pathic pain. Information regarding the potential of lacosamide to prolong the QTc interval is an important aspect of its safety profile.

A thorough QTc-trial has been conducted in 247 healthy male and female subjects according to ICH E14 guideline. The electrocardiographic effects and pharmacokinetic profile after multiple oral administrations of lacosamide (400 or 800 mg/day), moxifloxacin (positive control) or placebo were determined over 6 (lacosamide, placebo), 3 (moxifloxacin) treatment days, respectively. The primary variable was the change in the QTc interval from baseline based on the individual correction method (QTcl). Electrocardiograms were obtained by a Mortara continuous recorder. The relationship between plasma concentrations of lacosamide and changes in ECG parameters were determined by linear correlation analysis.

Lacosamide demonstrated no prolongation of the QTc interval. The difference in the maximum time matched change from Baseline in QTcI between the 400 mg/day lacosamide group and placebo was −4.3 ms (−6.3 ms in the 800 mg/day lacosamide group). In both cases, the upper limit of the 90%CI was below the 10 ms non-inferiority margin (−0.5 and −2.5 for 400 mg/day and 800 mg/day groups, respectively), thereby demonstrating that there was no increase of QTcI caused by lacosamide. No correlation between the plasma concentrations of lacosamide and time-matched changes in QTcI were evident in this trial.

There was no evidence of an association between lacosamide treatment (400 mg/day or 800 mg/day) and QTc prolongation in this trial. According to ICH E14, this trial can be considered as negative QTc trial.

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LOW POTENTIAL FOR DRUG–DRUG-INTERACTION OF LACOSAMIDE

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Lacosamide is a new drug being developed for the treatment of epilepsy and neuropathic pain. Preclinical and clinical data have been established in a series of trials. Information about the pharmacokinetic drug–drug-interaction (DDI) potential of lacosamide is an important part of its safety profile.

Regarding the DDI potential the results of several preclinical studies as well as of 9 Phase 1 trials ($n = 184$ subjects) and a Phase 2 trial ($n = 91$ patients) are presented.

In vitro, lacosamide is not substantially metabolized and shows no or low potential to inhibit or to induce CYP isoforms. Since lacosamide has low binding to plasma-proteins (<15%), drug displacement interactions are unlikely.

A phase 1 trial performed in CYP2C19 extensive and poor metabolizers demonstrated the minor relevance of CYP2C19 for the clearance of lacosamide.

Further DDI trials have been performed with carbamazepine (CYP450 inducer) and valproic acid (CYP450 inhibitor) under steady-state conditions. In these trials, lacosamide had no influence on rate or extent of absorption of carbamazepine or valproic acid and vice versa. DDI trials with digoxin and metformin showed no relevant influence of these drugs on lacosamide and vice versa. Lacosamide did not modify the pharmacokinetics and pharmacodynamics of the oral contraceptive Microgynon®. Coadministration of food did not alter the absorption of lacosamide.

In epileptic patients, lacosamide showed no influence on plasma levels of common antiepileptic drugs.

No DDI have been observed in these studies. Therefore, the data suggest that lacosamide has low potential for DDI in clinical use.

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APPLICATION OF LIDOCAINE PATCHES 5%: HOW MANY PATCHES NEED TO BE APPLIED ON A DAILY BASE IN ROUTINE CLINICAL PRACTICE?

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Lidocaine patches 5% became recently available for the treatment of post-herpetic neuralgia. In addition, a growing body of evidence has become available concerning the efficacy of this topical administration of lidocaine for the treatment of other neuropathic pain syndromes and even non-neuropathic pain syndromes. Study protocols have always prescribed the daily use