How do you switch between pregabalin and gabapentin for neuropathic pain, and vice versa?

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Background

Both gabapentin and pregabalin were originally developed as antiepileptic drugs. Both agents are also licensed for use in neuropathic pain.

The mechanism of action is similar for pregabalin and gabapentin. Both drugs bind to the α2δ subunit of voltage-gated calcium channels. Gabapentin has nonlinear pharmacokinetics, meaning careful titration of dose is required, whereas pregabalin possesses linear pharmacokinetics, which mean dosing regimes are more straightforward.

Pregabalin is recommended as a first-line treatment option for neuropathic pain by the National Institute for Health and Clinical Excellence. This recommendation was seen as controversial at the time of publication of the guideline, as gabapentin was in common use prior to this time.

Answer

There have been no clinically relevant pharmacokinetic interactions found between pregabalin and gabapentin, although pregabalin displaces gabapentin from receptors.

The manufacturer of both pregabalin and gabapentin advises that if they are to be discontinued, or the dose reduced or substituted with an alternative medication, the dose should be tapered gradually over a minimum of a week. However, this withdrawal is to minimise the risk of increased seizure frequency where they are being used for patients with seizure disorders.

The clinical importance of a slow withdrawal in patients with neuropathic pain remains unknown.

Literature Search

There is very limited evidence in the medical literature with regards to managing a switch between the two agents.

A conference abstract of a small study included 26 patients who were directly switched from gabapentin to pregabalin. The focus of the study was looking at unlicensed doses of pregabalin and gabapentin for the treatment of pain models outside of the pregabalin license. Patients were switched directly to pregabalin after stopping gabapentin with no dose tapering or wash out period. Most patients were switched to 150mg twice daily of pregabalin (above the recommended licensed starting dose in the UK). Unfortunately, there was no reported information on tolerability of this switching regime.

An open label study substituted gabapentin in patients with neuropathic pain due to peripheral neuropathy. The author describes an overnight switch from gabapentin to pregabalin, based on a conversion table which is described in the paper as "of the author’s creation" (table 1). No serious adverse effects appeared to have been caused by the switch. Patients who had not responded to gabapentin therapy appeared to have a higher likelihood of adverse effects such as sedation and dizziness, although these did not lead to treatment discontinuation after one week.

<table>
<thead>
<tr>
<th>Daily Dose of gabapentin pre-switch (mg/day)</th>
<th>Daily dose of pregabalin per day post switch (mg/day)</th>
<th>Dosing schedule of pregabalin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-900</td>
<td>150</td>
<td>75mg twice daily</td>
</tr>
</tbody>
</table>

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## Medicines Q&As

### Table 1: Dose conversion of gabapentin to pregabalin used in the Toth study.

*the table in the published study actually reads 75mg in the morning and 225mg in the evening. This error has been corrected in the above table.

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>Gabapentin Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>901-1500</td>
<td>225</td>
</tr>
<tr>
<td>1501-2100</td>
<td>300</td>
</tr>
<tr>
<td>2101-2700</td>
<td>450</td>
</tr>
<tr>
<td>2700 or higher</td>
<td>600</td>
</tr>
</tbody>
</table>

*75mg in the morning and 150mg in the evening*  
*150mg twice daily*  
*150mg in the morning and 300mg in the evening*  
*300mg twice daily*

### Yilmaz et al conducted a cross-over study design in which patients with neuropathic pain due to spinal cord injury were randomised into either the pregabalin or gabapentin group. Patients were titrated up to the highest tolerated dose up to 1800mg per day for gabapentin and 300mg per day for pregabalin for a total of 8 weeks. After a washout period of 2 weeks, they were switched to the other medication. Tolerability of this switching regime was not reported.

A small (n=32) study of patients with post-herpetic neuralgia saw patients switched from gabapentin to pregabalin at one sixth of the gabapentin dose. No serious side effects occurred, and no significant difference was found before and after substitution in the number of patients with somnolence and dizziness. A significant (p<0.05) increase in the number of patients with peripheral oedema was found after the switch.

### Manufacturer's Information

Pfizer, the manufacturer of both Lyrica® (pregabalin) and Neurontin® (gabapentin), advise that in the absence of clinical studies, licensed dosage information for both gabapentin and pregabalin should be consulted. They are unable to make any recommendations regarding initiating or switching.

An in-house pharmacokinetic simulation suggests that a regime of halving the original gabapentin dose, and introducing half the intended dose of pregabalin on day 0, then stopping gabapentin and doubling the pregabalin dose on day 4 leads to fairly stable drug levels of pregabalin equivalents. However, the efficacy and safety of this switching regime has not been established, and use in this way would fall out with the licenses of the products.

### Summary

In the absence of more detailed data, recommendations cannot be made about initiating or switching to gabapentin following pregabalin treatment or vice versa. The individual SPCs suggest that both agents should be discontinued over the course of a week, although whether this is relevant for patients with neuropathic pain remains unclear.

Any decisions made will need to be based on a clinical judgement, in partnership with the patient. Pain clinics or individual Primary Care Trusts may have developed local switching guidance which should be consulted where possible.

### Limitations

This Medicines Q&A does not consider the potential for differences in efficacy of pregabalin and gabapentin but merely considers how to manage a switch.

### Disclaimer

- Medicines Q&As are intended for healthcare professionals and reflect UK practice.
- Each Q&A relates only to the clinical scenario described.
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References

Quality Assurance

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Search strategy

Embase
PREGABALIN* AND GABAPENTIN* AND NEUROPATHIC PAIN*

Medline
Pregabalin.af AND gabapentin.af AND NEURALGIA*

eMC
NICE
PRODIGY
Micromedex
Manufacturer’s medical information department

References

9 Allen S. Pregabalin- is it any better than gabapentin? Presented at the IASP’s 11th World Congres on Pain: Sydney, Australia 2005, cited in: Personal Communication with Medical Information- Pfizer Ltd 27/11/2012
Toth C. Substitution of gabapentin therapy with pregabalin therapy in neuropathic pain due to peripheral neuropathy. Pain Medicine 2010; 11: 456-465


Personal Communication with Medical Information- Pfizer Ltd 27/11/2012