demographics and Profile

A total of 102 respondents (MS nurses, n = 52; pwMS, n = 50) completed the survey. Among the 52 MS nurses who participated in the survey, 16 were from the UK, 18 from Germany, and 18 from Italy. All the MS nurses were well experienced, with an average of 19 years of experience in nursing and approximately 10 years of experience in initiating, managing, and educating pwMS regarding self-injectable devices. On an average, they assisted approximately 94 pwMS per month. In addition, all eligible MS nurses reported having experience in training patients on the RebiSmart device. They also reported having experience in handling other self-assisted devices used for delivering a variety of self-injecting DMTs such as Copaxone[®] [glatiramer acetate] (80%), Plegridy[®] [peginterferon beta-1a] (68%), Avonex[®] [Interferon beta-1a] (68%), Kesimpta[®] [ofatumumab] (58%), Tysabri[®] [natalizumab] (50%), Betaseron[®] [Interferon beta-1b] (45%) and Extavia[®] [Interferon beta-1b] (27%). Of the 50 pwMS included in the survey, 18 were from Italy, 17 from the UK, and 15 from Germany. Among the current or recent RebiSmart 2.0 users (n = 27), 43% (n = 12) had used the device for 2 years or less. The participants' profiles and demographics are presented in Table 1.

Table 1 Respondent Profiles (n = 102)

Characteristics	MS nurses (N = 52)
Location, n (%)	
Germany	18 (34.6)
Italy	18 (34.6)
UK	16 (30.8)
Average time in practice, years	19
Average number of years initiating, managing, and educating pwMS on self-injectable devices, years	10
Average number of pwMS seen per month, n	94
Practice type (%)	
University/teaching hospital	36.5
Specialized MS center	42.3
Community hospital	15.4
Group private clinic	3.8
Private clinic	1.9
Time spent with pwMS, (%)	
Self-injection education	77.3
Educating on MS	9.6
Recording medical history	6.6
Monitoring health	6.5
Characteristics	PwMS (N = 50)
Location, n (%)	
Germany	15 (30)
Italy	18 (36)
UK	17 (34)
Female patients, n (%)	35 (70)
Age (years), n (%)	
20–34	11 (22)
35–49	17 (34)
50–65	22 (44)

(Continued)

Table 1 (Continued).

Characteristics	MS nurses (N = 52)	
	Symptoms	Diagnosis
Start of MS-related symptoms and diagnosis, n (%)		
1–5 years ago	8 (16)	8 (16)
6–10 years ago	15 (30)	16 (32)
11–15 years ago	9 (18)	10 (20)
15–30 years ago	17 (34)	15 (30)
30+ years ago	1 (2)	1 (2)
Current/Past RebiSmart 2.0 device user tenure, n (%)	(n = 27)	
<48 months	15 (57)	
48–120 months	7 (26)	
>120 months	5 (17)	

Abbreviations: pwMS, patients with multiple sclerosis; MS, multiple sclerosis.

Overall Receptivity to RebiSmart 3.0

Overall, 70% of the respondents, including MS nurses and pwMS, rated the RebiSmart 3.0 device “very” or “extremely” appealing, 53% were “very” or “extremely” interested in learning more about the device, and 71% stated they would be “very” or “extremely” comfortable using (58% pwMS) or educating patients on this device (83% MS nurses) (Figure 1). Compared with pwMS, MS nurses had an overall more positive initial reaction to the device, with 79% of the MS nurses vs 60% of the pwMS rating RebiSmart 3.0 “very” or “extremely” appealing.

Current or recent RebiSmart 2.0 users were slightly more receptive to RebiSmart 3.0 than RebiSmart 2.0 nonusers. Among current or recent RebiSmart 2.0 users (vs RebiSmart 2.0 nonusers), 67% (vs 52%) rated RebiSmart 3.0 “very” or

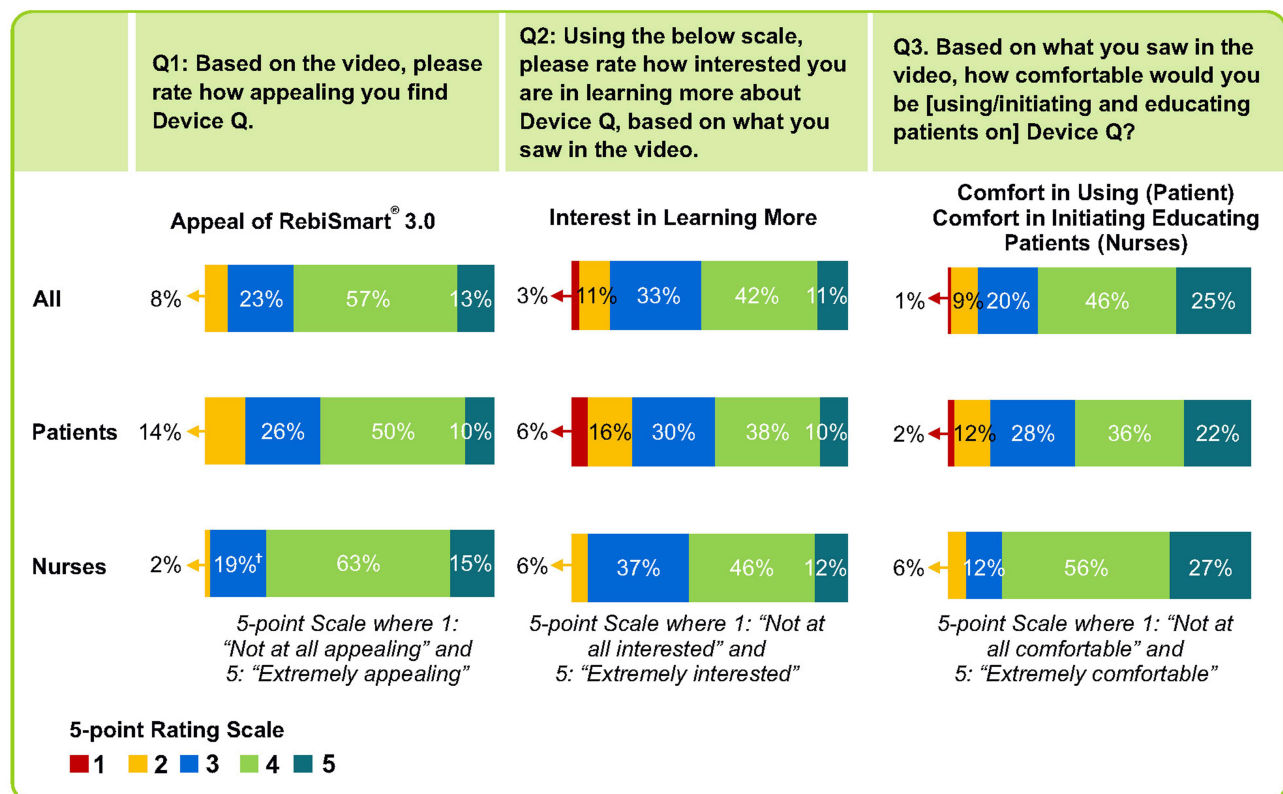


Figure 1 Overall receptivity to RebiSmart 3.0. [†]Indicates significantly higher than patients at 90% confidence.

“extremely” appealing, 52% (vs 43%) were “very” or “extremely” interested in learning more about the device, and 67% (vs 48%) stated they would be “very” or “extremely” comfortable using (pwMS) or educating pwMS (MS nurses) on this device. Of note, among the RebiSmart 2.0 users who rated RebiSmart 3.0 either “somewhat”, “not very” or “not at all” appealing (n = 9), majority (78%, n = 7) were “very” or “extremely” satisfied with their current RebiSmart 2.0 device. Similarly, among the RebiSmart 2.0 users who rated “somewhat”, “not very” or “not at all” interested in learning more about RebiSmart 3.0 (n = 13) and rated “somewhat”, “not very” or “not at all” comfortable using RebiSmart 3.0 (n = 9), 69% and 78% were highly satisfied with their current device.

Most Important Features of an Assistive Device

The top three features that were ranked as most important driver for their satisfaction with any self-assistive device by both pwMS and MS nurses were a customizable injection process, self-injection process, and hidden needle (Figure 2). The maximum difference analysis of the survey results revealed that pwMS ranked the self-injection process as the most important, whereas MS nurses ranked the customizable injection process as the most important device feature for user satisfaction. Focusing on the pwMS sample, customizable injection process was the most important feature for RebiSmart 2.0 users (n = 27) whereas self-injections process was the most important feature for RebiSmart 2.0 nonusers (n = 23, data not shown). In addition to the top three features, “very” or “extremely” satisfied current/recent RebiSmart 2.0 users (n = 22) identified size of device as another important feature for their satisfaction whereas features such as visual feedbacks and prompts were important for the “somewhat” “not very” or “not at all” satisfied RebiSmart 2.0 users (n = 5).

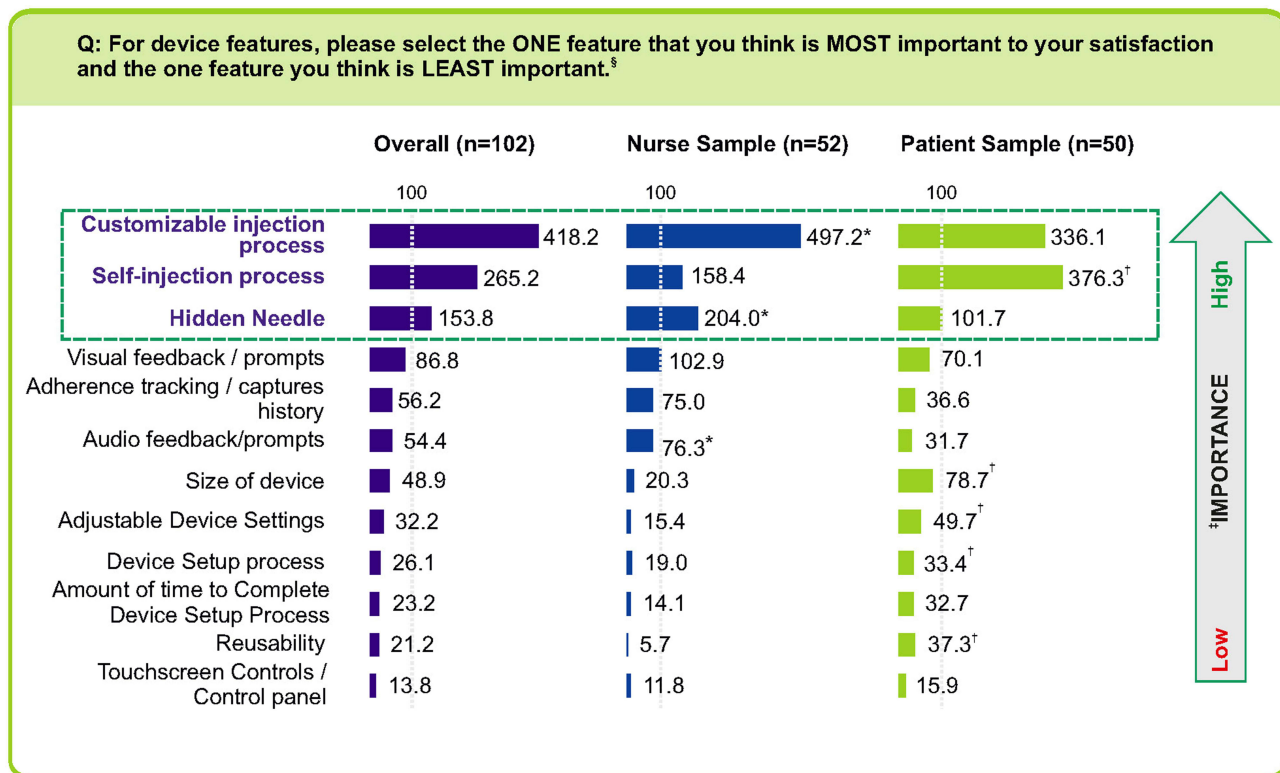


Figure 2 Importance of device features to user satisfaction: Anchored Probability Index. *Indicates significantly higher than patients at 90% confidence. [†]Indicates significantly higher than nurses at 90% confidence. [‡]The anchored maximum difference analysis was used for the relative ranking of the device features from greatest to least importance to user satisfaction. [§]This question was asked multiple times and only 4 features were shown at a time and were randomized in each screenshot; so the respondent would end up seeing a single feature listed on different screenshots.

Abbreviation: n, number of respondents.

Preference for RebiSmart 3.0 versus Other Assistive Devices

RebiSmart 3.0 outperformed other self-injecting devices for sc IFN β -1a on all tested features, including the top three ranked features (Figure 3). Overall, 81% and 50% of the respondents rated RebiSmart 3.0 and other devices as “very good” or “excellent” on the top three ranked features, respectively. MS nurses rated RebiSmart 3.0 higher than patients. With respect to the top three features, 89% of the MS nurses rated RebiSmart 3.0 “very good” or “excellent”, whereas only 55% rated other devices “very good” or “excellent” on the same features. Similarly, a higher proportion of pwMS (73%) rated RebiSmart 3.0 “very good” or excellent on the top three features, whereas only 44% gave the same rating to other devices for the same features. Focusing on the pwMS sample, both the RebiSmart 2.0 users (n = 27) and the RebiSmart 2.0 nonusers (n = 23) rated RebiSmart 3.0 performance higher than other self-assistive devices on nearly all features. Notably, more RebiSmart 2.0 users than RebiSmart 2.0 nonusers rated RebiSmart 3.0 performance higher than other self-assistive devices on all features, including the top three features: 85%, 89% and 78% of the RebiSmart 2.0 users vs 52%, 65% and 65% RebiSmart 2.0 nonusers rated RebiSmart 3.0 “very good” or “excellent”, on customizable injection process, self-injection process and hidden needle feature, respectively (Figure 4).

Moreover, highly satisfied (“very” or “extremely”) current or recent RebiSmart 2.0 users rated the performance of RebiSmart 2.0 and 3.0 device as similar, especially for the top three most important features, whereas less satisfied current or recent RebiSmart 2.0 users rated RebiSmart 3.0 performance as better than that of RebiSmart 2.0 on all features (data not shown).

Perceived Educational Gaps

Following a review of the video, 52% of the respondents reported having no questions or concerns about any of the RebiSmart electromechanical multidose autoinjector features. The proportion of respondents with questions or concerns for each feature did not differ significantly between pwMS and MS nurses except for the adherence tracking feature,

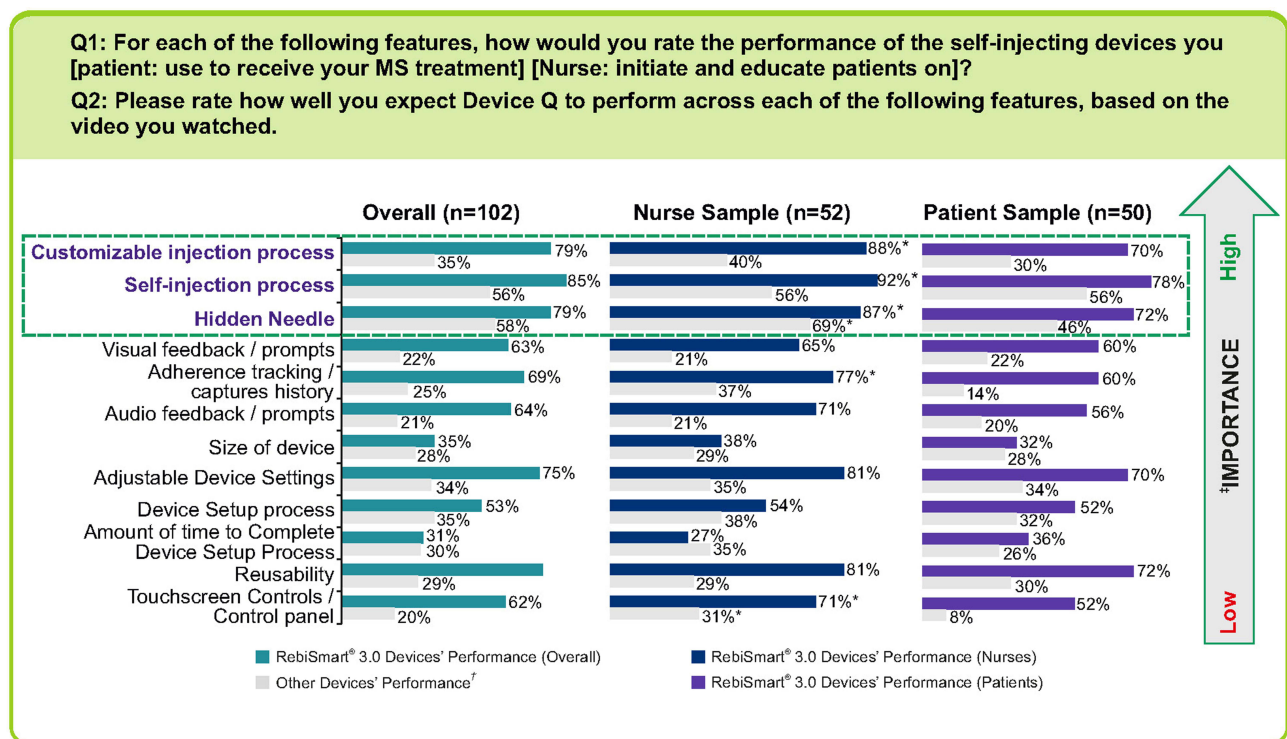


Figure 3 Performance of RebiSmart 3.0 vs other self-injecting devices on key features. *Indicates significantly higher than patients at 90% confidence. †RebiSmart® 2.0 Non-Users (n=23) that responded to questions on “Other devices performance”, were asked to consider the assistive device that they are currently using or recently used. ‡The anchored maximum difference analysis was used for the relative ranking of the device features from greatest to least importance to user satisfaction. **Abbreviations:** MS, multiple sclerosis; n, number of respondents.

Q1: For each of the following features, how would you rate the performance of the self-injecting devices you (patient) use to receive your MS treatment?

Q2: Please rate how well you expect Device Q to perform across each of the following features, based on the video you watched.

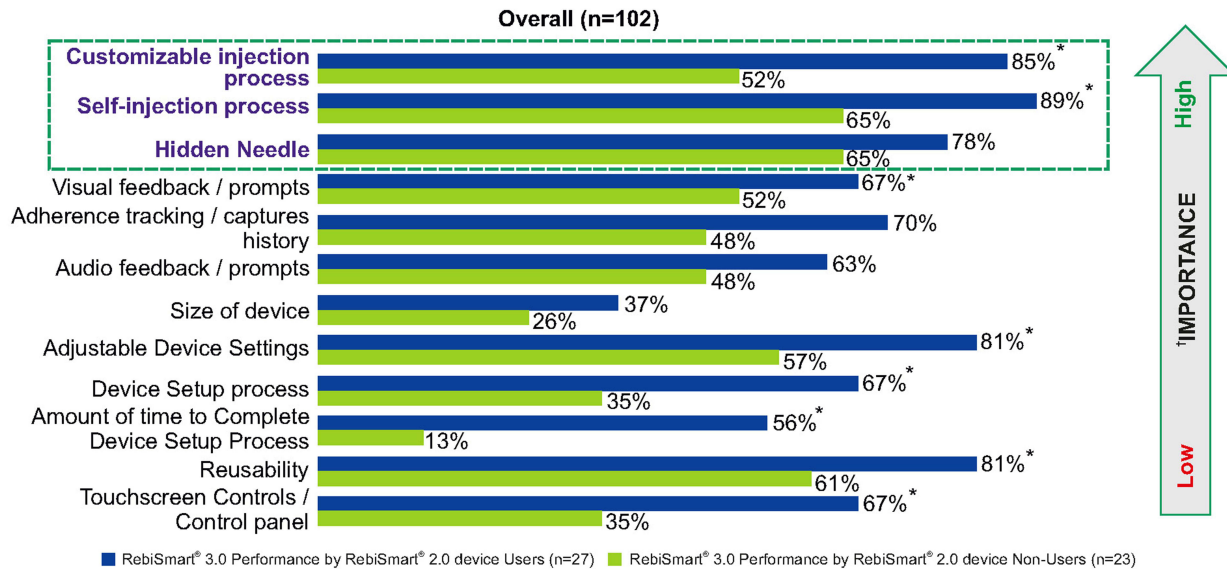


Figure 4 Performance of RebiSmart 3.0 by RebiSmart 2.0 users vs RebiSmart 2.0 non-users. Data refers to proportion of respondents rating the feature either very good (4) or excellent (5) on the 5-point scale. *Indicates significantly higher than RebiSmart® 2.0 device Non-Users at 90% confidence. †The anchored maximum difference analysis was used for the relative ranking of the device features from greatest to least importance to user satisfaction.

Abbreviations: MS, multiple sclerosis; n, number of respondents.

where a significantly higher proportion of MS nurses wanted more information on this feature than pwMS (17% vs 6%). A higher proportion of RebiSmart 2.0 nonusers had questions regarding the features compared with users, although the difference was not statistically significant (Figure 5).

Overall, 67% of the MS nurses recommended providing more information to pwMS on the customizable injection feature of RebiSmart 3.0, followed by the self-injection and device setup processes (42% for both; Figure 6). Patient demonstration materials were considered most helpful type of information by 88% of MS nurses for initiating and educating pwMS on self-assistive devices. In addition, MS nurses also considered instructions concerning device use (67%), take-home materials for patients (62%), and manufacturer support contact information for patients (46%), nurses/physicians (37%) as helpful types of information to initiate and educate pwMS on self-assistive devices.

Discussion

Several studies have shown that RebiSmart autoinjector device helps pwMS to adhere to the sc IFN therapy and consequently, may help to improve their clinical outcomes.^{6,17,18,26–28} The design of the device has continuously evolved to meet the evolving needs of pwMS. In this quest of unrelenting improvement, a recent formative usability study aimed at identifying recommendations for improvement to the existing RebiSmart device.¹⁹ The formative study of the upgraded device prototype identified several strengths (eg ease of use, size of the device, sound prompts, screen clarity and device safety etc.) and opportunities for improvement (consideration of dexterity among pwMS, modification of on-screen functionality).¹⁹ These recommendations from the formative usability study formed the basis of the upgraded device, RebiSmart 3.0. A subsequent summative usability study validated the safety of use of the RebiSmart 3.0 device and showed a favorable usability of the device in the user needs survey.²⁰

This multinational online discrete choice survey showed favorable initial reactions from pwMS and MS nurses to the RebiSmart 3.0 device, which is an upgraded version of the currently available RebiSmart 2.0 device. Following the video

Q: Which of these features of Device Q do you have questions or concerns about that you would like more information on?

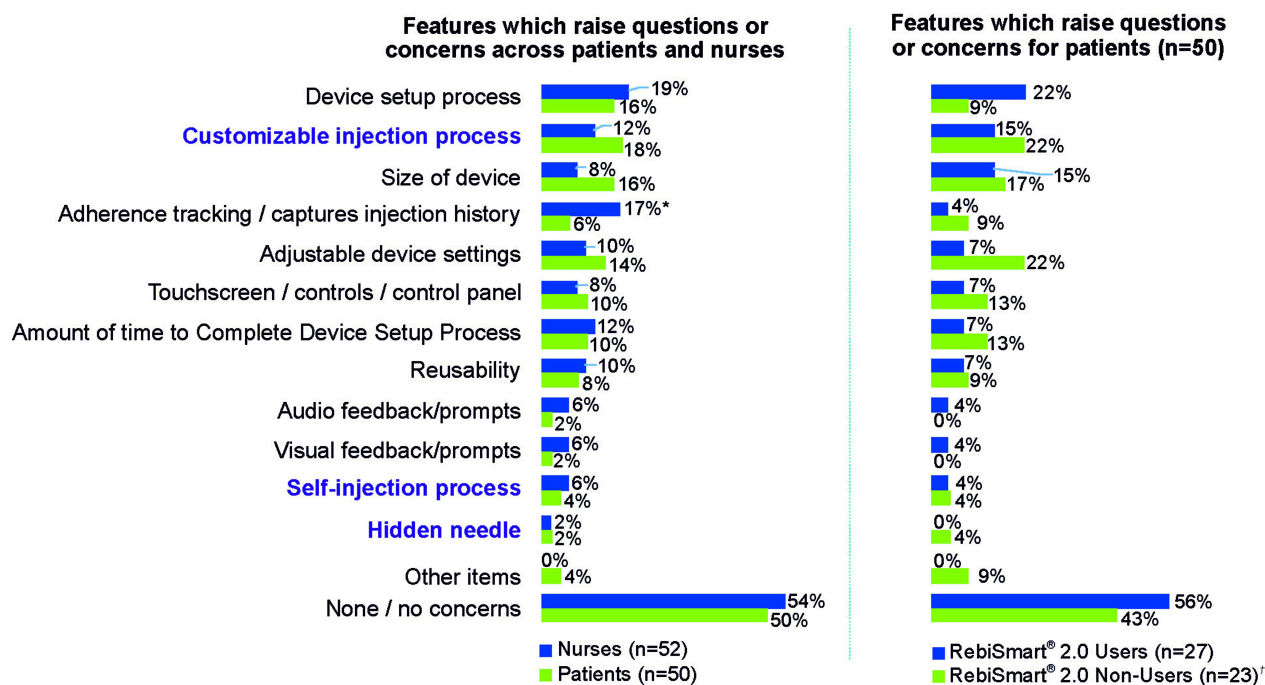


Figure 5 Features Which Raise Questions for Respondents (MS nurses and pwMS). *Indicates significantly higher than patients at 90% confidence. †RebiSmart® 2.0 Non-Users patients (n=23) that responded to questions on “Other devices performance”, were asked to consider the assistive device that they are currently using or recently used. Other devices included Avonex® pen and pre-filled syringe, Betaseron®/Betaferon® pre-filled syringe, ExtaviPro® 30G Autoinjector, Ypsomate®, glatiramer acetate pre-filled syringe and Plegridy® pen.

Abbreviation: n, number of respondents.

demonstration, majority of respondents (pwMS and MS nurses) rated RebiSmart 3.0 as appealing and stated that they would be comfortable using or educating their patients on this new device, respectively. Overall receptivity differed slightly between the nurses and patients and appeared to be driven by nurses. Both MS nurses and pwMS (including current and recent users of RebiSmart 2.0 device) rated the new RebiSmart 3.0 device performance higher on all tested device features compared to other self-injecting assistive devices.

The upgraded RebiSmart 3.0 device offers several incremental improvements designed to further increase ease of handling and convenience of use over the already established design. For example, RebiSmart 3.0 device is lighter, taller, and slimmer compared with the RebiSmart 2.0 device. The other incremental improvements such as injection button on the front in accordance with user preference, embedded Long Term Evolution Cellular connectivity, touchscreen for contemporary user experience, rechargeable and removable battery, improved shock absorption and robustness against liquid leakage, automated needle detachment function, skin sensor surrounding needle to ensure correct flat-on-skin positioning during injection is expected to further enhance the user experience. The upgraded version also offers improved adherence tracking features. For example, the device records the history (date and time) of cartridge changes and injection events providing information to the pwMS or doctor or MS nurse on treatment adherence. These data and the history of additional parameters (needle depth, injection speed, post injection hold time, cartridge type, titration on/off, dose reduction on/off) can be transferred via the onboard cellular data transmission to a central database.

In our survey, the three key features reported to be most appealing by the MS nurses and pwMS were the customizable injection process, self-injection process, and hidden needle. This is in line with previous studies wherein pwMS described an ideal assistive device as the one that would enable them to self-administer injections in a few simple steps, customize the injection process (for example, modify the needle insertion speed and injection depth, speed, and duration),^{29,30} and have a concealed/hidden needle.²⁶

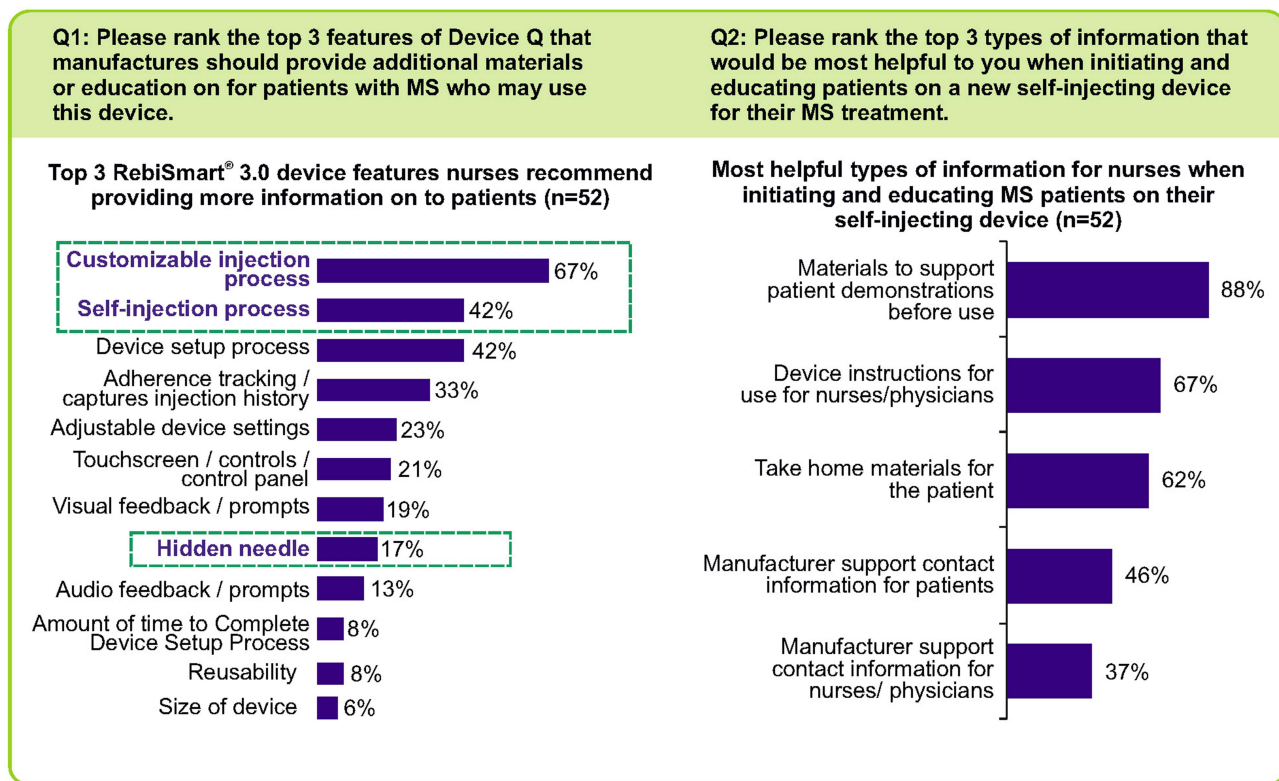


Figure 6 Nurses' recommendations.

Abbreviations: MS, multiple sclerosis; n, number of respondents.

Coyne et al reported that device training based on adult learning principles, routines, and rituals and at-home practice with a device trainer may reduce anxiety and unnecessary experimentation and improve injection therapy compliance.³¹ These device trainers can be well-informed MS nurses and can provide support to pwMS to help them cope with their needle-related fears. While pwMS can be trained on the self-injection technique, routines and rituals are mostly self-discovered by the pwMS, and when these are anchored with timely guidance and continual educational support, they may help pwMS gain more confidence regarding the self-injection process.³¹

Since MS nurses typically have more frequent clinical contact with pwMS than physicians, they can play a crucial role in educating pwMS about the disease and treatment they are receiving. This survey allowed us to understand the MS nurses' perspective on the key features of the RebiSmart 3.0 device that pwMS should be given additional information about that may potentially facilitate a smooth transition to it from their existing device or to start it as their first device. The majority of the MS nurses recommended providing more information to pwMS on the customizable injection process. Self-injection process and device set up process are other features which more than one third of participating MS nurses recommended providing more information to pwMS. The survey also indicated that MS nurses are more likely to have questions about the adherence tracking feature of the RebiSmart 3.0 device and thus would need to be provided with additional information on this feature. This observation was not unexpected. Given that the video was more focused on patients and only limited information could be conveyed through a short video, we anticipated that MS nurses would be interested to learn more on the aspects of setting up adherence tracking, especially the feature through which the specific adherence data can be sent directly to them from the patient's device. From the MS nurses' perspective, materials to support pwMS demonstration before use, device instruction for use for MS nurses or physicians and take-home materials for the pwMS are the most helpful types of information for them while initiating and educating the pwMS on the self-assistive device. To further address the educational gaps identified in this survey, additional materials such as patient training videos, MS nurses/pwMS quick guide leaflets and extended instruction for use has been created for use by MS nurses and pwMS.

This study was an online survey, and the results are based on responses to questions asked before and after a video was shown to the respondents and the respondents did not receive actual hands-on experience with the RebiSmart 3.0 device. We also recognize that the study had a small sample size; however, we tried to compensate for it by ensuring that there was a widespread geographic dispersion of the responses received to the greatest extent possible. The online survey design enabled us to reach a wider geographical audience and a greater variety of respondents. In this study, maximum difference analysis was used to measure the importance of an exhaustive list of features and anchored maximum difference analysis was used to rank the features based on ratings provided by the respondents. The advantage of using maximum difference analysis is that it leads to clearer differentiation among items and eliminates straight-lining and scale usage effects that can complicate rating scale analysis. Anchored maximum difference provides a reference point to support the understanding of intended actions, unlike non-anchored maximum difference scores, which are subjective and are not correlated with real-world action.

Conclusion

The results of our survey indicate that a customizable injection process (including injection speed, hold time, depth, and rotation guide), self-injection process, and hidden needle are three key features likely to influence the level of satisfaction of pwMS and MS nurses when evaluating self-injecting devices for MS treatments. Moreover, our survey identified key educational topics that MS nurses perceived essential for patients to derive maximum benefit from the upgraded RebiSmart 3.0 device. The MS nurses identified key needs for patient education on the use of the device and the suitable approaches (training videos and educational leaflets) to support MS nurses and their patients. The RebiSmart 3.0 is expected to provide improved MS nurses and patient experience than other self-assistive devices for administering sc IFN β -1a therapy.

Data Sharing Statement

Any requests for data by qualified scientific and medical researchers for legitimate research purposes will be subject to the healthcare business of Merck KGaA, Darmstadt, Germany's Data Sharing Policy. All requests should be submitted in writing to the healthcare business of Merck KGaA, Darmstadt, Germany's data sharing portal <https://www.merckgroup.com/en/research/our-approach-to-research-and-development/healthcare/clinical-trials/commitment-responsible-data-sharing.html>. When the healthcare business of Merck KGaA, Darmstadt, Germany's has a co-research, co-development, or co-marketing or co-promotion agreement, or when the product has been out-licensed, the responsibility for disclosure might be dependent on the agreement between parties. Under these circumstances, the healthcare business of Merck KGaA, Darmstadt, Germany's will endeavor to gain agreement to share data in response to requests.

Ethical Approval and Consent for Publication

The survey was conducted in accordance with the market research guidelines as per and General Data Protection Regulation (GDPR) and European Pharmaceutical Marketing Research Association (EphMRA).³² According to the latest EphMRA guidelines, any market research does not require Clinical Research Ethics Committee or Independent Review Board approval. Therefore, no formal ethics committee and IRB approval was required. All survey results were anonymized for the purpose of publication. In this report, the use of "patient" or "patients" refers to the feedback provided by the patient participants without attribution to any named individual. Participation was voluntary, and participants were entitled to withdraw at any stage of the process, or subsequently to ask that part or all of the record of their interview was destroyed or deleted. Adequate data protection was ensured, with data access strictly limited to the participants, Merck KGaA, Darmstadt, Germany and the survey support team. All participants provided written informed consent to participate in the survey.

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Author Contributions

The authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

SSC is an employee of EMD Serono, Billerica, MA, USA. DJ is an employee of Merck Serono Ltd (an affiliate of Merck KGaA), Feltham, United Kingdom. EVC was an employee of EMD Serono Research and Development Institute, Inc. (an affiliate of Merck KGaA), Billerica, MA, USA at the time of development of this manuscript. The authors report no other conflicts of interest in this work.

References

- Filippi M, Bar-Or A, Pielh F, et al. Multiple sclerosis. *Nat Rev Dis Primers*. 2018;4(1):43. doi:10.1038/s41572-018-0041-4
- Hanson KA, Agashivala N, Wyrwich KW, Raimundo K, Kim E, Brandes DW. Treatment selection and experience in multiple sclerosis: survey of neurologists. *Patient Prefer Adherence*. 2014;8:415–422. doi:10.2147/ppa.S53140
- Gromisch ES, Turner AP, Leipertz SL, Beauvais J, Haselkorn JK. Risk factors for suboptimal medication adherence in persons with multiple sclerosis: development of an electronic health record-based explanatory model for disease-modifying therapy use. *Arch Phys Med Rehabil*. 2020;101(5):807–814. doi:10.1016/j.apmr.2019.11.005
- Pozzilli C, Schweikert B, Ecari U, Oentrich W. BetaPlus Study group. Supportive strategies to improve adherence to IFN beta-1b in multiple sclerosis—results of the betaPlus observational cohort study. *J Neurol Sci*. 2011;307(1–2):120–126. doi:10.1016/j.jns.2011.04.026
- Bayas A. Improving adherence to injectable disease-modifying drugs in multiple sclerosis. *Expert Opin Drug Deliv*. 2013;10(3):285–287. doi:10.1517/17425247.2013.763793
- Rieckmann P, Ziemssen T, Penner JK, et al. Adherence to subcutaneous interferon beta-1a in multiple sclerosis patients receiving periodic feedback on drug use by discussion of readouts of their rebismart((R)) injector: results of the prospective cohort study REBIFLECT. *Adv Ther*. 2022;39(6):2749–2760. doi:10.1007/s12325-022-02100-w
- US FDA. BETACONNECT™ autoinjector. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/103471s5201lbl.pdf. Accessed February 09, 2024.
- Hoffmann FA, Trenova A, Llana MA, et al. Patient satisfaction with ExtaviPro 30G, a new auto-injector for administering interferon beta-1b in multiple sclerosis: results from a real-world, observational EXCHANGE study. *BMC Neurol*. 2017;17(1):156. doi:10.1186/s12883-017-0928-9
- US FDA. AVONEX (interferon beta-1a) injection, for intramuscular injection Initial U.S. Approval; 1996. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103628s5189lbl.pdf. Accessed February 09, 2024.
- US FDA. PLEGRIDY (peginterferon beta-1a) injection, for subcutaneous injection Initial U.S. Approval; 2014. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125499lbl.pdf. Accessed February 09, 2024.
- Devonshire VA, Verdun Di Cantogno E. Review of subcutaneous interferon beta-1a, delivered via the electronic self-injection device RebiSmart, for the treatment of multiple sclerosis. *Ther Deliv*. 2011;2(11):1455–1465. doi:10.4155/tde.11.116
- Lugaresi A. RebiSmart (version 1.5) device for multiple sclerosis treatment delivery and adherence. *Expert Opin Drug Deliv*. 2013;10(2):273–283. doi:10.1517/17425247.2013.746311
- Ebers GC; PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing/remitting multiple sclerosis. *Lancet*. 1998;352(9139):1498–1504. doi:10.1016/S0140-6736(98)03334-0
- Prisms Study Group the University of British Columbia, MS/MRI. Analysis Group. PRISMS-4: long-term efficacy of interferon-beta-1a in relapsing MS. *Neurology*. 2001;56(12):1628–1636. doi:10.1212/wnl.56.12.1628
- Filipi M, Jack S. Interferons in the treatment of multiple sclerosis: a clinical efficacy, safety, and tolerability update. *Int J MS Care*. 2020;22(4):165–172. doi:10.7224/1537-2073.2018-063

16. EMA. Rebif 22 micrograms solution for injection in pre-filled syringe SmPC; 2023.
17. Lugaresi A, De Robertis F, Clerico M, et al. Long-term adherence of patients with relapsing-remitting multiple sclerosis to subcutaneous self-injections of interferon beta-1a using an electronic device: the RIVER study. *Expert Opin Drug Deliv.* 2016;13(7):931–935. doi:10.1517/17425247.2016.1148029
18. Lugaresi A, Florio C, Brescia-Morra V, et al. Patient adherence to and tolerability of self-administered interferon beta-1a using an electronic autoinjector device: a multicentre, open-label, Phase IV study. *BMC Neurol.* 2012;12:7. doi:10.1186/1471-2377-12-7
19. Arnaud L. Evolution of the RebiSmart[®] autoinjector device in support of adherence to subcutaneous interferon beta-1a therapy for relapsing multiple sclerosis. Amsterdam, The Netherlands: ECTRIMS; 2022. Available from: https://www.merckneurology.com/content/dam/web/healthcare/biopharma/neurology/merckneurology/newDesign/congress/documents/ECTRIMS/Posters/ECTRIMS_Poster_blue_2_2022.pdf. Accessed February 09, 2024.
20. Lin Y. Evolution of the rebismart[®] autoinjector device to improve usability in support of adherence to subcutaneous interferon beta-1a therapy for relapsing multiple sclerosis. Cairo, Egypt: MENACTRIMS; 2022. Available from: <https://www.sciencedirect.com/science/article/pii/S2211034822008653>. Accessed February 09, 2024.
21. Burke T, Dishon S, McEwan L, Smrka J. The evolving role of the multiple sclerosis nurse: an international perspective. *Int J MS Care.* 2011;13(3):105–112. doi:10.7224/1537-2073-13.3.105
22. Calfee JE. A representative survey of MS patients on attitudes toward the benefits and risks of drug therapy; 2006.
23. Qualtrics. Getting started with maxdiff projects; 2023. Available from: <https://www.qualtrics.com/support/conjoint-project/getting-started-conjoints/getting-started-maxdiff/getting-started-with-maxdiff-projects/>. Accessed February 09, 2024.
24. Survey Analytics: maximum difference analysis; 2024. Available from: <https://www.surveyanalytics.com/maximum-difference-analysis.html>. Accessed February 09, 2024.
25. QuestionPro. Anchored maximum difference analysis; 2023. Available from: <https://www.questionpro.com/help/anchored-maxdiff.html>. Accessed February 09, 2024.
26. Devonshire VA, Feinstein A, Moriarty P. Adherence to interferon beta-1a therapy using an electronic self-injector in multiple sclerosis: a multicentre, single-arm, observational, phase IV study. *BMC Res Notes.* 2016;9:148. doi:10.1186/s13104-016-1948-z
27. Krol M, de Voer G, Osowski U. Patient adherence to subcutaneous IFN beta-1a injections using the RebiSmart[®] injection device: a retrospective real-world study among Dutch and German patients with multiple sclerosis. *Patient Prefer Adherence.* 2017;11:1189–1196. doi:10.2147/PPA.S130985
28. Valis M, Sarlakova J, Haluskova S, et al. An observational study demonstrating the adherence and ease of use of the injector device, RebiSmart[®]. *Expert Opin Drug Deliv.* 2020;17(5):719–724. doi:10.1080/17425247.2020.1742694
29. Lugaresi A, Rottoli MR, Patti F. Fostering adherence to injectable disease-modifying therapies in multiple sclerosis. *Expert Rev Neurother.* 2014;14(9):1029–1042. doi:10.1586/14737175.2014.945523
30. Bittner B, Schmit Chiesi C, Kharawala S, Kaur G, Schmidt J. Connected drug delivery devices to complement drug treatments: potential to facilitate disease management in home setting. *Med Devices.* 2019;12:101–127. doi:10.2147/MDER.S198943
31. Coyne M, Rinaldi A, Brigham K, et al. Impact of routines and rituals on burden of treatment, patient training, cognitive load, and anxiety in self-injected biologic therapy. *Patient Prefer Adherence.* 2022;16:2593–2607. doi:10.2147/PPA.S375037
32. EPHMRA. Code of conduct; 2022. Available from: <https://www.ephmra.org/sites/default/files/2022-08/EPHMRA%202022%20Code%20of%20Conduct.pdf>. Accessed February 09, 2024.

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