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Office de la propriété intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

REGISTERED MAIL

October 28, 2022

Our file no.: **RX-131/19**

Attn: Dr. Clark P. Holden
OSLER, HOSKIN & HARCOURT LLP
1900 - 340 Albert Street
OTTAWA Ontario
K1R 7Y6

Dear Sir/Madam:

Re: Request for Re-examination of Patent no. **2,760,802**

Title:	**LOW FREQUENCY GLATIRAMER ACETATE THERAPY**
Patentee:	YEDA RESEARCH AND DEVELOPMENT CO., LTD
Your file no.:	**PCA 30873**
Requester:	PHARMASCIENCE INC.

In accordance with subsection 48.3(3) of the *Patent Act*, the Re-examination Board (the Board) has completed a re-examination of the issued claims 1-66 of Canadian Patent number 2,760,802 (the '802 Patent). Pursuant to section 48.4(1) of the *Patent Act*, the Board has issued a Re-examination Certificate concurrent with this letter confirming claims 1-66 and incorporating in the patent proposed new claims, in part.

PROCEDURAL HISTORY

A compliant request for the re-examination of the issued claims 1-66 of the `802 Patent was received on October 15, 2019 from Pharmascience Inc. (the Requestor). Notably, a parallel proceeding involving the Requestor, the Patentee and their licensee to this patent, Teva Canada Innovation, concerning the infringement and validity of claims 1-66 of the '802 Patent, was underway before the Federal Court of Canada at that date.

In a notice issued pursuant to subsection 48.2(4) of the *Patent Act* dated February 12, 2020 (the Notice), the Board notified the Patentee that the request raised a substantial new question of obviousness with respect to all of the issued claims 1-66.

The Patentee submitted a reply to the Notice on May 29, 2020 in accordance with subsection 48.2(5) of the *Patent Act*, thereby commencing the re-examination proceeding[1]. In that reply, the Patentee made submissions in favour of the patentability of all of the issued claims 1-66.

The Board sent its first letter of the re-examination proceeding on July 17, 2020 (L1). In that letter the Board considered the Patentee`s submissions and provided reasons why, in its preliminary view, claims 1-66 would have been obvious contrary to section 28.3 of the *Patent Act*.

On October 19, 2020, the Patentee responded with further submissions in favour of the patentability of claims 1-66 and further requested that the Board incorporate newly proposed claims 67-78 to the '802 Patent (R-L1).

On December 17, 2020, the Patentee sent a supplemental response with further submissions and a letter informing the Board of the issuance by the Federal Court of a Confidential Judgment and Reasons in relation to Federal Court File No. T-2182-18 and T-2183-18. On January 7, 2021, the Patentee provided the Board with a copy of the public judgement upholding the claims of the patent (i.e., claims 1-66) in *Teva Canada Innovation v Pharmascience Inc*, 2020 FC 1158. Notably, Pharmascience Inc. had already filed a notice of appeal with the Federal Court of Appeal of Canada at that date.

The Board sent its second letter of the re-examination proceeding on February 22, 2021 (L2). In that letter the Board considered the Patentee`s submissions in respect of the new claims set 1-78 (i.e., issued claims 1-66 and the newly proposed claims 67-78) and provided its preliminary view that all of the claims would have been obvious and non-compliant with section 28.3 of the *Patent Act*. In addition, the Board expressed its preliminary view that the newly proposed dependent claims 68, 70, 72, 74, 76 and 78 lack utility and do not comply with section 2 of the *Patent Act*.

The Patentee responded to that second letter on March 22, 2021 (R-L2) providing additional submissions in favour of the patentability of claims 1-78. The Patentee further informed the Board that it had filed a motion with the Federal Court of Canada on March 19, 2021 to stay the re-examination proceedings pending the final resolution of the appeal that was underway. In its April 26, 2021 decision *Teva Canada Innovation v*

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[1] Pursuant to subsection 48.3(3) of the *Patent Act* a re-examination proceeding shall be completed within twelve months

Pharmascience Inc, 2021 FC 367, the Federal Court granted the motion staying the re-examination proceeding until a final judgment was rendered including any appeals.

The Federal Court of Appeal dismissed the appeal on January 6, 2022, upholding the validity of the issued claims 1-66 in its decision in *Pharmascience Inc. v Teva Canada Innovation*, 2022 FCA 2. Pharmascience Inc. sought leave to the Supreme Court of Canada to appeal that decision but the application was dismissed on September 29, 2022. With that dismissal, the decision in the Federal Court action became final, the order staying the re-examination proceeding lapsed and the Federal Court's order requiring the Board to complete the re-examination within 10 weeks of the stay expiring took effect.

On that same day, the Patentee provided the Board with submissions that (pages 1-2):

> (t)he trial decision by Justice Kane of the Federal Court…as affirmed by the Appeal Decision, now constitutes a final determination that the 802 Patent is valid, contrary to the position taken by Pharmascience in both the litigation and this re-examination…
>
> [and] the continuation of this re-examination is now precluded by the legal doctrines of issue estoppel and abuse of process.

The Patentee's submissions have been carefully considered in view of the claims set that is presently before us (i.e., claims 1-78). However, our view is that these submissions do not affect the Board's final decision, in light of the Patentee's submissions on March 22, 2021, to confirm the patentability of the issued claims and to incorporate the proposed claims, in part. We note that the proposed claims 67-78 were never before the Federal Court or the Federal Court of Appeal.

LEGISLATION AND LEGAL PRINCIPLES

Please refer to the principles of law relating to obviousness and utility as set out in our notice and our second letter L2, respectively.

ANALYSIS

Obviousness

The first step in the obviousness inquiry is to identify the person skilled in the art and their common general knowledge (CGK).

The characterization of the skilled person set out in our notice was a team of medical and scientific professionals, including a neurologist and a clinician, familiar with treating patients suffering from autoimmune diseases, including MS, and familiarity with treating

patients at risk of developing MS. In response, the Patentee's letter of May 29, 2020 did not dispute our characterization of the skilled person as a team. Rather, the Patentee's position was that a statistician ought to be added to the team (page 4, emphasis added):

> For the purpose of understanding the invention in the context of the prior art, the person skilled in the art is taken as being a team including a neurologist and clinician familiar with treating patients suffering from autoimmune diseases, including MS, and familiarity with treating patients at risk of developing MS, **and a statistician with experience in planning and interpreting clinical trials**.

In consideration of these submissions, we explained in L1 that we were unable to find any information based on the specification as a whole that would support adding a statistician to the team. However, we did agree with the Patentee that the skilled person as defined (i.e., a team of medical and scientific professionals including a neurologist and a clinician) would have the specific expertise they attributed to the statistician, namely experience in planning and interpreting clinical trials, and so that was added to the characterization of the skilled person.

We also revised the CGK in that letter in response to the Patentee's submissions to add the last four points (below) to the first three that were set out originally in our notice:

- copaxone (20 mg glatiramer acetate or "GA" injection) is a standard approved therapy for treating patients with RRMS;
- the approved GA dosage is 20 mg daily, although the optimal dosage is not known;
- the other standard and conventional disease modifying injectable therapies approved for treating RRMS include Avonex (interferon β-1a, once-a-week injection), Betaseron/Betaferon (interferon β-1b, every other day (EOD) injection) and Rebif (interferon β-1a, injection three times per week with at least one day between sc injections);
- a drug or treatment regimen must be subjected to a randomized, double-blinded Phase III clinical trial to obtain regulatory approval;
- smaller, unblinded investigational studies commonly follow regulatory approval, but a change in prescribing practice would require a proper Phase III clinical trial;
- a randomized, double-blind Phase III clinical trial (the "gold standard") is the ultimate test and so its results would supersede those of a Phase II trial to the extent that the Phase II results would fade into the background; and

- the knowledge required to understand the invention in the context of the prior art and to discern more powerful studies from those that are less reliable.

In that letter and again in our second letter we invited the Patentee to make further submissions on these characterizations of the skilled person and their CGK. Importantly, in response to our second letter, the Patentee disputed the second point of CGK that 20 mg GA daily was known to be the approved dosage but that the optimal dosage was not known (R-L2 on page 8). Instead, the Patentee indicated that the approved dosage of 20 mg GA daily would have been known as the optimal dose. In view of this submission, we have reconsidered the CGK.

The principles governing the assessment of CGK were stated in *Eli Lilly & Co v Apotex Inc*, 2009 FC 991 at para 97, upheld by 2010 FCA 240, citing *General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd*, [1972] RPC 457, [1971] FSR 417 (UKCA) at pages 482 and 483 (of RPC). In sum, CGK is a concept derived from a common sense approach to the practical question of what would in fact be known to an appropriately skilled addressee. Individual patent specifications and their contents do not normally form part of the relevant CGK, although there may be specifications which are so well known among those of the art that upon evidence of such a state of affairs they form part of such knowledge. Generally, scientific articles form part of the CGK provided they are generally known and generally regarded as a basis for further action by the bulk of those who are engaged in a particular art.

Established reference works (such as textbooks, review articles, handbooks, etc.) or demonstrated commonality of certain knowledge in a number of disclosures in the field are relevant to the inquiry. The common general knowledge at a certain date can be confirmed by subsequent publications, or by showing that the knowledge had been accepted in the field over a period of time: (see Manual of Patent Office Practice (CIPO) at § 12.02.02c).

References D2-D4 and D10-D12 cited originally in our notice were collectively considered as supporting the second point of CGK (please refer to the notice for the elaborated descriptions of these references). Specifically, these documents disclose that it was known that the early studies of GA had by-passed the usual dose-finding phase, that the standard 20 mg/day dosage had been chosen arbitrarily (D2-D4) and that the optimal dosage was not known (D10-D12). Importantly, the Patentee's response also specifically disputes that D2, D10 and D12 were part of CGK (R-L2 on page 9).

None of these documents qualify as an established reference work such as a review article. Rather, these documents consist of journal articles, conference abstracts and a

patent application that disclose small pilot or Phase II clinical studies. Even though these six publications each disclose that the optimal dosage was not known, there is no evidence on the record before us that these publications, individually or collectively, were generally known by the bulk of those in the field. There is no further evidence that it was known by the bulk of those in the field that the approved 20 mg/day GA formulation had been chosen arbitrarily without conducting the standard dose-finding studies. For these reasons, we agree with the Patentee that this knowledge is not appropriately considered as CGK of the skilled person.

At step 4 of our preliminary analysis of obviousness this point of CGK was particularly relevant to the skilled person's motivation to pursue the optimal GA regimen using one of the two known self-inject subcutaneous formulations: (from L2 at pages 15-16, citing the original passage from our notice)

> It was well-known in the art that the early therapeutic studies of GA had by-passed the usual dose-finding phase: the standard 20 mg/day dosage had been chosen arbitrarily (D2-D4), and the optimal dosing was not known (D10-D12).
>
> […]
>
> In our view, this information collectively supports that the CGK and prior art provided a specific motivation for the skilled person to pursue an optimal GA regimen with a lower dosing frequency

This conclusion was predicated in part on information that is no longer considered as CGK. Based on the record as it stands, for the reasons that follow, we no longer agree that the skilled person would have been motivated to determine the optimal dosing frequency of the existing GA formulations.

Since 20 mg/day was the approved on-market dosage our view is that it is more reasonable that the skilled person would have expected that the regimen had been identified as the optimal dosage regimen in the usual manner. In this view, it is reasonable that the skilled person would have accepted the statement from the D23[2] press release following the FORTE trial that 20mg/daily remained the optimal treatment dosage.

For these reasons, we agree with the Patentee's position that the skilled person with a motivation to solve the "long felt need" of "enhancing the patient experience whilst maintaining efficacy with no increase in side effects" (R-L1 at page 7) would more likely

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[2] Document D23 was submitted to the record with the Patentee's letter of May 29, 2020.

have abandoned the existing subcutaneous formulations in favour of an oral formulation, sustained release injectable formulation or a patch (R-L2, page 22). This position is supported by Dr. Prat's expert opinion[3] that the skilled person would more likely look to develop a formulation that could be administered orally or by patch, or alternatively a sustained release injectable formulation that could be administered monthly, every six months or annually (D31 at paras 305-306).

While the obvious to try factors need not all be met, they must all be considered and weighed before coming to a conclusion about whether it would have been more or less self-evident to the skilled person to try to obtain the invention (*Apotex Inc v Shire LLC*, 2021 FCA 52 at para 106, citing *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2020 FCA 30 at paras 89-90). The Board attributed significant weight to the motivation factor and, in having reconsidered the obvious to try factors in light of the above changes, our final view is that it would not have been more or less self-evident to the skilled person to try to obtain the invention. Our final conclusion is that the subject-matter of claims 1-78, which includes issued claims 1-66 and proposed claims 67-78, complies with section 28.3 of the *Patent Act*.

Utility of proposed claims 68, 70, 72, 74, 76 and 78

New claims 67-78 were proposed for the first time in the Patentee's letter R-L1. We note that these proposed claims were not before the Federal Court or the Federal Court of Appeal. As a result, our view is that the claim set before us is different. The Board has considered the proposed claims 67-78 in a manner consistent with the jurisprudence.

In the same manner as the issued claims, the proposed claims are each directed to using GA, or a medicament comprising GA, at a dosage of 40 mg subcutaneously three times per week to treat a patient suffering from a relapsing form of multiple sclerosis. In contrast to the first 66 claims, the frequency and severity of injection site reactions (ISRs) are prominently featured in all of claims 67-78.

Proposed claims 67 and 68 are representative (emphasis added):

> 67. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, while **inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily**, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising

[3] The expert report of Dr. Alexandre Prat from the Federal Court trial was submitted to the record with the Patentee's letter of December 17, 2020.

> 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.
>
> 68. The medicament of claim 67, wherein the medicament **induces both reduced severity and reduced frequency of injection site reactions**.

As with independent claim 67, inducing a reduced frequency of ISR relative to 20 mg daily is expressly asserted in all of the independent claims 69, 71, 73, 75 and 77. Likewise, as with dependent claim 68, inducing both reduced severity and reduced frequency of ISRs is expressly asserted in all of the dependent claims 70, 72, 74, 76 and 78.

Is it appropriate for the Re-examination Board to consider the utility of the proposed claims?

The proposed claims were considered for the first time in our second letter wherein we explained our statutory obligation to consider all of the patentability requirements for any new claims that may be proposed during a re-examination proceeding (L2 at page 21, emphasis in the original):

> In accordance with paragraph 48.4(1)(*c*) the Board shall issue a certificate incorporating in the patent any proposed amended or new claim determined to be patentable. Accordingly, proposed claims must satisfy the requirements of patentability, including utility.

In response to that letter, the Patentee submitted that the utility defect identified by the Board is not an appropriate matter for review in the re-examination proceeding because some of the issued claims include an improvement in the severity of ISRs and so the analysis presented is not a substantial "new" question of patentability as contemplated in section 48.2 of the *Patent Act* (R-L2 at page 25).

Section 48.2 of the *Patent Act* requires a re-examination board to determine whether a compliant request for re-examination has raised a substantial new question of patentability affecting any of the issued claims contained within the patent concerned:

> **Determination to be made by board**
>
> **48.2(2)** A re-examination board shall, within three months following its establishment, determine whether a substantial new question of patentability

> affecting any claim of the patent concerned is raised by the request for re-examination.
>
> ...
>
> **48.2(4)** Where a re-examination board has determined that a request for re-examination raises a substantial new question affecting the patentability of a claim of the patent concerned, the board shall notify the patentee of the determination and the reasons therefor.

Section 48.2 of the *Patent Act* applies to the claims contained in the original issued patent at the time when the request for re-examination was made, not to new claims that may be proposed later in the re-examination proceeding. Re-examination is a two-stage process: *Camso Inc v Soucy International Inc*, 2016 FC 1116 at paras 8-9 [*Camso*], citing *Novozymes A/S v Canada (Commissioner of Patents)*, 2007 FCA 129. It is the first stage that is governed by section 48.2, and it is only in the second stage that amendments or new claims may be proposed: *Camso* at paras 8-9

> Re-examination pursuant to sections 48.1 to 48.5 of the Act is a two-step process. Both stages do not involve the same parties. The first stage involves the filing of a request by a requester (section 48.1), the establishment of a re-examination board by the Commissioner in response to this request (section 48.2(1) and the preliminary decision by the re-examination board as to whether the request raises a substantial new question of patentability (section 48.2(2) to (4)).
>
> The second stage follows the re-examination board's determination that a substantial new question of patentability is raised (section 48.2(4))...Only the patentee is given notice of such determination (section 48.2(4)) and is entitled to make submissions (section 48.2(5)), to propose amendments to the patent (section 48.3(2) and to receive a copy of the certificate (section 48.4(2)). Only the patentee is given a right to appeal (section 48.5).

Since the provisions under section 48.2 of the *Patent Act* govern the first stage of the process, we are unable to agree that they prohibit the Board from considering the patentability of new claims that are proposed for the first time during the second stage of the proceeding.

Pursuant to paragraph 48.4(1)(c) of the *Patent Act*, any amended or new claim that is proposed during the second stage must be determined to be patentable in order to be incorporated in the patent. For this reason, our view is that the utility of the proposed claims is an appropriate matter for the Board to review.

Was the utility of dependent claims 68, 70, 72, 74, 76 and 78 established as of the filing date?

In our second letter, we provided our preliminary views and reasoning as to why the claimed therapeutic efficacy (including the various clinical and MRI-efficacy outcomes claimed), the reduced frequency of ISRs and the improved tolerability asserted within one or more of the proposed independent claims 67, 70, 72, 74, 76 and 78 had each been established. We further expressed our preliminary view that, based on the record before us, the utility of inducing ISRs of reduced severity that was further asserted in each of the dependent claims 68, 70, 72, 74, 76 and 78 had not been established as of the filing date. We invited submissions in response to our preliminary analysis and expressly informed the Patentee that evidence establishing that the asserted utility had been demonstrated as of the filing date could be accepted and it was open to the Patentee to provide the Board with such evidence if it wished (L2 at pages 21-23, emphasis added):

> The first step is to identify the subject-matter of the invention as claimed.
> …
> Our preliminary view is that the skilled person would construe the above assertions relating to efficacy, tolerability and the frequency and severity of ISRs (where applicable for each respective claim) as part of the subject-matter of the invention as claimed. While it would be erroneous to expand the subject-matter of a claim beyond what it says, it is appropriate to consider matter that is expressly asserted within the claim as part of the invention as claimed: *Bristol-Myers Squibb Canada Co v Apotex Inc*, 2017 FCA 190, para 37, citing *AstraZeneca*, para 61.
>
> The second step is to determine whether the claimed subject-matter is capable of a practical purpose or an actual result. The claimed efficacies and MRI-outcomes, improved tolerability and reduced frequency and severity of ISRs are actual results that are asserted as part of the claimed inventions.
> Since utility is measured against the subject-matter of the invention as claimed, our preliminary view is that these asserted results are the utility that must have been established by either demonstration or sound prediction as of the filing date. This is a longstanding principle that has not been varied by *AstraZeneca*: *Bauer Hockey Corp v Easton Sports Canada Inc*, 2010 FC 361, para 289; *AZT*, para 92.
>
> *Demonstration*
>
> On pages 31-35 of the patent's description a number of positive statements are made indicating that the claimed efficacies and MRI-outcomes had been

established by demonstration prior to the filing the application. There is no obligation to include such data in the application, however if an invention's utility is questioned, utility must be shown to have been demonstrated or soundly predicted as of the filing date: *Manual of Patent Office Practice* §19.01, 19.01.02. Having no reason to question these statements, the Board accepts the statements on pages 31-35 as indicating that the specific assertions relating to efficacy had been established by demonstration prior to filing the application.

Notably, even though the Phase III GALA study outlined in the example had not been completed before the application was filed, establishing utility by demonstration does not require Phase III results: the standard for establishing utility is lower than the standard for obtaining regulatory approval. Statements of demonstration based on smaller, less powerful studies or preclinical data would generally suffice.

In contrast to the various efficacy measures claimed, no such statements of demonstration are made in the results section or elsewhere indicating that improved tolerability, less frequent ISRs or less severe ISRs, relative to 20 mg/day, had been demonstrated as of the filing date.

Evidence establishing that the demonstration had been carried out as of the filing date can be accepted and it is open to the Patentee to provide such evidence, if it wishes.

Sound prediction

Factual Basis

The safety and tolerability of daily administration of GA at 20 mg and 40 mg had already been established and were known to be comparable. Further, a regimen requiring three injections per week would self-evidently involve significantly fewer injections than a daily regimen. These facts were known or would have been self-evident to the skilled person reading the specification as of the filing date.

Line of reasoning and disclosure of same

Lowering the injection frequency from seven to three per week would significantly lower the number of injections administered. In our view, the skilled person would reasonably expect that reducing the frequency of injection would in turn reduce the frequency of reactions associated with injections.

> Further, the skilled person would understand that fewer injections and fewer injection-related reactions would equate to improved tolerability. This would have been self-evident to the skilled person reading the specification, in our preliminary view.
>
> Our preliminary view is therefore that reduced frequency of ISRs and improved tolerability compared to the 20 mg daily regimen was soundly predicted as of the filing date. As such, the utility of proposed claims 67, 69, 71, 73, 75 and 77, insofar as it relates to reduced frequency of ISRs and improved tolerability, would have been soundly predicted as the filing date.
>
> By contrast, there is no line of reasoning disclosed in the description or known from the CGK from which the skilled person can infer that the severity of ISRs associated with the 40TIW would be reduced relative to 20 mg daily. Since the safety and tolerability of the 20 mg and 40 mg doses were known to be about the same, the reasonable inference would have been that the severity of ISRs would be about the same. Accordingly, our preliminary view is that the utility of proposed claims 68, 70, 72, 74, 76 and 78, insofar as it relates to inducing a reduced severity of ISRs, was not soundly predicted as of the filing date.
>
> **As stated above evidence establishing that the demonstration had been carried out as of the filing date can be accepted.**

The Patentee's response to our second letter did not provide any submissions disputing or addressing any of our preliminary views in respect of the lack demonstration or lack of sound prediction that less severe ISRs are induced relative to 20 mg/day, nor was any evidence of demonstration as of the filing date provided. In this view, and for the reasons set out above, we are unable to determine that is was established as of the filing date that the subject-matter of proposed claims 68, 70, 72, 74, 76 and 78 was capable of the additional actual result of inducing less severe ISRs in the manner asserted in each of those dependent claims. Our conclusion is therefore that the subject-matter of these dependent claims lack the utility that is required by section 2 of the *Patent Act*.

CONCLUSIONS

The Board has concluded that claims 1-78 are non-obvious and compliant with section 28.3 of the *Patent Act*.

The Board has further concluded that proposed independent claims 67, 69, 71, 73, 75 and 77 are useful and compliant with section 2 of the *Patent Act*. In contrast, the additional utility that is expressly claimed in dependent claims 68, 70, 72, 74, 76 and 78

was not established by demonstration or sound prediction, contrary to section 2 of the *Patent Act*.

In accordance with paragraph 48.4(1)(c) of the *Patent Act* the proposed claims 67, 69, 71, 73, 75 and 77 shall be incorporated in the '802 Patent.

COMPLETION OF RE-EXAMINATION

Please find enclosed a Certificate of Re-examination issued under section 48.4(1) of the *Patent Act* confirming the patentability of issued claims 1-66 and incorporating the new proposed claims 67, 69, 71, 73, 75 and 77 submitted by the Patentee with the letter of October 19, 2020.

Please also find enclosed a Registration Certificate indicating that the enclosed Certificate of Re-examination has been registered as an "Other Document" against CA Patent number 2,760,802.

Under section 48.5 of the *Patent Act*, no appeal may be taken by the Patentee from the decision of the Re-examination Board after three (3) months from the date a copy of the Certificate of Re-examination is sent by registered mail to the Patentee.

Chairperson
Cara Weir

Member
Geneviève Fortier

Member
Isabelle Gagné

c.c. Kavita Ramamoorthy
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Canadian Intellectual Property Office

BUREAU DES BREVETS
CONSTAT DE RÉEXAMEN

PATENT OFFICE
CERTIFICATE OF RE-EXAMINATION

Nº de brevet - Patent No: **2,760,802**

Par la présente, les soussignées certifient que le brevet susmentionné a été réexaminé selon les paragraphes 48.1 à 48.3 de la *Loi sur les brevets* et que le Conseil de réexamen convient de ce qui suit:

The undersigned hereby certify that the above-noted patent has been re-examined pursuant to section 48.1 to 48.3 of the *Patent Act* and that the Re-examination Board has determined the following:

(i)	Les revendications / Claims	1-66	du brevet susmentionné sont brevetables / of the above noted patent are hereby confirmed to be patentable.
(ii)	Les nouvelles revendications/ New claims	67, 69, 71, 73, 75 and 77	(soumises le 19 octobre, 2020 / submitted October 19, 2020) sont brevetables et font partie du brevet susmentionné à compter de ce jour / are patentable and have been incorporated into the above noted patent as of this date.

Cara Weir	Geneviève Fortier	Isabelle Gagné
Présidente	Membre	Membre
Chairperson	Member	Member

Daté à Gatineau (Québec), ce 28ieme jour d'octobre, 2022
Dated at Gatineau, Quebec, this 28th day of October, 2022

Canada

Innovation, Sciences et Développement économique Canada
Office de la propriété intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

Courtoisie - Certificat d'enregistrement (document(s) connexe(s))
Courtesy - Certificate of Registration (Related Document(s))

SMART & BIGGAR LP
P.O. BOX 2999
STATION D
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Détails du certificat
Certificate Details

Date du certificat: Certificate Date:	**2022/10/28**
N° d'enregistrement: Registration N°:	**05854383**
Votre n° de référence: Your Reference N°:	29382-12

Document enregistré:	AUTRE DOCUMENT
Document Registered:	OTHER DOCUMENT

Les dossiers du Bureau des brevets indiquent qu'un document a été enregistré relativement à la (aux) demande(s) et/ou au(x) brevet(s) suivants:

Patent Office records indicate that a document has been registered for the following application(s) and/or patent(s):

Demandes/Applications:

2,706,802

CLAIMS:

1. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from relapsing-remitting multiple sclerosis or who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

2. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection to treat a human patient who is suffering from relapsing-remitting multiple sclerosis or who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis.

3. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from relapsing-remitting multiple sclerosis or who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, wherein the medicament comprises a 40mg dose of glatiramer acetate and wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every week with at least one day between each subcutaneous injection, and wherein the medicament is a pharmaceutical composition having a pH in the range of 5.5 to 8.5.

4. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every week with at least one day between each

subcutaneous injection to treat a human patient who is suffering from relapsing-remitting multiple sclerosis or who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, and wherein the medicament is a pharmaceutical composition having a pH in the range of 5.5 to 8.5.

5. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate each week with at least one day between each subcutaneous injection.

6. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate each week with at least one day between each subcutaneous injection to treat a human patient who is suffering from a relapsing form of multiple sclerosis.

7. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, wherein the medicament is prepared for a regimen consisting of a single subcutaneous injection of a 40mg dose of glatiramer acetate on three days during each week with at least one day between each subcutaneous injection.

8. Glatiramer acetate for use in a regimen consisting of a single subcutaneous injection of a 40mg dose of glatiramer acetate on three days during each week with at least one day between each subcutaneous injection to treat a human patient who is suffering from a relapsing form of multiple sclerosis.

9. A medicament comprising glatiramer acetate for use in

treating a human patient who is suffering from a relapsing form of multiple sclerosis, wherein the medicament is prepared for a regimen consisting of subcutaneous injections for at least 6 months of 1ml of a pharmaceutical composition comprising 40mg/ml of glatiramer acetate on only three days during each week with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

10. Glatiramer acetate for use in a regimen for treating a human patient suffering from a relapsing form of multiple sclerosis which regimen consists of subcutaneous injections for at least 6 months of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only three days during each week with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

11. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, wherein the medicament is prepared for a regimen which is more tolerable than and as effective as a regimen of 20mg of glatiramer acetate s.c. daily, the regimen consisting of subcutaneous injections for at least 6 months with 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only three days during each week with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the

pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

12. Glatiramer acetate for use in a regimen for treating a human patient suffering from a relapsing form of multiple sclerosis which regimen is more tolerable than and as effective as a regimen of 20mg of glatiramer acetate s.c. daily, the regimen consisting of subcutaneous injections for at least 6 months with 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only three days during each week with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

13. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

14. Glatiramer acetate for use in a regimen for treating a human patient suffering from a relapsing form of multiple

sclerosis, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, the regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

15. A medicament comprising glatiramer acetate for use in reducing the frequency of relapses by 30% or more as compared to placebo in a human population, for reducing brain atrophy, for reducing the cumulative number of enhancing lesions on T1-weighted images, or for reducing the level of disability as measured by EDSS Score of a human patient suffering from a relapsing form of multiple sclerosis, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

16. Glatiramer acetate for use in a regimen for reducing the frequency of relapses by 30% or more as compared to placebo

in a human population, for reducing brain atrophy, for reducing the cumulative number of enhancing lesions on T1-weighted images, or for reducing the level of disability as measured by EDSS Score of a human patient suffering from a relapsing form of multiple sclerosis, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, which regimen consists of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

17. A medicament comprising glatiramer acetate for use in improving the tolerability of glatiramer acetate treatment of a human patient suffering from a relapsing form of multiple sclerosis which is as effective as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

18. Glatiramer acetate for use in a regimen for improving the tolerability of glatiramer acetate treatment of a human patient suffering from a relapsing form of multiple sclerosis which is as effective as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, which regimen consists of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

19. A medicament comprising glatiramer acetate for use in improving the tolerability of glatiramer acetate therapy reducing the frequency of relapses, reducing brain atrophy, reducing the cumulative number of enhancing lesions on T1-weighted images, or reducing the level of disability as measured by EDSS Score, of a human patient suffering from a relapsing form of multiple sclerosis as effectively as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled

syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

20. Glatiramer acetate for use in a regimen for improving the tolerability of glatiramer acetate therapy reducing the frequency of relapses, reducing brain atrophy, reducing the cumulative number of enhancing lesions on T1-weighted images, or reducing the level of disability as measured by EDSS Score, of a human patient suffering from a relapsing form of multiple sclerosis as effectively as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced severity of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, which regimen consists of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

21. The medicament of claim 9 or claim 11, or glatiramer acetate of claim 10 or claim 12, wherein the subcutaneous injections occur for at least 12 months.

22. The medicament of claim 1 or claim 3, or glatiramer acetate of claim 2 or claim 4, wherein the human patient is suffering from relapsing-remitting multiple sclerosis.

23. The medicament of claim 1 or claim 3, or glatiramer acetate of claim 2 or claim 4, wherein the human patient has experienced a first clinical episode and has MRI features consistent with multiple sclerosis.

24. The medicament of any one of claims 1, 3, 5 or 7, or glatiramer acetate of any one of claims 2, 4, 6 or 8 wherein the medicament is prepared as a pharmaceutical composition having a pH in the range of 5.5 to 7.0 or the glatiramer acetate is present in a pharmaceutical composition having a pH in the range of 5.5 to 7.0, wherein the pharmaceutical composition comprises 40 mg/ml glatiramer acetate and mannitol.

25. The medicament of any one of claims 1, 3, 5, 9, 11, 13, 15, 17, 19 or 21-24 or glatiramer acetate of any one of claims 2, 4, 6, 10, 12, 14, 16, 18, 20-24, wherein during each week or each seven days the subcutaneous injections are on day 1, day 3 and day 5 of such week or seven days; day 1, day 3 and day 6 of such week or seven days; day 1, day 4 and day 6 of such week or seven days; day 2, day 4 and day 6 of such week or seven days; day 2, day 4 and day 7 of such week or seven days; day 2, day 5 and day 7 of such week or seven days; or day 3, day 5 and day 7 of such week or seven days.

26. The medicament of claim 7 or glatiramer acetate of claim 8, wherein the three days during each week are selected from the group consisting of day 1, day 3 and day 5; day 1, day 3 and day 6; day 1, day 4 and day 6; day 2, day 4 and day 6; day 2, day 4 and day 7; day 2, day 5 and day 7; and day 3, day 5 and day 7.

27. A medicament comprising glatiramer acetate for use in increasing the time to a confirmed relapse in a human patient who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

28. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection to increase the time to a confirmed relapse in a human patient who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis.

29. A medicament comprising glatiramer acetate for use in reducing the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reducing the mean number of new T2 lesions in the brain of a human patient, reducing the cumulative number of enhancing lesions on T1-weighted images in a human patient, reducing the total volume of T2 lesions in a human patient, reducing the number of new hypointense lesions on enhanced T1 scans in a human patient or reducing the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient has experienced a single demyelinating event and is at high risk of developing clinically definite multiple sclerosis, and wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

30. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection to reduce the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reduce the mean number of new T2 lesions in the brain of a human patient, reduce the cumulative number of enhancing lesions on T1-weighted images in a human patient, reduce the total volume of T2 lesions in a human patient, reduce the number of new hypointense lesions on enhanced T1

scans in a human patient or reduce the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient has experienced a single demyelinating event and is at high risk of developing clinically definite multiple sclerosis.

31. The medicament of any one of claims 1, 3, 23-25 or 27, or glatiramer acetate of any one of claims 2, 4, 23-25 or 28, wherein the first clinical episode comprises a clinical episode of optic neuritis, blurring of vision, diplopia, involuntary rapid eye movement, blindness, loss of balance, tremors, ataxia, vertigo, clumsiness of a limb, lack of coordination, weakness of one or more extremity, altered muscle tone, muscle stiffness, spasms, tingling, paraesthesia, burning sensations, muscle pains, facial pain, trigeminal neuralgia, stabbing sharp pains, burning tingling pain, slowing of speech, slurring of words, changes in rhythm of speech, dysphagia, fatigue, bladder problems, bowel problems, impotence, diminished sexual arousal, loss of sensation, sensitivity to heat, loss of short term memory, loss of concentration, or loss of judgment or reasoning.

32. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31, wherein the human patient has MRI features consistent with multiple sclerosis.

33. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29, 31 or 32, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31 or 32, wherein the human patient has at least 1 cerebral lesion detectable by an MRI scan and wherein the lesion is associated with brain tissue inflammation, myelin sheath damage or axonal damage.

34. The medicament or glatiramer acetate of claim 33, wherein the lesion is a demyelinating white matter lesion visible on brain MRI and wherein the white matter lesion is at least 3 mm in diameter.

35. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-34, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-34, wherein the human patient has at least 2 cerebral lesions detectable by an MRI scan and suggestive of multiple sclerosis.

36. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-35, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-35, wherein the regimen is effective for reducing the frequency of relapses in the human patient, reducing the mean cumulative number of Gd-enhancing lesions in the brain of the human patient, reducing the mean number of new T2 lesions in the brain of the human patient, reducing the cumulative number of enhancing lesions on T1-weighted images in the human patient, reducing brain atrophy in the human patient, increasing the time to a confirmed relapse in the human patient, reducing the total number of confirmed relapses in the human patient, reducing the progression of MRI-monitored disease activity in the human patient, reducing the total volume of T2 lesions in the human patient, reducing the number of new hypointense lesions on enhanced T1 scans in the human patient, reducing the total volume of hypointense lesions on enhanced T1 scans, reducing the level of disability as measured by EDSS Score in the human patient, reducing the change in EDSS Score in the human patient, reducing the change in Ambulation Index in the human patient, reducing the level of disability as measured by EuroQoL (EQ5D) questionnaire

in the human patient, or reducing the level of disability as measured by the work productivity and activities impairment – General Health (WPAI-GH) questionnaire in the human patient.

37. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-36, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-36, wherein the regimen is effective for reducing the frequency of relapses or exacerbations in the human patient.

38. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-36, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-36, wherein the regimen is effective for reducing the frequency of relapses in the human patient.

39. The medicament or glatiramer acetate of claim 38, wherein the regimen is effective for further reducing the cumulative number of enhancing lesions on T1-weighted images of the human patient.

40. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-36, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-36, wherein the regimen is effective for reducing the cumulative number of enhancing lesions on T1-weighted images.

41. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-40, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-40, wherein the regimen is effective for reducing brain atrophy and for reducing the frequency of relapses by 30% or more as compared to placebo in a human population.

42. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-41, or glatiramer acetate of any

one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-41, wherein the regimen is effective for reducing the level of disability of the human patient as measured by EDSS Score.

43. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-42, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-42, wherein the regimen is effective for reducing the frequency of relapses as effectively as administration of 20mg of glatiramer acetate s.c. daily.

44. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-43, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-43, wherein the regimen is effective for reducing brain atrophy as effectively as administration of 20mg of glatiramer acetate s.c. daily.

45. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-44, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-44, wherein the regimen is effective for reducing the cumulative number of enhancing lesions on T1-weighted images as effectively as administration of 20mg of glatiramer acetate s.c. daily.

46. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-45, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-45, wherein the regimen is effective for reducing the level of disability of the human patient as measured by EDSS Score as effectively as administration of 20mg of glatiramer acetate s.c. daily.

47. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13,

15, 17, 19, 21-27, 29 or 31-46, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-46, wherein the regimen is effective for treating the human patient with or inducing reduced frequency and severity of immediate post injection reactions and injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily.

48. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29 or 31-47, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30 or 31-47, wherein the regimen is effective for alleviating a symptom of relapsing-remitting multiple sclerosis in the human patient.

49. A medicament comprising glatiramer acetate for use in reducing frequency of relapses or exacerbations in a human patient suffering from relapsing-remitting multiple sclerosis wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

50. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection to reduce frequency of relapses or exacerbations in a human patient suffering from relapsing- remitting multiple sclerosis.

51. A medicament comprising glatiramer acetate for use in reducing the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reducing the mean number of new T2 lesions in the brain of a human patient, reducing the cumulative number of enhancing lesions on T1-weighted images in a human patient, reducing the total volume

of T2 lesions in a human patient, reducing the number of new hypointense lesions on enhanced T1 scans in a human patient or reducing the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient is suffering from relapsing-remitting multiple sclerosis, and wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

52. Glatiramer acetate for use in a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection to reduce the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reduce the mean number of new T2 lesions in the brain of a human patient, reduce the cumulative number of enhancing lesions on T1-weighted images in a human patient, reduce the total volume of T2 lesions in a human patient, reduce the number of new hypointense lesions on enhanced T1 scans in a human patient or reduce the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient is suffering from relapsing-remitting multiple sclerosis.

53. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29, 31-49 or 51, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31-48, 50 or 52, wherein the regimen is further effective for reducing the mean cumulative number of Gd-enhancing lesions in the brain of the human patient, reducing the mean number of new T2 lesions in the brain of the human patient or reducing the cumulative number of enhancing lesions on T1- weighted images in the human patient.

54. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13,

15, 17, 19, 21-27, 29, 31-49, 51 or 53, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31-48, 50 or 52-53, wherein the regimen is effective for treating the human patient with or inducing reduced frequency of immediate post injection reactions or of injection site reactions in the human patient relative to administration of 20mg glatiramer acetate s.c. daily.

55. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29, 31-49, 51 or 53-54, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31-48, 50 or 52-54, wherein the regimen is effective for improving tolerability in the human patient relative to 20mg glatiramer acetate s.c. daily , wherein the increased tolerability comprises reduced frequency of immediate post injection reactions or reduced frequency of injection site reactions, each relative to the frequency experienced with 20 mg glatiramer acetate s.c. daily.

56. The medicament or glatiramer acetate, of any one of claims 47, 54 or 55, wherein the immediate post injection reaction is palpitations, feeling hot, flushing, hot flushes, tachycardia, dyspnoea, chest discomfort, chest pain, non-cardiac chest, asthenia, back pain, bacterial infection, chills, cyst, face edema, fever, flu syndrome, infection, injection site erythema, injection site hemorrhage, injection site induration, injection site inflammation, injection site mass, injection site pain, injection site pruritus, injection site urticaria, injection site welt, neck pain, pain, migraine, syncope, tachycardia, vasodilatation, anorexia, diarrhea, gastroenteritis, gastrointestinal disorder, nausea, vomiting, ecchymosis, peripheral edema, arthralgia, agitation, anxiety, confusion, foot drop, hypertonia,

nervousness, nystagmus, speech disorder, tremor, vertigo, bronchitis, dyspnea, laryngismus, rhinitis, erythema, herpes simplex, pruritus, rash, skin nodule, sweating, urticaria, ear pain, eye disorder, dysmenorrheal, urinary urgency, or vaginal moniliasis.

57. The medicament or glatiramer acetate, of any one of claims 47, 54 or 55, wherein the injection site reaction is erythema, hemorrhage, induration, inflammation, mass, pain, pruritus, urticaria, or welt that occurs immediately around the site of injection.

58. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29, 31-49, 51 or 53-57, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31-48, 50 or 52-57, wherein the human patient has not received glatiramer acetate prior to initiation of the regimen.

59. The medicament of any one of claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21-27, 29, 31-49, 51 or 53-58, or glatiramer acetate of any one of claims 2, 4, 6, 8, 10, 12, 14, 16, 18, 20-28, 30, 31-48, 50 or 52-58, wherein the glatiramer acetate is present in 1ml of a pharmaceutical composition in a prefilled syringe for self administration.

60. Use of glatiramer acetate for the manufacture of a medicament for use in treating a human patient who is suffering from relapsing-remitting multiple sclerosis or who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

61. Use of glatiramer acetate in the manufacture of a medicament for use in increasing the time to a confirmed relapse in a human patient who has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

62. Use of glatiramer acetate in the manufacture of a medicament for use in reducing the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reducing the mean number of new T2 lesions in the brain of a human patient, reducing the cumulative number of enhancing lesions on T1-weighted images in a human patient, reducing the total volume of T2 lesions in a human patient, reducing the number of new hypointense lesions on enhanced T1 scans in a human patient or reducing the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient has experienced a first clinical episode and is at high risk of developing clinically definite multiple sclerosis, and wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

63. Use of glatiramer acetate in the manufacture of a medicament for use in reducing frequency of relapses or exacerbations in a human patient suffering from relapsing-remitting multiple sclerosis wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous

injection.

64. Use of glatiramer acetate in the manufacture of a medicament for use in reducing the mean cumulative number of Gd-enhancing lesions in the brain of a human patient, reducing the mean number of new T2 lesions in the brain of a human patient, reducing the cumulative number of enhancing lesions on T1-weighted images in a human patient, reducing the total volume of T2 lesions in a human patient, reducing the number of new hypointense lesions on enhanced T1 scans in a human patient or reducing the total volume of hypointense lesions on enhanced T1 scans in a human patient, wherein the human patient is suffering from relapsing-remitting multiple sclerosis, and wherein the medicament is prepared for a regimen of three subcutaneous injections of a 40mg dose of glatiramer acetate every seven days with at least one day between each subcutaneous injection.

65. The use of any one of claims 60-64, wherein the medicament is a pharmaceutical composition comprising 40 mg/ml glatiramer acetate and mannitol, and having a pH in the range of 5.5 to 7.0.

66. The use of any one of claims 60-65, wherein the medicament is to be administered using a prefilled syringe by self administration.

New Claims
Accompanying Response to the July 17, 2020 Preliminary Opinion

67. A medicament comprising glatiramer acetate for use in treating a human patient who is suffering from a relapsing form of multiple sclerosis, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

68. The medicament of claim 67, wherein the medicament induces both reduced severity and reduced frequency of injection site reactions.

69. Glatiramer acetate for use in a regimen for treating a human patient suffering from a relapsing form of multiple sclerosis, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, the regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

70. The glatiramer acetate use of claim 69, wherein the glatiramer acetate use induces both reduced severity and reduced frequency of injection site reactions.

71. A medicament comprising glatiramer acetate for use in reducing the frequency of relapses by 30% or more as compared to placebo in a human population, for reducing brain atrophy, for reducing the cumulative number of enhancing lesions on T1-weighted images, or for reducing the level of disability as measured by EDSS Score of a human patient suffering from a relapsing form of multiple sclerosis, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

72. The medicament of claim 71, wherein the medicament induces both reduced severity and reduced frequency of injection site reactions.

73. Glatiramer acetate for use in a regimen for reducing the frequency of relapses by 30% or more as compared to placebo in a human population, for reducing brain atrophy, for reducing the cumulative number of enhancing lesions on T1-weighted images, or for reducing the level of disability as measured by EDSS Score of a human patient suffering from a relapsing form of multiple sclerosis, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, which regimen consists of one

subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

74. The glatiramer acetate use of claim 73, wherein the glatiramer acetate use induces both reduced severity and reduced frequency of injection site reactions.

75. A medicament comprising glatiramer acetate for use in improving the tolerability of glatiramer acetate treatment of a human patient suffering from a relapsing form of multiple sclerosis which is as effective as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, wherein the medicament is prepared for a regimen consisting of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

76. The medicament of claim 75, wherein the medicament induces both reduced severity and reduced frequency of injection site reactions.

77. Glatiramer acetate for use in a regimen for improving the tolerability of glatiramer acetate treatment of a human patient

suffering from a relapsing form of multiple sclerosis which is as effective as administration of 20mg of glatiramer acetate s.c. daily, while inducing reduced frequency of injection site reactions in the human patient relative to administration of 20mg of glatiramer acetate s.c. daily, which regimen consists of one subcutaneous injection of 1ml of a pharmaceutical composition comprising 40mg of glatiramer acetate on only each of three days during each week of treatment with at least one day without a subcutaneous injection of the pharmaceutical composition between each day on which there is a subcutaneous injection, wherein the pharmaceutical composition is in a prefilled syringe, and wherein the pharmaceutical composition further comprises mannitol and has a pH in the range 5.5 to 7.0.

78. The glatiramer acetate use of claim 77, wherein the glatiramer acetate use induces both reduced severity and reduced frequency of injection site reactions.