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EXCLUSIVE INTERVIEW

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Lamotrigin Desitin® (Plexxo®) – the special generic product – Value in Epilepsy Therapy –

– Epilepsy Expert from Bonn in an Interview with NeuroNews –

Financial pressures in public health are persistently on the increase. One consequence thereof is the rising use of long-established generic products for several indications. In the field of anti-epileptic therapy as well, we find an increasing number of generic successor products in the market. The question of dealing with generic products in the specific target group of epilepsy patients is of great significance for the neurologist. The risks associated with switching between different commercial drugs based on a specific active substance must be justifiably low from the perspective of the treating physician as well as the perspective of the affected patient. The editorial office of NeuroNews had an opportunity to conduct an exclusive interview on this subject with Prof. C. Elger, Director of the Department of Epileptology at the University Clinic of Bonn. In addition to the general problem of substitution of generic products in epilepsy treatment, the conversation was focused on the active substance lamotrigine which is being offered in the German market by several companies, e.g. Desitin Arzneimittel GmbH since June 2005 in the form of various generic products. The trade name for Lamotrigin Desitin® in Czech Republic, Romania, Poland, Hungary and Slovakia is called Plexxo®. All dosage strengths of Plexxo® tablets are divisible.

Source: Department of Epileptology, University of Bonn

Interview with Prof. Dr. Christian Elger, Director of the Department of Epileptology, University of Bonn, and exclusive teaching professor for epileptology in Germany.

NeuroNews: *Prof. Elger, what is your personal view of the problem of switching from an original product to a generic product in epilepsy therapy?*

Prof. Elger: Generally, in epilepsy therapy one must look at two aspects or risks when switching from the original product to a generic product. First of all – and this appears to be the most important aspect – one must look at the seizure situation. Given the tolerance ranges for evidence of bioequivalence between the original product and the generic product – as stipulated in the marketing authorization conditions for generics – there may be a relative decrease in plasma levels after the patient has been switched. In some cases the decrease may be such that the patient's plasma levels are too low for seizure protection, and this may cause him to experience a seizure relapse, which could have far-reaching social and medical consequences for the patient. A second aspect is tolerance. Here again, due to the previously mentioned differences in bioavailability there may be a relative increase in plasma levels after the switch has been made, and this may lead to side effects. Therefore, any change in

Photo: University of Bonn

Clinic of Epileptology, University of Bonn

medication must be discussed individually with the patient and he must be adequately informed about the risks connected with the change. Furthermore, one should keep in mind a general rule of thumb – repeated and indiscriminate switching from one generic product to another should be avoided in epilepsy therapy. If one plans to switch a patient one should carefully select a suitable generic product and ensure it is not replaced by a different one at the pharmacy and is not replaced by a different generic product when subsequent prescriptions are issued.

NeuroNews: *What factors influence the success or failure of switching from one medication to the other?*

Prof. Elger: On the one hand there are substance-specific properties that influence bioavailability. Poorly water-soluble substances are known to possess a narrow therapeutic range and non-linear kinetics, and lead to greater problems when the medication is switched. Phenytoin, for instance "fulfils" all of these criteria and may therefore cause problems of a greater magnitude. Carbamazepine also fulfils the first two criteria but is rated slightly more positively because of its partly non-linear kinetics. Lamotrigine is moderately water-soluble but appears to be more suitable for generic substitution because of its relatively wide therapeutic range and its linear kinetics. In addition to these substance-specific aspects, of course the bioequivalence study with the formulation of the respective generic product is also very important. The lesser the deviations in pharmacokinetic parameters between the generic product and the original product, the better its bioequivalence is rated. Finally, of course, the patient's psychosocial situation is also important. Particularly epilepsy patients are known to react very sensitively to changes in their medication. Frequent problems have been encountered when the patient is switched from one medication to another and has not been properly informed. The problems mainly concern tolerance.

»When selecting the generic, the quality and particulary the practical features of the substance are of great importance. Lamotrigin Destin® (Plexxo®) possesses these properties.«

NeuroNews: *What prerequisites must a generic product fulfil, in your opinion, in order to justify or render possible a switch in medication even in patients who are largely free of seizures?*

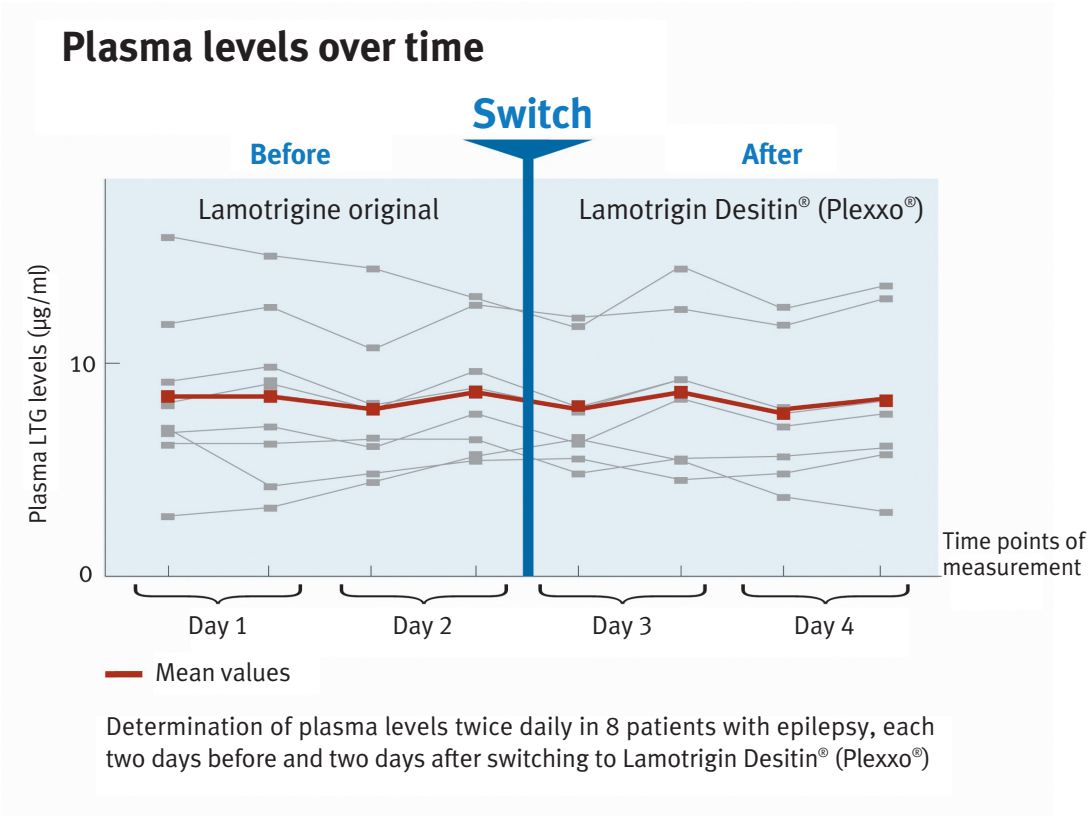
Prof. Elger: Here I believe the quality of production – which should be uniform and of a high standard – is of prime importance to render possible a switch. Apart from that, one should be able to rely on the fact that the production is handed over to a new manufacturer who then may introduce minimal changes in the quality of the product – without the knowledge of the prescribing physician. In addition to these aspects, the results of bioequivalence studies needed for the marketing authorization of a generic product must be published so that the prescribing physician is fully aware of them. The greater the agreement in pharmacokinetic data between the original product and the generic product – based on these studies – the more positively one may rate the generic. Finally, positive experiences from switching medication in clinical practice, such as those reported in studies from this setting, should ideally be available for perusal.

NeuroNews: *Which lamotrigine patients do you prescribe the divisible Lamotrigin Desitin® (Plexxo®)?*

Prof. Elger: Given the well known problem in public health, it is no longer permissible to prescribe an original product from the very start when generics of high quality are available. The same applies to epilepsy therapy. Therefore, all of our patients who are started on lamotrigine for the first time receive a generic lamotrigine product. The fact that the tablets can be divided is so useful in routine practice that I believe this substance should be treated as the standard in lamotrigine therapy. This advantage is of great significance when starting a patient on the treatment and is also important when "fine-tuning" the treatment or adjusting the dose to the patient's individual needs. In both settings the tablets need not be replaced – which makes life much easier for the doctor as well as the patient. As errors are avoided, the administration is simpler and also easier to explain to the patient.

NeuroNews: *We are aware of the fact that many of your patients have been switched to Lamotrigin Desitin® (Plexxo®). What has your experience been in this regard?*

Prof. Elger: We have experienced no problems thus far while switching our lamotrigine patients. On the contrary – the fact that the tablets are divisible has made it much easier to start dose titration.



Source: Prof. Elger, Bonn/Germany

NeuroNews: *What were the factors that convinced you of the safety of switching a patient from the original product Lamictal® to Lamotrigin Desitin® (Plexxo®)?*

Prof. Elger: The good bioequivalence of Lamictal® and Lamotrigin Desitin® (Plexxo)® was proved in the marketing authorization study which was conducted in healthy subjects in accordance with international guidelines. Furthermore, in our own study we measured plasma levels in 8 patients twice daily for 2 days, before and after switching to Lamotrigin Desitin® (Plexxo®), and found no difference in plasma concentrations.

NeuroNews: *Would you, in principle, switch all patients who receive Lamictal® to Lamotrigin Desitin® (Plexxo®)?*

Prof. Elger: Such sweeping statements are not meaningful and I will refrain from making them. In principle, first of all one has to consider the patient's individual situation and his anxieties. If the patient can be convinced of the fact that the use of a generic product is meaningful in terms of reducing costs, and is practically devoid of any risks, we do most certainly use this alternative. However, if the patient is very anxious about experiencing a relapse we let him continue his original medication.

NeuroNews: *When switching epilepsy patients from lamotrigine – what would you advise practicing physicians to do?*

Prof. Elger: The neurologist should first consider how much time he will have to invest in updosing the patient with the original product Lamictal®. He will immediately realize the advantages of a tablet that can be divided, and will gladly use the alternative available to him.

NeuroNews: *Professor Elger, thank you very much for this interview.*

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