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Dosage Regimens at the EPO

9th September 2025

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Overview

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- Background **to dosage regimens at the EPO**
- Hurdles to Patentability
  - (a) Novelty
  - (b) Inventive Step
  - (c) Added Matter
  - (d) Sufficiency
- Protecting large molecule dosing regimens
  - (a) Assessment by EPO
  - (b) Arguments in support of patentability
- Drafting Considerations
- Case Study

Legal Basis for Dosage Regimens

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- **Article 53 (c) EPC**

European patents shall not be granted in respect of:.....(c) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; this provision shall not apply to products, in particular substances or compositions, for use in any of these methods.

- **Article 54 (4) & (5) EPC**

(4) Paragraphs 2 and 3 [defining the state of the art] shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to in Article 53(c), provided that its use for any such method is not comprised in the state of the art.

(5) Paragraphs 2 and 3 [defining the state of the art] shall also not exclude the patentability of any substance or composition referred to in paragraph 4 for any specific use in a method referred to in Article 53(c), provided that such use is not comprised in the state of the art.

Legal Basis cont…

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- **G2/08**

Art. 54(4) and (5) EPC acknowledge the notional novelty of substances or compositions even when they are already comprised in the state of the art, provided they are claimed for a new use in a method which Art. 53(c) EPC excludes from patent protection. The notional novelty, and thus, non-obviousness, if any, is not derived from the substance or composition as such, but from its intended therapeutic use.

Art. 54(5) EPC refers to "any specific use"

…..so novelty and inventiveness can reside in a dosage regime……

A substance (X) for use in the treatment of disease (Y) wherein substance (X) is for administration at a dose of (Z) [amount/time]

Value

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- Adds to the patent thicket
- Can be filed as a divisional from API/formulation applications containing suitable dosage information and data
- More usually filed for life cycle management – additional patent years beyond API protection
- Label claim – easier to catch infringers

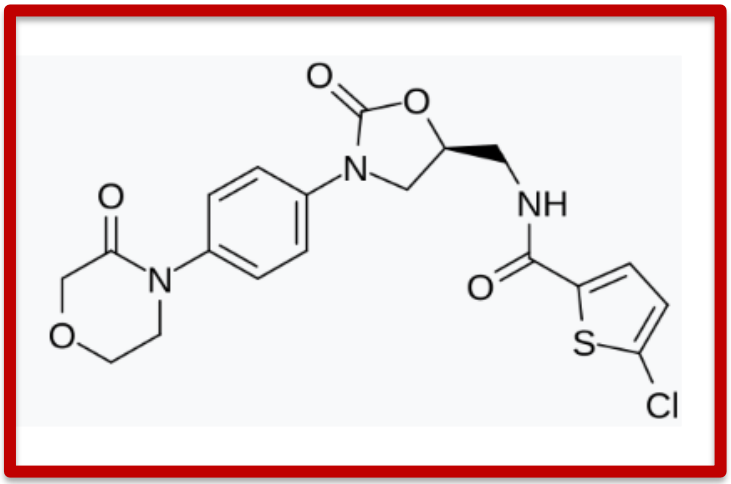
Bayer's Xarelto® - rivaroxaban

Compound patent expired December 2020

SPC provided protection until April 2024

Dosage regime expires in January 2026

- additional 2 years patent protection!!!
- 2023 - $4.7 billion sales
- Q1 2025 - $ 700 million sales



Prior Art

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- Usually own prior art - boilerplate from previous applications
  investor relations
  regulatory submissions

- **CONFLICT!** Clinical protocols are published before data is generated but data is need to support sufficiency
- Beware of EU's CTIS (The Clinical Trials Information System) (CTIS)
  - online system for the regulatory submission, authorisation and supervision of clinical trials in the EU & EEA
  - revised transparency rules in force since 18 June 2024 with launch of a new version of the CTIS public website
  - no longer possible to defer the publication of certain data and documents
  - data and documents are published according to the established timelines for the trial category, population age and trial phase

Prior Art cont…

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Clinical trial plans that disclose only dosage regimens (without results) are generally not novelty-destroying but they may still be used for obviousness

- **T2506/12** Lack of novelty for 2nd medical use requires a disclosure that the treatment of the disease with the API is effective and safe
- **T1123/16** D1 (phase II clinical trial) was deemed CPA (same medical condition, substance and treatment objective) but it did not disclose a therapeutic effect as there was no data
- **T0239/16** Announcement of clinical trials even without data indicates reasonable expectation of success unless the art suggest otherwise (clinical trials are based on existing favourable scientific data and are not conducted in a 'try-and-see basis')

Patentees must carefully manage the timing of dosage regime patent filings to avoid conflicts with publicly available trial data

Patentability Barriers

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Inventive Step – small molecular therapeutics

- EPO's starting position is that determining dosage regimes is routine experimentation (confirmed by **T1409/06** reason 3.2.1)
- If clinical trial protocol is CPA, EPO assumes a reasonable expectation of success unless there are existing prejudices (**T 2963/19)**
- **IT IS DIFFICULT!!!**

Consider including features in addition to the preferred dosage regimen (a specific dose or range and frequency of administration) in the claims, i.e. features of the *specific* formulation, condition being treated, patient group and/or administration mode.

- A narrow claim to marketed product (label claim) will be more defendable and enforceable

T 2963/19

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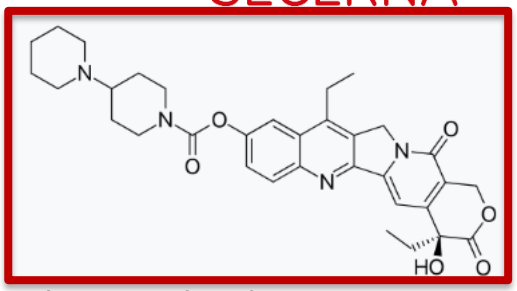

Liposomal irinotecan for use in a method of treating pancreatic cancer in a human patient, wherein the patient exhibits evidence of recurrent or persistent pancreatic cancer following primary chemotherapy and wherein the patient has failed prior treatment with gemcitabine or become resistant to gemcitabine, the method comprising co-administration of an effective amount each of liposomal irinotecan, 5-fluorouracil (5-FU) and leucovorin to the patient in at least one cycle wherein the cycle is a period of 2 weeks and, for each cycle:

(a) liposomal irinotecan is administered to patients not homozygous for the UGT1A 1 *28 allele on day 1 of each cycle at a dose of 80 mg/m**(2)and to patients homozygous for the UGT1A1 *28 allele on day 1 of cycle 1 at a dose of 60 mg/m**(2)and on day 1 of each subsequent cycle at a dose of 60 mg/m**(2)or 80 mg/m**(2);

(b) 5-FU is administered at a dose of 2400 mg/m**(2); and

(c) leucovorin is administered at a dose of 200 mg/m**(2)(l form) or 400 mg/m**(2)(l+d racemic form);

and wherein in each cycle, the liposomal irinotecan is administered prior to the leucovorin, and the leucovorin is administered prior to the 5-FU

T 2963/19 cont…

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- Appeal of opposed patent (revoked for lack of inventive step)
- CPA was clinical trial protocol D15b (no results)
- Problem was defined as the provision of actually effective and safe treatment of defined patients
- BoA accepted that the development of the therapy represented a particular challenge, due to the poor prognosis and low success rates of previous clinical trials;
- BoA also noted that the approval of a clinical study is a risk/benefit assessment, which does not necessarily imply an expected positive outcome; and
- BoA was not convinced that the disclosure of D15b **itself** provided the skilled person with a reasonable expectation that the treatment would be safe and effective

T 2963/19 cont…

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BUT

- There were also reports of beneficial triple treatment of gemcitabine refractory pancreatic cancer patients involving non-liposomal irinotecan with 5-FU and leucovorin, the FOLFIRI regimen, in Phase 2 studies and the report of benefits from treatment of such patients with liposomal irinotecan with or without 5-FU and leucovorin in Phase 1 investigations
- Patentee had leaned into the FOLFIRI regime to help support sufficiency

SO

- Lack of inventive step was upheld

T 1411/23 (13 May 2025)

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- HDM2-p53 interaction inhibitors for use in treating TP53 wild-type tumors with a specific intermittent administration regimen (administration on day 1 and day 8 of a 28 days cycle; minimum of 2 cycles)
- Distinguishing feature over CPA D3: specific administration schedule (one administration every 3 weeks in D3, versus administration on days 1 and 8 of a 28 days cycle in the claims
- Alleged technical effect: reduction of the incidence of severe grades of thrombocytopenia while maintaining a similar efficacy (i.e. improved dosage regime)
- Patent contained data comparing 2 administration schedules but there were also differences in the doses administered so BoA concluded that the data did not convincingly support the alleged technical effect
- Objective technical problem reformulated as an alternative dosage regime
- OBVIOUS

Patentability Barriers cont…

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❖ Added Matter

Article 123(2) EPC (Amendments)

(1) The European patent application or European patent may be amended in proceedings before the European Patent Office, in accordance with the Implementing Regulations. In any event, the applicant shall be given at least one opportunity to amend the application of his own volition.

(2) The European patent application or European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

(3) The European patent may not be amended in such a way as to extend the protection it confers.

Patentability Barriers cont…

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- **Added Matter**

Enlarged Board of Appeal G2/10

- So-called “gold standard” for assessing amendments
- Would the skilled person derive the subject matter as amended directly and unambiguously using common general knowledge from the application as filed.

Added Matter (2)

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- **Originally filed broad claims**

  An antibody specific to target X for use in the treatment of a (broadly defined) disease (e.g inflammatory disorder), wherein antibody X is for administration in a dosage of A to B

- Often need to limit during prosecution in response to support/ inventive step objections
- Article 83 EPC (**sufficiency**) objections - may be to definition of product. Objection is that only the specific antibody e.g. rituximab has been shown to have therapeutic effect.
- Limitation to specific CDRs may not overcome objection
- Article 56 EPC (**inventive step**) objections may be to breadth of medical use
- Amendments may have to be made to narrow plurality of features
- Each amendment could raise risk of contravening Article 123(2) EPC

Added Matter (3)

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❖ **Claim (hypothetical) – Amendments in red**

*An antibody specific to target X (**rituximab**) for use in the treatment of a (broadly defined) disease (e.g inflammatory disorder) **rheumatoid arthritis**, wherein antibody X **rituximab** is for administration in a dosage of 1g to 3g **1g, followed by 1g after 2 weeks***

- ❖ Amend to specific antibody e.g. rituximab to overcome Article 83/84 EPC objections
- ❖ Amend to dosage A as only have data for A e.g. 1g
- ❖ Amend to timing e.g. clinical trial of 1 every 2 weeks
- ❖ Amend to specific disease e.g. RA

Each restriction to a feature may represent a selection from a list! Multiple selections may contravene Article 123(2) EPC!

Added Matter (4)

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- **Types of Article 123(2) EPC Objections**
- Amendments arise as selection from multiple lists
- Amendments taken from an Example
  - Specific dosage and timing
  - Example contain full clinical trial protocol
  - Example may include other features from clinical trial e.g exclusion criteria, biomarker patient selection
  - Amendment may be considered to be an intermediate generalisation
- Amendment to cover dosage regimen not envisaged by Examples

Added Matter – Antibody Case Law

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- **T0363/18**
- *"Use of an anti-CD20 antibody comprising human gamma 1 constant regions in the manufacture of a medicament for treatment of chronic lymphocytic leukemia (CLL) in a human patient, wherein the medicament is for administration to the human patient at a dosage of 500 to 1500 mg/m**(2), and wherein the anti-CD20 antibody is rituximab".*
- Divisional application and therefore it was Article 76(1) EPC in question.
- Correction allowed to amend *mg/m^3 to mg/m^2.*
- BOA accepted a skilled person would derive directly and unambiguously from the disclosure in example 3 the particular dosage of **500 to 1500 mg/m^2** of the active compound rituximab
- BOA also considered that example 3 discloses the use of the particular dose of **500 to 1500 mg/m^2** of **rituximab** in the explicit context of a sequence of administration by infusion of four doses of rituximab for the therapeutic treatment of human CLL patients, the first dose given being a particular and lower one than the three subsequent doses in the range of **500 to 1500 mg/m^2** Thus, the administration of rituximab in a specific amount followed by *increased, identical amounts within a specific range, at a specified frequency (weekly) and for a certain duration (four doses)*, forms part of the dosage regimen described in example 3.

Added Matter – Antibody Case Law

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- **T0363/18 cont.**
- However, BOA unable to identify in example 3 the disclosure of aspect ii) of the definition of the claimed subject-matter (see point 6, above, i.e. the aspect "**treatment of CLL in a human patient"** as referred to in general in the claim) in particular in combination with aspect iii) (i.e. the particular dosage of 500 to 1500 mg/m^2 of rituximab).
- *"Indeed, example 3 discloses dosages of rituximab of **500 to 1500 mg/m^2** in the context of a particular therapy of human CLL patients, characterised by four administrations of the active compound in a stepped-up regimen (see point 12)".*
- This is, however, different from disclosure of a treatment of CLL in a human patient by the sole dose of 500 to 1500 mg/m^2 of rituximab.
- **REVOKED DUE TO ADDED MATTER**

Added Matter – Case Law

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- **T 0235/22**
- *Amendments to claim 1 included:*
- a selected primer agent (the same agent as the anti-CD47 agent)
- a selected anti-CD47 agent (anti-CD47 antibody)
- a selected dosage regimen (where (a) and (b) are separated by 3 to 21 days)
- for the treatment of a particular disease (cancer);
- in a particular subject (primates)
- *Reasons for Decision:*
- Each amendment was either a general definition (features (iv) to (vii) and (ix)) or a preferred embodiment of the invention (features (i) to (iii), (viii)). The skilled person would therefore have derived the combination of these features with the subject-matter of claim 1 as filed in a direct and unambiguous manner.

Decision - no added matter

Patentability Barriers

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Sufficiency – small molecular therapeutics

The claimed efficacy must be *credible at the filing date* of the patent, based on the information provided in the patent application together with the common general knowledge of the person skilled in the art at the filing date.

T799/16

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- A sustained release 4-aminopyridine composition for use in a method of increasing walking speed of a patient with multiple sclerosis, wherein said composition is administered twice daily in a dose of 10 milligrams of 4-aminopyridine
- Sufficiency of preparing sustained-release dosage forms of 4-aminopyridine was acknowledged
- Sufficiency of the credibility of the alleged therapeutic efficacy across the whole scope was challenged as the claims did not exclude the treatment of non-responders.
- Application as filed acknowledged that only a proportion of patients, estimated to be about one third, responded to treatment with 4-aminopyridine
- BoA confirmed that the existence of non-responders is not a reason to deny sufficiency of disclosure, and the treatment of non-responders does not have to be excluded or disclaimed

T799/16 cont…

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Because…

…The existence of a substantial proportion of patients who are non-responders is a common phenomenon observed with drugs in many treatment areas, such as diabetes, migraine or cancer. It is common practice to treat patients with a drug and change their medication should it turn out that they do not respond to the treatment. If it can be shown that a relevant proportion of patients benefits from a treatment and that it has acceptable safety, the criterion of sufficiency of disclosure is met, since the person skilled in the art has the necessary technical information to perform the treatment.

Patentability of Dosage Regimens - Biologics

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Inventive Step

- Are biologic dosage regimens treated differently by the EPO?
- Different arguments in support of IS for biologics can be used by Proprietors

Arguments used to support inventiveness of antibody dosage regimens

- Case Law which relates to small molecule dosage regimen is not applicable
- Antibodies should be treated differently from small molecules, since they have potentially complex pharmacodynamics. Also, half life and elimination rate of antibodies depends on factors such as dose of antibody and level of expression of target antigen which in turn can vary depending on disease state. Other considerations include target-mediated clearance and anti-drug antibodies
- Other arguments - no reasonable expectation of success from previous clinical trials/ report of clinical trial
- Previous failed clinical trials indicates no reasonable expectation of success
- Not feasible to run clinical trials to test effects in isolation so technical effect of administration regimen as a whole must be assessed

Patentability of Biologics Dosage Regimens

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T1927/22

- *1. A pharmaceutical composition comprising a PCSK9 inhibitor for use in reducing lipoprotein(a) (Lp(a)) levels in a patient who exhibits a* ***serum Lp(a) level above 30*** *mg/dL and who is diagnosed with or identified at being at risk of developing a cardiovascular disease or disorder prior to or at the time of administration of the composition, or who is diagnosed with or identified as being at risk of developing a thrombotic occlusive disease or disorder prior to or at the time of administration of the composition; and wherein the PCSK9 inhibitor is* ***an antibody or antigen-binding fragment thereof that specifically binds PCSK9.“***
- BOA accepted that claim was novel over prior art uses of anti-PCSK9 antibodies due to specified Lp(a) level.
- BOA concluded that there was doubt in the art regarding any link between PCSK9 inhibitors and Lp(a) levels. Animal studies were difficult in this context. As such there was no reasonable expectation of success.

INVENTIVE!

Patentability of Biologics Dosage Regimens

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- **T0810/22 - formulation**

1. A stable liquid pharmaceutical formulation of an anti-human PD-1 antibody for use in a method of treatment by therapy, wherein the formulation consists essentially of:

a) 25 mg/mL of the anti-human PD-1 antibody in aqueous solution;

b)70 mg/mL sucrose;

c) 0.2 mg/mL polysorbate 80; and

d) 10 mM Histidine buffer at pH 5.5, wherein the antibody is h409A11."

- The antibody h409A11 is also known as pembrolizumab (Keytruda).
- The closest prior art discussed the therapeutic uses of anti-PD1 antibodies, including pembrolizumab, but not their preparation as a stable formulation suitable for human use. No formulations of pembrolizumab were disclosed.
- Technical effect was the high degree of stability that is necessary for Phase III trials and marketing. As such, the objective technical problem was formulated as the provision of a formulation of pembrolizumab that can be marketed for human therapeutic use.

Patentability of Biologics Dosage Regimens

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- **T0810/22**
- Other prior art documents provided considerable disclosure of approaches for efficient formulation of biopharmaceuticals such as antibodies.
- However, BOA considered that hindsight was required to apply these teachings to pembrolizumab specifically and select the claimed formulation out of other suitable formulations.
- BOA - claimed formulation to be the result of an optimisation process for late clinical development and marketing rather than the outcome of a quick routine search for a formulation with sufficient stability. Thus, the claims were deemed to be inventive over the prior art

INVENTIVE!

Patentability of Biologics Dosage Regimens

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- **EP3107575 – under appeal (T0563/24) following opposition upholding patent in amended form**
- Claims are to a combination IL-4R antagonist (dupilumab) + LABA + ICS in specific dosages
- Aux Req allowed as included patient class
- *A combination therapy comprising:*
  - *i) one or more maintenance doses of an ICS,*
  - *ii) one or more maintenance doses of a LABA.*
  - *iii) a loading dose of about 400 to about 600 mg of an IL-4R antagonist, and*
  - *iv) one or more maintenance doses of about 200 to about 300 mg of the IL-4R antagonist. administration every other week (q2w) or every fourth week (q4w). wherein the ICS and LABA are administered for the duration of administration of the IL-4R antagonist for for use in a method of reducing an asthma patient's dependence on ICS and/or LABA for the treatment of one or more asthma exacerbations comprising: (a) selecting a patient who has moderate-to-severe asthma that is uncontrolled with a background asthma therapy comprising an ICS, a LABA, or a combination thereof; and (b) administering said combination therapy to the patient.*

Patentability of Biologics Dosage Regimens

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- **EP3107575 cont. – under appeal (T0563/24) following opposition upholding patent in amended form**
- **Decision of OD**
- OD ruled that claim was directed towards group of patients *"for whom therapy was known to be more difficult than the general group of asthma patients."*

*"The case law decisions in this field balance (like in other technical fields) the positive and negative pointers derived from the technical background of each case. Here, the indication in D1 that further studies were needed to better define the dosing regimen, and the disclosure of a clinical trial protocol already proposing the claimed administration pattern are **clear pointers** in favour of the opponents. However, the problem to solve is now not as general as for claims 1 and 2, and requires the provision of an effective treatment against asthma exacerbation in a **specific patient population** for whom asthma control is know to be difficult to achieve. This last pointer, added to the fact that dupilumab is a first-in-class antibody modulating both IL-4 and IL-13 signalling with very limited clinical use before D1 speaks against the idea that studies concerning dupiliumab in the patient population in claim 3 would be routine"*

Drafting Considerations

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- Consider where may the claims end up
- Claims with a narrow scope that are on label may be very useful particularly in biologics space
- Consider drafting multiple statement of invention with differing scope, different combination of features
- Statements of invention and claims exactly to clinical trial dosages
- Include sub-categories of patient class, biomarkers etc.
- Timing of filing is critical – need data or to be at least plausible but be aware of clinical trial prior art
- Examples to contain at least some data from clinical trial

Semaglutide

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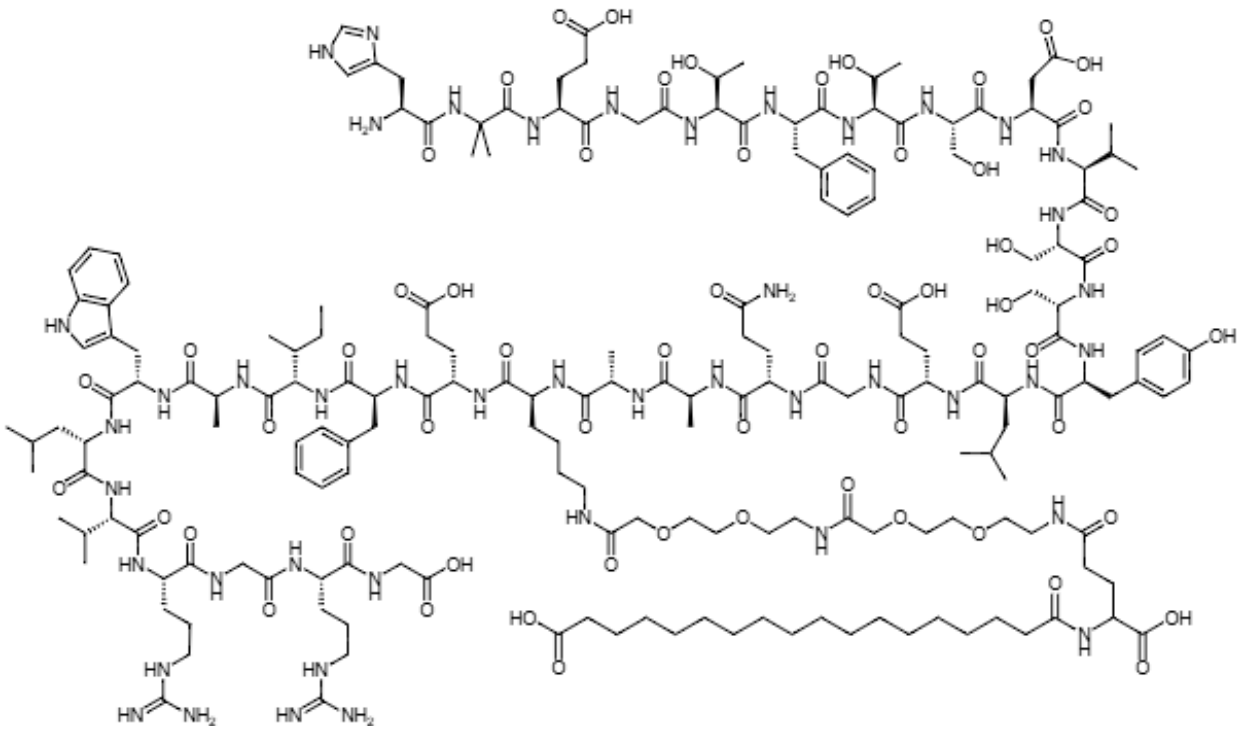

Glucagon-like peptide-1 (GLP-1) receptor agonist which mimics the natural hormone GLP-1 and binds to GLP-1 receptors in the brain

Ozempic® **– type 2 diabetes (injectable)**
Rybelsus® **– type 2 diabetes (tablet)**
Wegovy® **– weight loss**

Semaglutide: Novo Nordisk patent portfolio

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WEGOVY		
8129343	Dec. 5, 2031	Compound patent
8536122	Mar. 20, 2026	Compound patent
9764003	Jun. 21, 2033	Method for reducing body weight
10888605	Aug. 24, 2038	Formulation patent
11318191	Feb. 17, 2041	Formulation patent
11752198	Aug. 24, 2038	Formulation patent
12029779	Oct. 10, 2038	Method for reducing body weight

Semaglutide: Novo Nordisk patent portfolio

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US976403 B2

- A method for reducing body weight , comprising administering semaglutide subcutaneously once weekly in an amount of at least 0.7 mg and up to 1.6 mg to a subject in need thereof, wherein said semaglutide is administered without another therapeutic agent.

EP2866825 as granted

- A composition comprising the GLP-1 agonist semaglutide and one or more pharmaceutically acceptable excipients for use in the prevention or treatment of obesity, wherein said use comprises administration of said GLP-1 agonist in an amount of at least 0.7 mg per week; and said composition (i) comprises an isotonic agent, (ii) is in the form of an aqueous formulation comprising at least 80% w/w of water, or (iii) is in the form of an aqueous formulation with pH between 3 and 10.

Semaglutide: Novo Nordisk patent portfolio

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EP2866825 (T170/22)

- Filed 21 June 2013 (earliest priority date 1 July 2012)
- Granted
- Opposed by (01): Teva Pharmaceutical Industries Ltd, Tel Aviv (IL)
  (02): Generics [UK] Limited, Hatfield (GB)
  (03): Galenicum Health S.L.U., Esplugues de Llobregat (ES).
- OD revoked the patent for lack of inventive step (sufficiency was acknowledged):
  - D10 (WO2011/138421 A) disclosed a combination comprising a GLP-1 receptor agonist and a DPP-4 inhibitor which is linagliptin…. In view of semaglutide, a once weekly subcutaneous injection in an amount of 0.1 to 1.6 mg is described (p. 43, lines 1 and 13)
    - Skilled person would have considered using the 1.6 mg maximum dose so the technical problem is limited to the formulation
    - Formulation in claim is obvious
    - Reasonable expectation of success for treatment of obesity

Semaglutide: Novo Nordisk patent portfolio

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US12029779 B2

A method for reducing body weight of a subject in need thereof, comprising administering semaglutide subcutaneously to the subject in an amount of about 2.4 mg weekly.

EP3694538 (pending)

Semaglutide for use in weight management of a subject in need thereof, wherein said semaglutide is administered subcutaneously to said subject in an amount 2.2 -2.7 mg per week.

Semaglutide: Novo Nordisk patent portfolio

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EP3694538 (pending)

ED objections:

(1) therapeutic (treating and/or preventing obesity, treating and/or preventing overweight) and non-therapeutic (reducing body weight, preventing weight gain) aspects;
(2) higher doses not supported by examples; and
(3) lack of inventive step because actual dosage regime needed to avoid GI side effects i.e. once daily administration with dose escalation starting with a very low dose is not reflected in the claims.

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Thank you for listening

Any questions?

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