

Lyrica – the effect of the litigation on pregabalin prescribing

October 2018

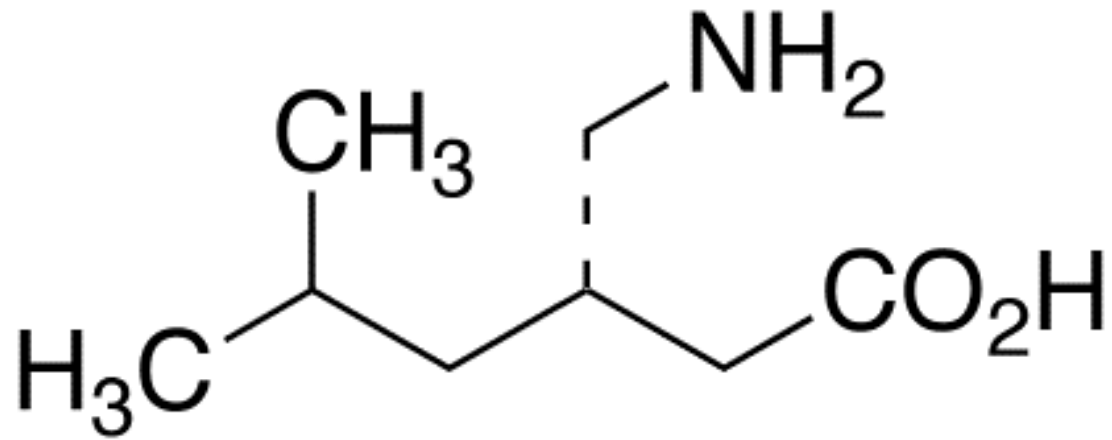
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Background

Pregabalin



Patents on Pregabalin

- Originally protected by EP0641330 – a product patent – expired on 18 May 2013.
- Patent granted on basis of antiseizure treatment (but product claims not limited to a particular use).
- Owned by Northwestern University – licensed to Warner-Lambert (subsidiary of Pfizer).
- EP 0934061 – second medical use patent – expired 16 July 2017; owned by Warner-Lambert.
- Claimed: Use of [pregabalin] or a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for treating [neuropathic] pain.

The litigation

- Pfizer had marketing authorisation to sell pregabalin (“Lyrica”) for the treatment of epilepsy, generalised anxiety disorder (“GAD”) and neuropathic pain.
- Data exclusivity ended on 8 July 2014; Actavis (and others) applied for marketing authorisation for “skinny label” product (“Lecaent”), limited to off-patent indications of epilepsy and generalised anxiety disorder, granted on 16 February 2015.
- Pfizer began patent infringement proceedings.

The decisions

- All judges at all three instances agree that the patent is invalid (for all material claims), because only treatment of inflammatory pain is rendered plausible by the data in the patent.
- What remains totally unclear is what is required to infringe a second medical use patent (where there is a lawful market for the same drug in the same presentation that is off-patent).
- Perhaps more importantly, what is required **not** to infringe a second medical use patent?

The issue is how prescribing works

- A doctor is not bound by the authorised indication for a drug – can prescribe any drug for any indication.
- Not supposed to prescribe “off-label” unless medical reason.
- Doctors are also supposed to prescribe generically (by INN not brand).
- A pharmacist must dispense a branded drug against a branded prescription; against a generic prescription can dispense any brand.
- The prescription usually does not indicate what the drug is being prescribed for.



The first interim decision

Mr Justice Arnold identifies the problem

- “[I]t is more or less common ground between all concerned that the best solution to the problem which arises in this case is to try to ensure that prescribing doctors prescribe pregabalin for the treatment of pain by reference to the brand name Lyrica rather than by reference to the generic name pregabalin.”
- “[I]t does not lie within the power of either Warner-Lambert or Actavis to ensure that this happens. It depends ultimately on the behaviour of the prescribers.”



The fourth interim decision

Action against the NHS

- Following the logic of the judge's comments in the first interim decision, Pfizer sought a court order against NHS England, which Arnold J granted.
- NHS England did not really oppose the order, but wanted a court to decide the matter, not to have to make the decision themselves.
- This was a new form of court order arising from patent litigation, unprecedented in the UK.
- Order was against a non-party to the litigation, NHS England.

The court order

- Required NHS England to issue guidance to Clinical Commissioning Groups, that if pregabalin was prescribed for treatment of pain, it should be prescribed by brand name Lyrica.
- If doctor prescribes brand name (Lyrica), pharmacist **MUST** dispense that brand; if doctor prescribes generic name (pregabalin), pharmacist can dispense any brand or generic ...
- ... even if the generic has a “skinny label”.
- This decision was not appealed and order remained in place until patent expired.



The final first instance decision

Judge's thoughts on infringement

- “the best solution to the problem of protecting the monopoly conferred by a second medical use patent while allowing lawful generic competition for non-patented indications of the substance in question is to separate the patented market for the substance from the non-patented market by ensuring that prescribers write prescriptions for the patented indication by reference to the patentee's brand name and write prescriptions for non-patented indications by reference to the generic name of the substance (the INN)”.

Judge's thoughts on infringement

- “I consider that it behoves patentees who want their second medical use patents enforced to provide NHS England with all the information and assistance it requires to enable it to issue appropriate guidance as and when required. I also consider that it behoves generic companies who want their interests in obtaining untroubled access to lawful markets protected to cooperate with NHS England as well.”

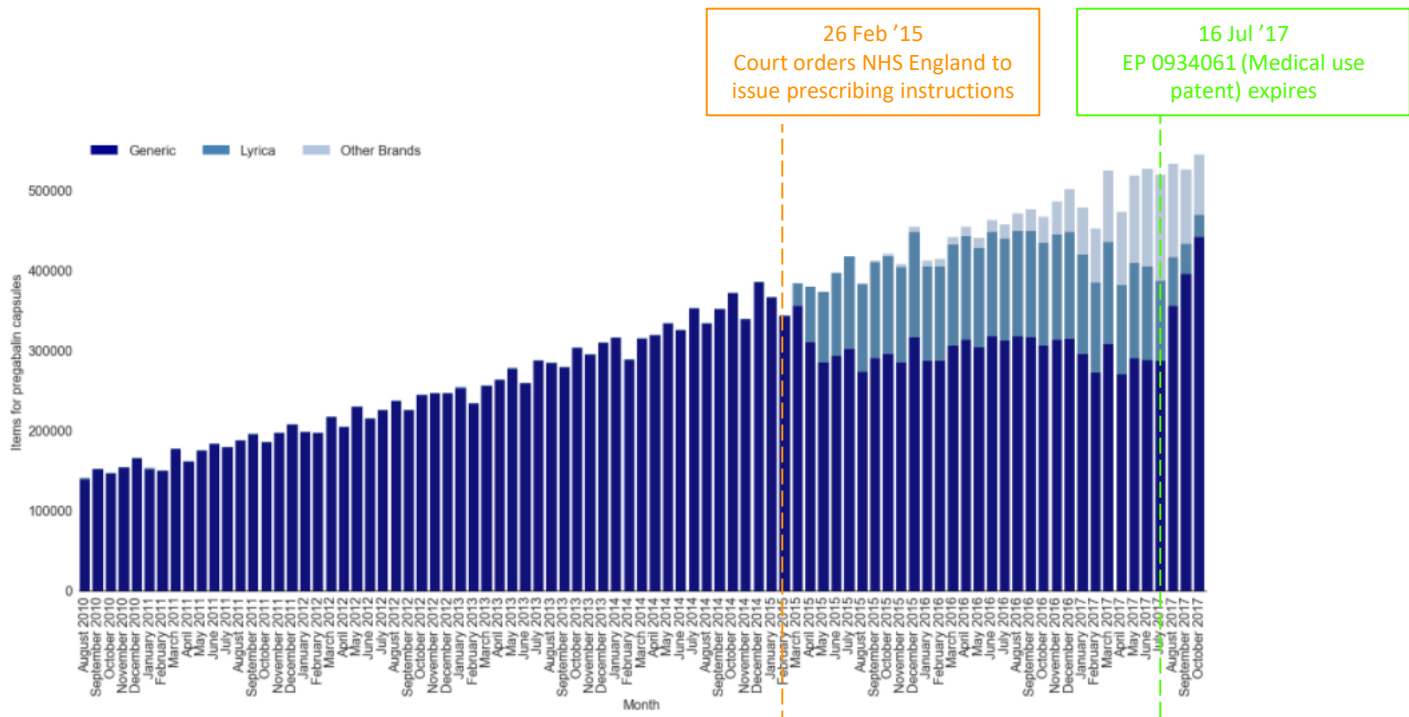


The effect on prescribing patterns

Did Arnold's solution work? (No, not really!)

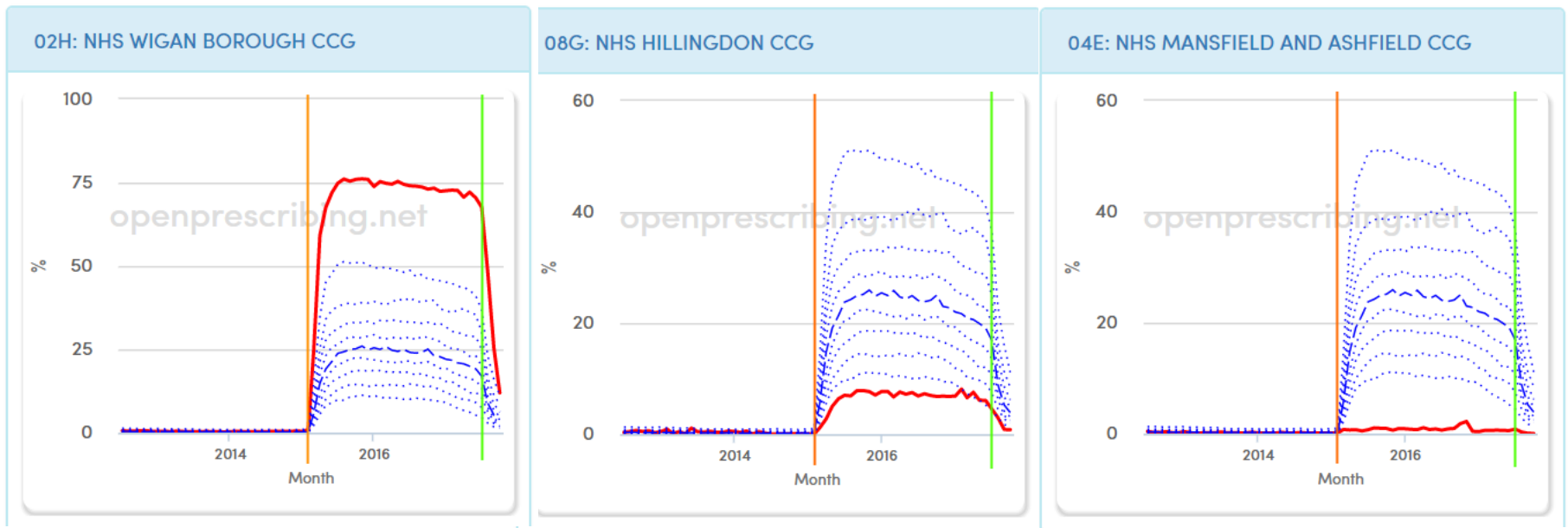
- Prescribing data up to expiry of the patent shows that although prescriptions for “Lyrica” increased and those for “pregabalin” decreased, they did not get anywhere near the 70% that would be expected if corresponded to all prescriptions for pain.
- Doctors reluctant to abandon generic prescribing to respect patent.
- But happy to abandon generic prescribing for budget reasons, because there was a large rise in “branded generic” prescriptions reimbursed at a lower price (mainly Alzain from Dr. Reddy's; not Lecaent).

Prescribing for generic pregabalin, Lyrica, other brands 2013-2017



- 26 Feb '15
Court orders NHS England to issue prescribing instructions
- 16 Jul '17
EP 0934061 (Medical use patent) expires

Prescribing for generic pregabalin, Lyrica 2012-2017

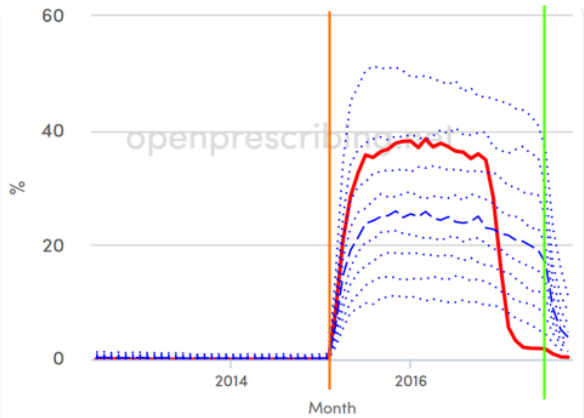


Thanks to openprescribing.net/measure/lyrica/ for these visualisations

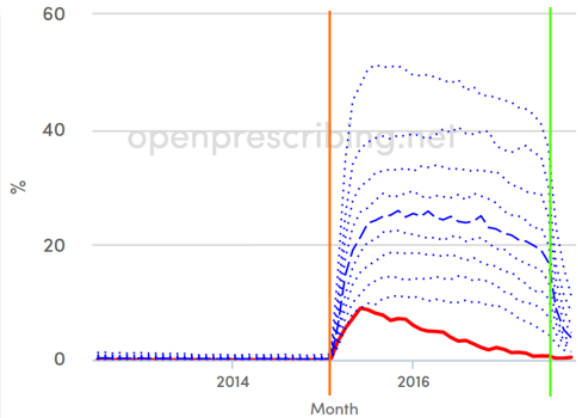
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Prescribing for generic pregabalin, Lyrica 2012-2017

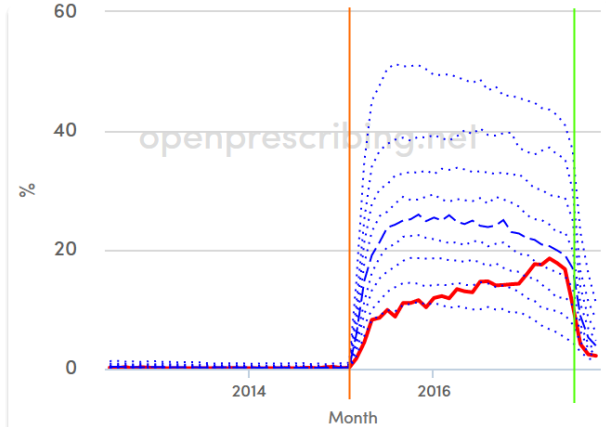
13T: NHS NEWCASTLE GATESHEAD CCG



06M: NHS GREAT YARMOUTH AND WAVENEY CCG



08M: NHS NEWHAM CCG



Thanks to openprescribing.net/measure/lyrica/ for these visualisations



Where did the money go?

Drug pricing and reimbursement

- Category C drugs are not readily available as a generic and are reimbursed at a price based on an individual supplier.
- Pregabalin was in this category, and the pharmacist would be reimbursed based on the Lyrica price even if another brand was dispensed.
- On 1 August 2017 (ie 2 weeks after patent expiry), pregabalin was recategorised to Category M and the reimbursement price plummeted from £64.40 for 56 capsules (irrespective of strength) to between £1.84 and £3.54 (depending on strength).
- Excess prescribing cost in period between final first instance judgment and patent expiry is over £500 million.

It's complicated

- Only prescribing as “branded generic” (e.g. Alzain) resulted in a direct saving in prescription cost.
- If Lyrica dispensed, whether for a branded prescription or generic prescription, money goes to Pfizer as excess profit.
- If a generic dispensed (against generic prescription) then some money goes to pharmacist as excess profit, and some goes to generic company (who can charge higher price during this period).
- BUT excess pharmacy profit is compensated by reduced direct NHS payment.

Is Pfizer liable for any of this?

- Pfizer gave cross-undertaking in damages to both Actavis and NHS England.
- But for Actavis, decreased sales may have been more than compensated by higher price achievable in this period.
- NHS has paid higher prescription reimbursement, but some of that has gone to NHS pharmacies and can be recouped.
- Higher reimbursement cost also arguably partially due to NHS policy on drug classification.
- Has the NHS suffered a quantifiable loss that can be proved?



The mystery of the SPCs

SPCs on EP0641330

- In UK, SPC applied for in October 2004 and granted in February 2005.
- Similar SPCs in other countries across Europe.
- But then in May 2013 the renewal fees required to bring SPCs into force upon expiry of EP0641330 were not paid, so that they lapsed.
- If the SPCs had been brought into force, the use patent would likely never have been litigated, as the SPCs would have lasted until May 2018 (use patent expired in July 2017).
- This has never been adequately explained.



Thank you!
Any questions?

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