Second medical use claims
The *pregabalin* litigation in Europe

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Outline

- Background and patent situation
- The dilemma of the Swiss-type claim
- Litigation in UK, DE, FR, ES, NL, DK and SE

Please interrupt – please ask questions!

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Your speaker in brief

- M Sc degree in Molecular Biotechnology Engineering from Uppsala
- With Awapatent since 1999
- Qualified as European Patent Attorney in 2003
- CEIPI Diploma in European patent litigation 2011
- Patent applications, freedom-to-operate, litigation and strategic counselling for life science companies large and small, as well as to investors and to patent firms from outside Europe
- Member of the board of **AIPPI Sweden**
- Member of **AIPPI** Standing Committee on Pharma and Biotechnology
- Sweden's elected member of **epi**'s biotechnology committee
- Member of Awapatent's board of directors, advisory board and practice group for life science, and responsible for developing European work from Chinese clients

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Awapatent – key facts

- One of Europe's leading IP firms – founded in 1897
- Employee-owned
- Head office in Malmö; 15 more offices in Sweden, Denmark, Germany and China
- 300 employees, including 160 patent attorneys and attorneys-at-law
- Specialists within all areas of technology and all aspects of IP
- Vision:

  "AWA shall become the leading IP firm by combining IP law with business knowledge"

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An example of pharma patent litigation in Europe – *pregabalin*

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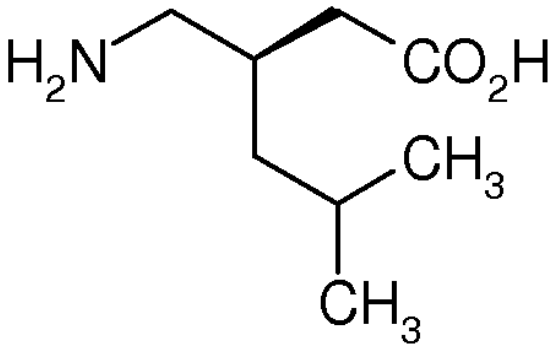
Background



Pregabalin

or (S)-3-(aminomethyl)-5-methylhexanoic acid

- Entered the market in 2004

- Authorized for treatment of
  1. Epilepsy
  2. Generalized anxiety disorder (GAD)
  3. **Neuropathic pain**

Pain indication was 88 % of Lyrica market in 2014

Total global sales of Lyrica® in 2016:

4 966 000 000 USD

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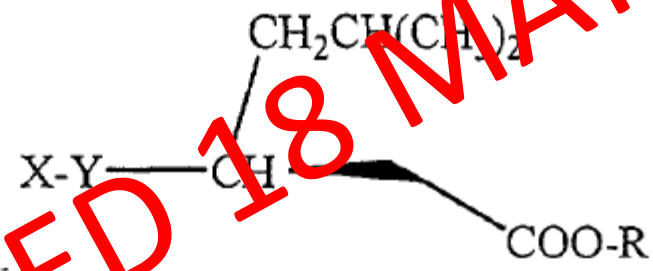
Background

Patent in Europe for pregabalin as such, and for treating epilepsy and GAD: EP 641 330

Claims

1. An S(+) enantiomer of a compound having the general formula (I)



(I)

[0036] The compounds according to the invention can be used in pharmaceutical compositions as an antidepressant, anxiolytic, antipsychotic, antiseizure, antidyskinesic, or antisymptomatic for Huntington's or Parkinson's diseases when an effective amount of the compound together with a pharmaceutically acceptable carrier is used. That is, the present invention provides a pharmaceutical composition for the suppression of seizures resulting from epilepsy, the treatment of cerebral ischemia, Parkinson's disease, Huntington's disease and spasticity and also possibly for antidepressant, anxiolytic, and antipsychotic effects. These latter uses are expected due to functional similarities to other known compounds having these pharmacological activities. The pharmaceutical compositions can be used for treating such disorders in mammals, including humans, suffering therefrom by administering to such mammals an effective amount of the compound in unit dosage form.

EXPIRED 18 MAY 2013!

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Background

Patent in Europe for treating pain: EP 934 061

Claims

1. Use of (S)-3-(aminomethyl)-5-methylhexanoic acid or a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for treating pain.

= "Swiss-type" claim
(i.e. a claim to a new medical use, pre-EPC2000)

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Background

In 2015, several pregabalin generics entered the European market…

…and the scene was set…

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The dilemma

- Selling pregabalin for treatment of epilepsy or GAD is free of patent protection
- A generic can market a product under an authorization that “carves out” or removes the patented indication
- This results in a package label called a “skinny label”
- Actavis and other generic companies received a carve-out authorization to sell pregabalin for epilepsy and GAD, but not for pain

…but what if the pharmacies, doctors and pricing bodies don’t care about patents…?

- Given the relative size of the pain market vs. the other indications, it appears highly likely, even inevitable, that generic pregabalin is sold for treatment of pain

The dilemma

Pfizer: “Patent infringement!”

Generics: “Not our fault!”

Pharmacies & regulatory bodies: “Huh?”

So, who infringes a Swiss-type claim?

Courts all over Europe are trying to decide!

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Litigation in the UK – preliminary injunctions

(Generally, UK prescriptions do not mention the treated indication)

- Pfizer sought a preliminary injunction against Actavis which would force them to go to great lengths to ensure that their product is not sold for pain treatment

- First instance decision 21 Jan 2015: NO such injunction

  "the word "for" in Swiss form claims imports a requirement of subjective intention on the part of the manufacturer that the medicament or pharmaceutical composition will be used for treating the specified condition" – this requirement was not found to be met

- Appeal decision 28 May 2015: still NO injunction

  …but a different and broader analysis of the test for infringement:

  "the manufacturer who knows (…) or could reasonably foresee that some of his drug will intentionally be used for pain is making use of the patentee's inventive contribution"

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Litigation in the UK – full trial on validity and infringement

- First instance decision 10 Sep 2015: the patent is INVALID for insufficiency

  …and, as an *obiter dicta*, it wasn't infringed either…

- Appeal decision 13 Oct 2016: upheld, i.e. the patent is INVALID

  …and yet another long discussion about the infringement issue…

  "The intention will be negatived [i.e. there will be no infringement] *where the manufacturer has taken all reasonable steps within his power to prevent the consequences* [i.e. infringing use] *occurring. In such circumstances his true objective is a lawful one (…)."*

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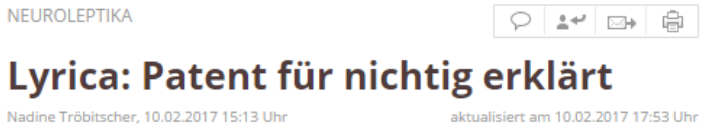
Litigation in Germany – injunctions and invalidity

- In Germany, infringement and validity are decided by separate courts

- Generic, “skinny label” pregabalin from various vendors was being put forward for subsidies through tenders for “rebate contracts”, without any limitation to non-patented uses

- Pfizer sued for preliminary injunctions in infringement court
- First instance decision 2 Apr 2015: injunctions GRANTED
- One appeal pending, but hearing 2 Mar 2017 was cancelled

- Generic Hexal sued for invalidity in Federal Patent Court
- First instance decision 24 Jan 2017: patent INVALID
- Pfizer intends to appeal


NEUROLEPTIKA

Lyrica: Patent für nichtig erklärt

Nadine Tröbitscher, 10.02.2017 15:13 Uhr aktualisiert am 10.02.2017 17:53 Uhr

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Litigation in France

- First instance decisions 26 Oct 2015 and 2 Dec 2016: NO infringement

- The defendants (generics) had obligation to ensure that patented use was avoided, but
- the Court found that defendants had made adequate efforts
- Ongoing validity trials – one first instance decision upheld the patent and is now under appeal

Litigation in Spain

- First instance decision 23 Jun 2015: NO preliminary injunction

- Some competent authorities had already taken measures, at Pfizer's request, to avoid generics being prescribed or dispensed for the treatment of pain

Litigation in the Netherlands

- Until 2009, the Dutch medical agency CBG would publish product information with “carved-out” indications if patent protected
- In 2009, this practice was changed and full labels published

- Pfizer sued the Dutch state for infringement in the patented indication

- First instance decision 15 Jan 2016:
  - NO infringement, because CBG was not actually trading in pregabalin, merely providing information without any commercial gain
  - BUT CBG acts unlawfully when publishing full label

De voorzieningenrechter:

5.1. beveelt de Staat binnen vier weken na betekening van dit vonnis de *full label* SmPC en bijsluiter van generieke pregabaline producten die bestemd zijn voor de Nederlandse markt die toegankelijk zijn via de website van het CBG te vervangen door versies van deze documenten waarin een *carve out* is opgenomen, gelijk de papieren versies van de SmPC en bijsluiter voor de pregabaline producten;

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Litigation in Denmark

- First instance decision 25 Jun 2015:
- NO preliminary injunction against Krka (the generic)
  - Pfizer had proposed two alternative injunctions
    - …but the first one was considered unenforceable
    - …and the second one already complied with by Krka
- GRANTED injunction against 220 different pharmacies
  - Subjective intent by manufacturer not required
- Decision led to new rules on substitution

Litigation in Sweden

- First instance decision 12 Aug 2016: patent VALID
- No infringement allegations (yet)

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In summary

- Several appeals are still pending, and outcomes are uncertain

- The need for European harmonization is obvious
  - Unified Patent Court
  - Patent linkage system?

- Lord Justice Floyd in the UK appeal decision:

“These cases continue to show a spectrum of different approaches. Some countries have gone for the "only packaging will do" approach. Some countries look more generally for some element of encouragement of the use of the drug for the new use by the manufacturer before being prepared to find infringement. Others look to see what steps have been put in place in the marketplace to prevent use for the prohibited indication. I do not think a universal principle has yet emerged.”

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Questions and discussion

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Thank you for your attention!

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