Understanding and meeting injection device needs in multiple sclerosis: a survey of patient attitudes and practices

Elisabetta Verdun di Cantogno1
Susan Russell2
Tom Snow2

1Global Clinical Development Unit, Merck Serono S.A. – Geneva, Switzerland; 2Global Marketing, Merck Serono S.A. – Geneva, Switzerland

Background: All established disease-modifying drugs for multiple sclerosis require parenteral administration, which can cause difficulties for some patients, sometimes leading to suboptimal adherence. A new electronic autoinjection device has been designed to address these issues.

Methods: Patients with relapsing multiple sclerosis currently receiving subcutaneous or intramuscular interferon beta-1a, interferon beta-1b, or glatiramer acetate completed an online questionnaire (July 4–25, 2008) that surveyed current injection practices, experiences with current injection methods, and impressions and appeal of the new device.

Results: In total, 422 patients completed the survey, of whom 44% used autoinjectors, 43% prefilled syringes, and 13% syringes and vials; overall, 66% currently self-injected. Physical and psychological barriers to self-injection included difficulty with injections, needle phobia, and concerns over correct injection technique. Only 40% of respondents were “very satisfied” with their current injection method. The new electronic autoinjector was rated as “very appealing” by 65% of patients. The benefits of the new device included the ability to customize injection settings and to review dosing history.

Conclusion: New technologies may help patients overcome physical and psychological barriers to self-injection. The combination of a reliable and flexible autoinjection device with dose-monitoring technology may improve communication between health care professionals and patients, and improve treatment adherence.

Keywords: adherence, autoinjection, subcutaneous interferon beta-1a, multiple sclerosis

Background

Multiple sclerosis is a chronic degenerative disease of the central nervous system, and is the most common disabling neurological condition affecting young adults.1,2 Because multiple sclerosis is currently incurable, patients require long-term treatment that delays or stops the progression of irreversible disability. Currently, the first-line therapies for relapsing forms of multiple sclerosis are interferon (IFN) beta-1a 44 µg or 22 µg administered subcutaneously three times weekly (Rebif®, Merck Serono S.A., Geneva, Switzerland); IFN beta-1a 30 µg administered intramuscularly once weekly (Avonex®, Biogen Idec Inc, Cambridge, MA); IFN beta-1b 250 µg administered subcutaneously every other day (Betaferon®/Betaseron®, Bayer Schering Pharma AG, Berlin, Germany; Extavia®, Novartis AG, Basel, Switzerland); and glatiramer acetate 20 mg administered subcutaneously daily (Copaxone®, Teva Pharmaceutical Industries Ltd, Petah Tikva, Israel). All these first-line disease-modifying drugs for multiple sclerosis require parenteral self-administration, by either subcutaneous or intramuscular injection.3
Adherence to multiple sclerosis treatment is important to ensure optimal clinical outcomes. However, the debilitating nature of the disease itself, together with the need for long-term, frequent, parenteral drug administration, means that adherence is a challenge for many patients. A recent multicenter observational study of 2648 patients reported that 25% of 2566 patients for whom data were available (643 patients) were nonadherent (defined as missing at least one disease-modifying drug injection over a four-week period). Among these nonadherent patients, 32% reported injection-related reasons for their nonadherence.

There are limited prospective data on factors that influence adherence to disease-modifying drugs. However, contributing factors to nonadherence that have been identified include problems with injecting, perceived lack of efficacy, and adverse events. Patients who are required to self-inject often react with fear, avoidance, anxiety, or disgust, with some asking family members to administer the treatment to avoid self-injection. However, dependence on others for injection may also reduce treatment adherence. Other injection-related barriers to adherence include injection site reactions and injection pain. In an observational study that surveyed patients via online questionnaires, factors directly related to the injection of therapy accounted for 32% of the reasons given for missing injections, including “tired of shots”, “skin reactions”, and “pain at injection site”. Additionally, many patients with multiple sclerosis have reduced manual dexterity, which can make the correct self-injection procedure physically problematic.

In response to these potential problems with injecting, various injection technologies have been introduced, which are designed to improve convenience and the safety and reliability of injections, and to reduce pain and anxiety. These technological developments include thinner needles, prefilled syringes for manual injection, and autoinjection devices (or “autoinjectors”). Autoinjectors automatically insert the needle and deliver a controlled dose, and are available for all first-line disease-modifying drugs used for multiple sclerosis with the exception of intramuscular IFN beta-1a, for which an injection device is available, but the injection process remains partially manual. Autoinjectors have been shown to provide a number of benefits, including a reduced risk of injection site reactions, reduced discomfort, and greater ease of use compared with manual syringe injections.

A recent cross-sectional, questionnaire-based survey of 3006 patients with multiple sclerosis examined patients’ reasons for using or for being reluctant to use an autoinjector for the subcutaneous administration of IFN beta or glatiramer acetate. The reasons most commonly cited by patients for using an autoinjector were “certainty that the injection was being carried out correctly” (47.1% of patients) and the ability to administer injections at sites on the body that were previously inaccessible (41.1%). A major reason for not using an injection device, cited by 34.4% of patients, was that patients wanted control of the injection, including control of the speed and depth of needle insertion, as well as the duration of the injection. The survey also found that treatment adherence was greater among patients who always used an autoinjector (79% stated that they never missed an injection) than in those who used a prefilled syringe (71% stated that they never missed an injection). However, over 20% of patients who always used an autoinjector still reported that they sometimes missed an injection.

Adherence to treatment in multiple sclerosis thus remains suboptimal, indicating that patients may still have unmet needs. In the survey by Bayas et al., patients were also asked to identify the characteristics that an ideal autoinjector should have. The most frequently cited characteristics included the ability to carry out the injection simply and swiftly in just a few steps, drug release only with skin contact, prevention of accidental activation, and the opportunity to adjust needle insertion speed, as well as injection depth, speed, and duration. Advances in delivery technology towards this ideal profile may, therefore, offer greater patient convenience and increase adherence.

A new electronic, multidose autoinjector (RebiSmart™, Merck Serono S.A., Geneva, Switzerland) has been developed for administering subcutaneous IFN beta-1a. This device offers a number of innovative features designed to improve the convenience and comfort of subcutaneous IFN beta-1a administration. Patients using this device have the facility to improve injection comfort by adjusting the needle insertion speed, needle depth, injection speed, and injection time (the time between the end of injection and needle retraction). In addition, interactive onscreen instructions, together with clear visual and audible signals, provide guidance for correct use. The device also features a dosing log that records the date, time, and dosage of every injection. This function may help patients to avoid missing doses, and thus potentially improve adherence.

Here we report the results of an online survey of patients diagnosed with relapsing multiple sclerosis and currently receiving treatment with subcutaneous IFN beta-1a, intramuscular IFN beta-1a, subcutaneous IFN beta-1b, or glatiramer acetate. The aims of the survey were to investigate patients’ injection practices in the normal clinical
setting, to evaluate their experiences with current injection methods, and to assess their reactions to the new electronic autoinjector.

**Methods**

Eligible patients in Canada, France, Germany, Italy, Spain, and the US were recruited from an online panel of patients and completed an online, self-administered questionnaire during July 4–25, 2008. Patients were eligible if they were aged 18–65 years, had a diagnosis of relapsing multiple sclerosis or had experienced a demyelinating event suggestive of multiple sclerosis, were currently receiving IFN beta or glatiramer acetate, had been injecting treatment for at least two months prior to participating in the survey, and were not affiliated with any medical marketing, market research, or pharmaceutical company.

Patients were shown a series of slides describing the new electronic, multidose autoinjector, its key features, and the injection procedure, including insertion and removal of the drug cartridge and needle. The questionnaire was designed to collect information on current injection practices, patients’ attitudes to and experience with current treatment, and impressions and appeal of the new electronic autoinjector (Table 1). The questionnaire consisted mainly of multiple-choice questions and took approximately 30 minutes to complete. Three of the questions asked patients to indicate their attitudes on a scale of 0–10, ranging from “not at all” (score of 0) to “very comfortable/satisfied/appealing” (score of 10). For question 9 (satisfaction with the patient’s current injection method), a score of 0–2 was categorized as “unsatisfied”, 3–7 as “moderately satisfied”, and 8–10 as “very satisfied”. The responses to questions 1 and 10 were also categorized using these score ranges.

**Results**

**Demographics, patient clinical characteristics, and current therapy**

In total, 422 patients completed the survey in Canada (n = 35, 8%), France (n = 35, 8%), Spain (n = 45, 11%), Germany (n = 50, 12%), Italy (n = 47, 11%), and the US (n = 210, 50%). Patient demographic and clinical characteristics are presented in Table 2. Respondents had been receiving injected therapy for a mean of 4.2 years. The most common current therapy was subcutaneous IFN beta-1a, which was being received by 189 respondents (45%). A further 85 respondents (20%) were currently receiving treatment with intramuscular IFN beta-1a, 60 (14%) with subcutaneous IFN beta-1b, and 88 (21%) with glatiramer acetate.

**Current injection habits**

Overall, a similar proportion of respondents used prefilled syringes (43%) and autoinjectors (44%), while a smaller percentage (13%) used syringes and vials (Figure 1). However, when analyzed by current drug used, the percentage of respondents using autoinjection devices was smaller among patients taking intramuscular IFN beta-1a (15%) than among patients taking subcutaneous IFN beta-1a (54%), IFN beta-1b (42%), or glatiramer acetate (51%, Figure 1).

Approximately two-thirds (66%) of respondents self-injected, while 19% had someone else administer the injection. The remaining 15% of patients sometimes self-injected and sometimes had someone else inject their medication. Rates of self-injection were similar among patients treated with subcutaneous IFN beta-1a (71%), IFN beta-1b (65%), or glatiramer acetate (70%), but lower among those receiving intramuscular IFN beta-1a (51%). Patients reported a number of physical and psychological reasons for not currently self-administering injections (Figure 2). The most common reason was physical difficulty with injecting (57% of respondents), whereas pain on injection was cited by only 10% of respondents. The most common psychological reasons for not self-injecting included dislike of looking at needles (39%), dislike of the thought of injecting (37%), and a lack of confidence in their ability to inject correctly (32%). When patients were asked to rate their satisfaction with their current injection method on a scale of 0–10 (0 = not at all satisfied, 10 = very satisfied), the mean score was 6.7 (median 7.0, range 0–10). Overall, 40% of respondents were “very satisfied” (score of 8–10) with their current injection method (Table 3), with a lower percentage among users of vials and syringes (23%) than among users of prefilled syringes (39%) or autoinjectors (46%).

**Attitudes to technology**

Most respondents were very comfortable in general with new technologies. On a scale of 0–10 (0 = not at all comfortable, 10 = very comfortable), the mean score was 8.0 (median 8.0, range 0–10), and 69% of patients scored between 8 and 10; 29% were somewhat comfortable (score of 3–7), and only 2% were uncomfortable (score of 0–2). Approximately one-third (35%) of respondents described themselves as early adopters of new technologies, while 57% described themselves as cautious adopters, and only 8% as late adopters.

**Reactions to the new electronic autoinjection device**

When patients were asked how appealing the new electronic autoinjection device was compared with their current method...
Table 1  Survey questionnaire

| Question                                                                 | Response                                                                                           |
|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| 1. Thinking generally about new technologies, how comfortable           | Scale of 0 (not at all) to 10 (very comfortable)                                                    |
| would you say you were with technical electronic instruments            |                                                                                                    |
| such as computers and mobile phones?                                    |                                                                                                    |
| 2. Which of the following best describes your approach to new           | 1. I am always one of the first to try new technologies (early adopter)                            |
| technologies?                                                           | 2. I tend to wait until others have tried and tested a new technology before                     |
|                                                                         |   using it myself (cautious adopter)                                                               |
|                                                                         | 3. I am usually amongst the last to start using a new technology (late adopter)                    |
| 3. Which of the following types of MS do you currently have?            | 1. Relapsing–remitting                                                                            |
|                                                                         | 2. Secondary progressive                                                                           |
|                                                                         | 3. Clinically isolated syndrome                                                                    |
|                                                                         | 4. Don’t know                                                                                     |
| 4. How long ago were you first diagnosed with MS?                       | Length of time                                                                                    |
| 5. For how long have you been injecting this MS treatment?              | Length of time                                                                                    |
| 6. Which of the following do you currently use to inject your MS        | 1. A syringe that requires you to fill from a vial                                                 |
| treatment?                                                              | 2. A prefilled syringe                                                                            |
|                                                                         | 3. Autoinjection device                                                                           |
| 7. Do you currently inject yourself or do you have someone else         | 1. I inject myself                                                                                  |
| inject for you?                                                         | 2. Someone else injects me                                                                         |
|                                                                         | 3. Both                                                                                            |
| 8. For which of the following reasons do you not currently inject your   | 1. I find it physically difficult to inject myself                                                |
| treatment yourself?                                                    | 2. It hurts to inject myself                                                                       |
|                                                                         | 3. I don’t like looking at needles                                                                  |
|                                                                         | 4. I don’t like the thought of having to inject myself                                              |
|                                                                         | 5. I don’t trust I will inject myself correctly                                                    |
|                                                                         | 6. I find the syringe/injection device unsafe                                                     |
|                                                                         | 7. Other                                                                                          |
| 9. How satisfied would you say you were with the injection method you   | Scale of 0 (not at all) to 10 (very satisfied)                                                     |
| currently use for administering treatment?                              |                                                                                                    |
|                                                                                       | Questions after viewing presentation on the new electronic, multidose autoinjector                  |
|                                                                                       | 10. How appealing is this new injection device compared                                            |
|                                                                                       | with your current method?                                                                         |
|                                                                                       | Scale of 0 (not at all) to 10 (very appealing)                                                     |
|                                                                                       | 11. Which of the following do you feel are the key benefits of this new electronic device that    |
|                                                                                       | would encourage you to ask your nurse or doctor about it?                                          |
|                                                                                       | 1. Ability to tailor injection settings to individual patient needs                                |
|                                                                                       | 2. Reliable monitoring of regular dosing                                                           |
|                                                                                       | 3. Could allow for easier access to various injection sites                                        |
|                                                                                       | 4. Simple uncomplicated procedure                                                                  |
|                                                                                       | 5. Hidden needle                                                                                   |
|                                                                                       | 6. Sounds, lights, and onscreen prompts ensure correct and confident delivery of dose             |
|                                                                                       | 7. Looks easy to grip and handle the device                                                        |
|                                                                                       | 8. Compact                                                                                        |
|                                                                                       | 9. Ability to download dosing information to computer                                              |
|                                                                                       | 10. Looks less like a medical device                                                               |
|                                                                                       | 11. Other                                                                                         |
|                                                                                       | 12. There are no benefits                                                                         |
|                                                                                       | 1. The device may malfunction                                                                     |
|                                                                                       | 2. Requires a screwdriver to change batteries                                                      |
|                                                                                       | 3. Too many steps to prepare the injection                                                        |
|                                                                                       | 4. Too many steps involved in actually injecting                                                   |
|                                                                                       | 5. Could be too large to handle comfortably                                                        |
|                                                                                       | 6. Information screen could be difficult to read                                                   |
|                                                                                       | 7. Patient is less in control of the injection                                                     |
|                                                                                       | 8. Dosing log implies a lack of physician’s trust                                                  |
|                                                                                       | 9. Other                                                                                          |
|                                                                                       | 10. There are no drawbacks                                                                        |

Notes: *Respondents could give more than one reason, benefit, or drawback; *other benefits or drawbacks cited by patients were recorded.

Abbreviation: MS, multiple sclerosis.
Table 2 Patient demographic and clinical characteristics

| Characteristics                                |        |        |
|-----------------------------------------------|--------|--------|
| Age, years                                    | Mean (SD) | 43 (10.7) |
|                                               | Median (range) | 44 (18–64) |
| Age range, n (%)                              | 18–30 years | 72 (17) |
|                                               | 31–40 years | 122 (29) |
|                                               | 41–50 years | 126 (30) |
|                                               | 51–65 years | 102 (24) |
| Sex, n (%)                                    | Male | 127 (30) |
|                                               | Female | 295 (70) |
| Clinical form of MS, n (%)                    | Clinically isolated syndrome | 40 (9) |
|                                               | Relapsing–remitting | 300 (71) |
|                                               | Secondary progressive | 57 (14) |
|                                               | Unknown | 25 (6) |
| Time since diagnosis of MS, years             | Mean (SD) | 8.4 (6.7) |
|                                               | Median (range) | 6 (1–41) |
| Length of time injecting MS therapies, years  | Mean (SD) | 4.2 (3.6) |
|                                               | Median (range) | 3.2 (0.2–36.5) |

Abbreviations: MS, multiple sclerosis; SD, standard deviation.

on a scale of 0–10 (0 = not at all appealing, 10 = very appealing), the overall mean score was 7.7 (median 8.0, range 0–10). Approximately two-thirds (65%) of patients found the new device “very appealing” (score of 8–10), with a higher proportion among current users of subcutaneous IFN beta-1a (73%) and IFN beta-1b (70%) than among users of intramuscular IFN beta-1a (54%) and glatiramer acetate (56%) favoring the new device. Overall, the new device was rated as moderately appealing (score of 3–7) by 30% of patients, and not at all appealing (score of 0–2) by 5%.

Questions 11 and 12 presented the patients with lists of several potential benefits and drawbacks of the new device. Overall, 96% of respondents identified a benefit that would encourage them to ask their nurse or doctor about the new device. The most appealing benefits were the ability to tailor injection settings (such as speed of injection and depth of needle insertion) to individual needs (cited by 39% of respondents), and the dosing log that allows reliable monitoring of regular dosing (cited by 38%, Figure 3). Overall, 23% of respondents considered that the device had no drawbacks. The most frequently stated drawback was fear that the device might malfunction, which was cited by 37% of respondents.

Discussion
This survey of patients with relapsing multiple sclerosis indicates that patterns of self-injection practice and satisfaction with current injection methods are broadly similar across the two groups in the US and the European Union/Canada. Auto-injection devices and prefilled syringes were used by most respondents, but the use of autoinjectors was considerably less common among patients treated with intramuscular IFN beta-1a than in patients receiving other disease-modifying drugs, which reflects the lack of a fully automated injection device for use with this treatment.

A third of respondents reported that they relied on others (at least part of the time) to administer injections. The percentage of patients who self-injected among those receiving medications for which an autoinjector is available (ie, subcutaneous IFN beta-1a, IFN beta-1b, and glatiramer acetate) was 65%–71%. In contrast, the percentage of patients receiving intramuscular IFN beta-1a who self-injected was 51%. While it should be noted that the routes of administration are different in these two cases and there may be differences in clinical characteristics between these populations, these data could suggest that self-injection might be more acceptable if an autoinjector is available than if the injection must be performed manually.

The percentage of patients who were either unsatisfied or only moderately satisfied with their current method of administration ranged from 54% among patients using an autoinjection device to 60% among patients using a prefilled syringe and 78% among those using vials and syringes. These findings indicate that even among patients already using an autoinjection device, there is scope for improvements in autoinjector design that may increase patient satisfaction with their injection method. It should be noted that 9% of subcutaneous IFN beta-1a patients reported using a syringe and vial although this drug was not available in such a delivery format at the time of the survey.

Results from this multinational survey indicate that patients reacted favorably to the new electronic autoinjection device. The design improvements that were found to be most appealing to patients were the dosing log and the ability to tailor injection settings to suit individual needs. The new electronic autoinjector appraised in this survey has also been evaluated in another study, which assessed ease of use and suitability in 106 patients with multiple sclerosis who had the opportunity to use the device.13 Most patients considered the device suitable for self-injection, with 95% of patients rating it as “easy” or “very easy” to use, and over 80% of patients rating individual features, such as dose history, confirmation of end of injection, audible and visual signals, and display of last injection time and date, as “useful” or “very useful”. Additional international user trials will further
Figure 1 Current method of injection administration. 
Abbreviations: IFN, interferon; im, intramuscular; sc, subcutaneous.

Figure 2 Reasons given for not self-injecting. Respondents could give more than one reason (values total more than 100%). Physical (total) score is the percentage of respondents selecting one or both of the two physical reasons; psychological (total) score is the percentage of patients selecting one or more of the psychological reasons.
validate the new device in patients with relapsing-remitting multiple sclerosis.\textsuperscript{14}

It should be acknowledged that patient characteristics outside the scope of this analysis, such as patient age and length of time previously injecting therapy, could influence patient responses to these questions. The online format of this survey may have selected for patients who are more comfortable with technology. This survey confirms the findings of previous studies that have found that barriers to self-injection include both physical factors, such as injection pain, and psychological factors, including anxiety about the use of needles.\textsuperscript{5,8} However, this survey also found that over two-thirds of respondents were “very comfortable” with new technologies. These results suggest that new technologies such as those incorporated in the new electronic autoinjection device could potentially help large numbers of patients to, at least partially, overcome some of the physical and psychological barriers to self-injection. In particular, the ability to adjust speed and depth of needle insertion and injection speed and time may allow patient comfort to be maximized. Concealment of the needle may also reduce needle-related anxiety. Evidence from the field of diabetes suggests that use of an

\begin{table}[h]
\centering
\caption{Satisfaction with current injection method}
\begin{tabular}{lrrrr}
\hline
Method of injection & Satisfaction score & & & \\
 & Mean & Median & Range & Category (percentage of patients) \\
 & & & & 0–2 & 3–7 & 8–10 \\
 & & & & “unsatisfied” & “moderately satisfied” & “very satisfied” \\
\hline
All patients (n = 422) & 6.7 & 7.0 & 0–10 & 6 & 54 & 40 \\
Vial and syringe (n = 53) & 5.9 & 6.0 & 1–10 & 8 & 69 & 23 \\
Prefilled syringe (n = 183) & 6.7 & 7.0 & 0–10 & 6 & 55 & 39 \\
Autoinjection device (n = 186) & 6.9 & 7.0 & 0–10 & 5 & 49 & 46 \\
\hline
\end{tabular}
\end{table}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Benefits of the new autoinjection device most commonly cited by patients. Respondents could cite more than one benefit (values total more than 100%).}
\end{figure}
automatic injection device that conceals the needle during the entire injection process is associated with significantly reduced pain perception.\textsuperscript{15} Furthermore, by providing reassurance regarding correct injection technique and improving the comfort of the injection, this new autoinjector may improve adherence. Importantly, the dosing log incorporated into the device provides an objective means by which to assess adherence to subcutaneous IFN beta-1a treatment and may facilitate discussion between patients and health care professionals, which may, in turn, improve adherence and treatment decision-making.

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