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Dr Bernard Schmidt graduated in pharmacy and received his Ph.D. in 1985. After a post-doc stint in France, he joined the Pharmaceuticals Business Group of Bayer AG in 1987, where he specialized in drug development, starting with *in vitro* drug screening and then moving on to behavioural, endocrine and finally safety pharmacological evaluations of developmental drug candidates for human therapy. Since 2001, he has been with the Animal Health Division of Bayer HealthCare AG, where he is currently responsible for the clinical development of new veterinary products in the field of non-infectious diseases.

Therapeutic experience with Catosal® in the treatment of metabolic disorders: new clinical results

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Metabolic disorders in cows

Post-parturient metabolic disorders in dairy cows have a tremendous impact on cattle health and farm economy. These disorders can be due either to impaired electrolyte homeostasis (e.g. hypocalcaemic paresis) or to disturbed energy metabolism (e.g. ketosis). Besides the acute life-threatening features of metabolic disorders in severe cases, they are predisposing factors for puerperal disorders and may lead to reproductive disorders.

Catosal®

Catosal® (synonyms: Coforta® and Phosphorum B12®) has been widely used in the treatment of metabolic disorders since 1958. This tonic and metabolic stimulant is available as a ready-to-use solution for parenteral injection. It contains as active ingredients 10 g butafosfan and 5 mg cyanocobalamin (vitamin B12) per 100 ml solution and is currently registered in 58 countries, including 16 in Europe.

Efficacy studies in cattle

Based on the framework described by Sommer (1975), the prophylactic effect of Catosal® administration during the dry period on the prevalence of puerperal complications and fertility disorders has been demonstrated in numerous clinical studies (Wiedenroth, 1979; Palmer, 1980; Schuh, 1994). Another study by Krdžalić and Curčić (1976) provided evidence for the efficacy of Catosal® in indigestion and subclinical ketosis in cows. However, despite the broad perception of clinical benefits associated with the well-established use of Catosal® in the supportive treatment of clinical ketosis (primary or secondary to other conditions such as abomasal displacement, hypocalcaemic paresis, retention of placenta or endometritis) or disorders of electrolyte metabolism such as hypocalcaemic paresis, randomised controlled clinical studies to demonstrate the efficacy of the product have not been reported in the past.

New clinical results in ketosis

In two recent randomised and negatively controlled studies, the effects of Catosal® in cows with ketosis associated with abomasal displacement to the left were investigated. The first of these trials was performed as an open label study at the University of Leipzig (Fürl et al., 2006). Thirty animals were allocated to each of a Catosal® and a saline group, and this treatment was administered 2 hours before surgical repositioning of the abomasum at a dose volume of 5 ml /100 kg body weight. Catosal® positively affected the return of feed intake, rumen motility and rumination, especially during the first 24 h post surgery. These effects were paralleled by beneficial effects on the blood concentrations of bilirubin, β -hydroxybutyrate (BHB), non-esterified fatty acids, and aspartate aminotransferase (ASAT) activity. The differences to control values of these variables were all statistically significant ($p < 0.05$). Under the specific conditions of the study, no effects of Catosal® were observed with regard to pulse and respiration rate, body temperature, abomasal emptying rate or



antioxidative status. The efficacy and safety of Catosal® in the treatment of ketosis associated with abomasal displacement to the left was confirmed in the first multicentre, controlled, randomised and masked field study on Catosal® conducted in compliance with Good Clinical Practice (GCP) standards (Lohr *et al.*, 2006). Overall, 120 cows were allocated to a Catosal® treatment group or to a negative control group (saline). The test medications were administered at the beginning of surgical repositioning of the abomasum, as well as 24 and 48 hours afterwards, at a dose volume of 5 ml/100 kg body weight. The results showed significant differences in clinical parameters (proportion of healthy animals and rumen activity at 48 and 72 hours after surgery) and near-significant differences ($p=0.0592$) in the reduction of BHB levels compared to the negative control group.

New clinical results in parturient paresis

A randomised, controlled and masked multicentre field study on the efficacy and safety of Catosal® as supportive treatment of parturient paresis was performed in the Republic of South Africa (Delpont *et al.*, 2006) in compliance with GCP standards. Dairy cows with the confirmed condition received a standard electrolyte infusion, followed by an injection of either Catosal® or saline at a dose volume of 5 ml/100 kg body weight. The changes in serum calcium levels within 24 hours after treatment served as the primary parameter for efficacy. Calcium levels increased from baseline in both study groups, with a tendency ($p=0.0958$) towards better recovery being observed in the Catosal® group ($n=15$) as compared to saline-treated controls ($n=14$). Although statistical significance was not achieved, the higher level may be clinically relevant in terms of the risk of relapse. Under the conditions of the study, no treatment-related effects were observed on the levels of serum phosphorus or magnesium. Serum levels of non-esterified fatty acids were slightly elevated in both groups, but without statistically significant group differences. Serum levels of BHB acid were in the reference range at the start of the study, and some of the saline-treated animals developed subclinical ketosis during the study. However, the difference in BHB levels at the end of the study (24 hours after treatment) was not confirmed statistically. None of the study animals developed clinical ketosis.

(n = 15) ???
(n = 14) ???



Conclusion and outlook

All three clinical studies summarised in this review provide substantial evidence for the efficacy and safety of Catosal® as a supportive treatment of ketosis and parturient paresis in cattle. They also indicate possibilities for improving clinical results further by repeated administration of Catosal® at intervals of 24 hours if required. Further clinical studies are currently being performed to provide further evidence of the efficacy of Catosal® in the (supportive) treatment of cattle disorders according to current standards of GCP. This is being done not only for scientific reasons but also to refine the indication claims, to find new indications for Catosal®, and to defend the periodic renewals of marketing authorisations for this important product which would be sorely missed by many veterinarians.

References

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