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ESOC 2025

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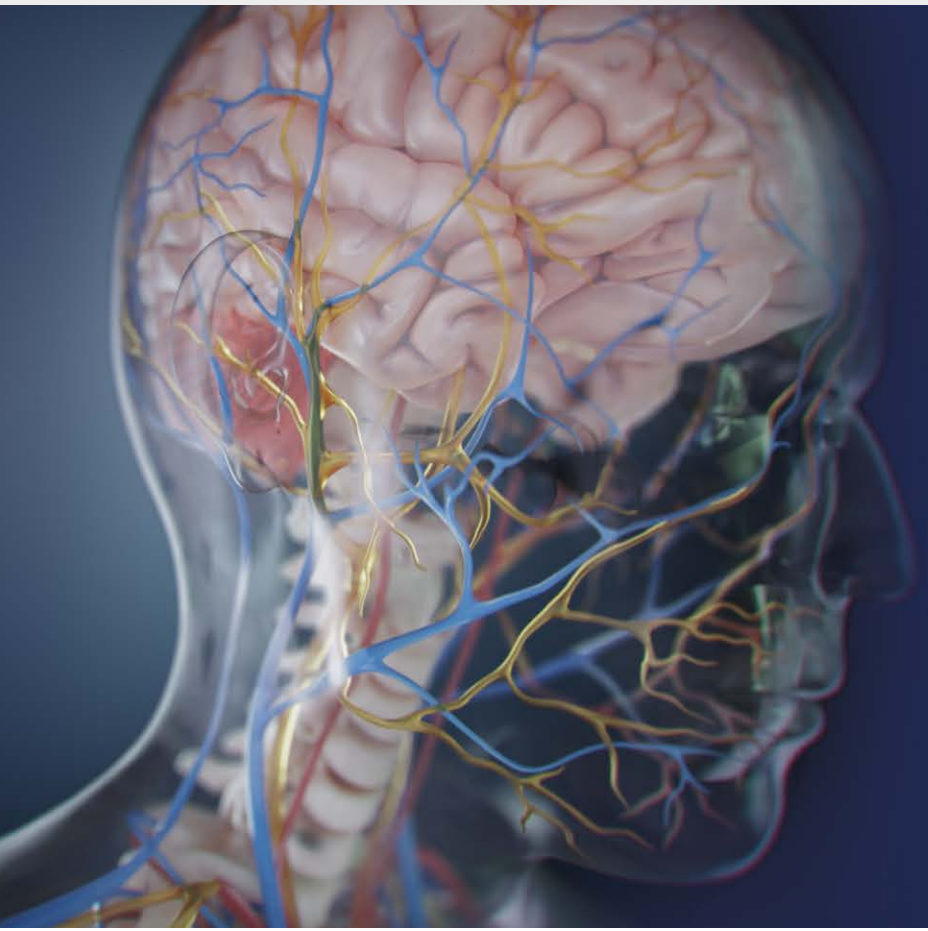

Cerebroprotective Treatment Strategies in Stroke

Evidence from 3 new studies

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In May 2025, the European Stroke Organisation Conference (ESOC) was held in Helsinki, bringing together leading clinicians and researchers from around the world. The conference served as a premier platform for presenting and discussing the latest advances in stroke prevention, acute treatment, rehabilitation and long-term recovery.

The official symposium hosted by EVER Pharma focused on emerging cerebroprotective treatment strategies in acute ischemic stroke. The session highlighted new clinical evidence from three studies.

Dr. Jacek Staszewski presented findings from his recently published **WIM** (Wojskowy Instytut Medyczny) study, which explored the safety and efficacy of Cerebrolysin following mechanical thrombectomy (MT).

Dr. Michael Brainin followed with results from the **ESCAS** (Efficacy and Safety of Cerebrolysin in the Treatment of Aphasia After Acute Ischemic Stroke) study, highlighting the benefits of combining Cerebrolysin with speech therapy for aphasia recovery, and presented preliminary **C-REGS2** (Cerebrolysin REGistry Study in Stroke) data on post-stroke treatment effectiveness.

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Andrei Alexandrov

MD
Professor, Clinical Scholar – Neurology and Translational Neurosciences, Chair – Neurology
University of Arizona College of Medicine, Phoenix, USA

Introduction

Dr. Andrei Alexandrov opened the symposium by highlighting a key challenge in stroke care: although MT is a highly effective reperfusion therapy, around 50% of patients still fail to achieve good recovery. This underscores the urgent need for adjunctive treatments that can enhance outcomes. He posed the central question of the session – can Cerebrolysin help improve results after stroke? *(Figure 1)*

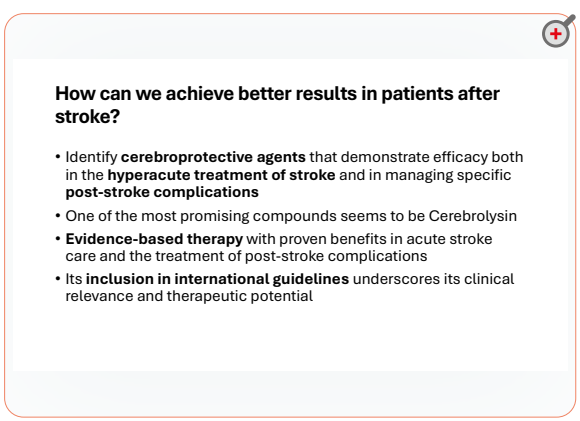

Figure 1

Dr. Alexandrov emphasized that a growing body of clinical and experimental evidence supports the safety and cerebroprotective effects of Cerebrolysin. He referenced the CARS study by Dr. Muresanu, which showed significant motor function improvements in patients with severe deficits, such as arm weakness. Similar benefits have been observed in patients with aphasia and in broader measures like activities of daily living and quality of life.

He also noted the increasing inclusion of Cerebrolysin in national and international treatment guidelines. Most recently, the German Society of Neurology recommended its use to reduce disability and enhance motor recovery, while the European Academy of Neurology has endorsed it for moderate to severe strokes. *(Figure 2 & 3)*

Dr. Alexandrov characterized Cerebrolysin as a uniquely brain-targeted neurorestorative therapy, developed with the innovative concept of engaging the brain's intrinsic capacity for repair and regeneration. Unlike conventional pharmacologic agents that act on a single molecular target, Cerebrolysin exhibits a multimodal approach. This allows it to support the injured brain across the various stages of neural recovery – hyperacute, subacute and chronic phases – by delivering a combination of neurotrophic and neuroprotective effects. *(Figure 4 & 5)*

In conclusion, he emphasized that ongoing research is helping us fully understand how Cerebrolysin supports overall recovery after a stroke – which is consistent with the original vision of its development and offers new hope for better outcomes.

Figure 2

Figure 3

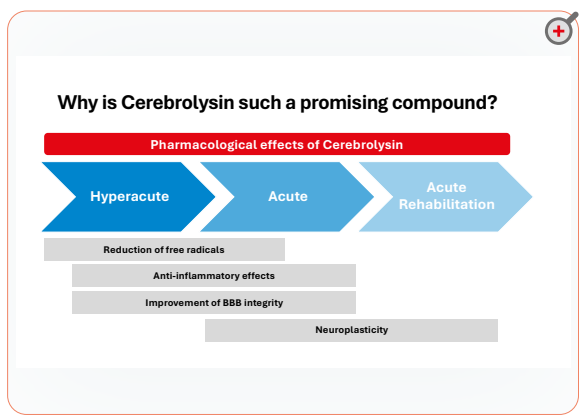

Figure 4

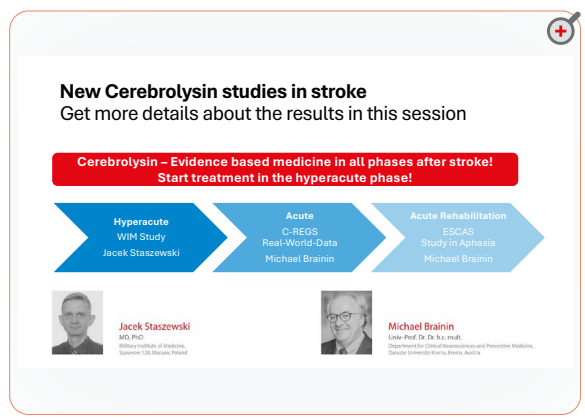

Figure 5

Jacek Staszewski

MD, PhD
Clinical Neurologist
Military Institute of Medicine Warsaw, Poland

Cerebroprotection as an Adjunct to Mechanical Thrombectomy.

WIM Study Results

ABSTRACT

Background and Aims: We hypothesized that Cerebrolysin, a multimodal cerebroprotective agent, enhances the efficacy and safety of mechanical thrombectomy (MT) <6 hours of stroke onset in patients with good collateral status and effective recanalization (mTICI 2b-3).

Methods: A single-center, prospective, open-label, single-arm study with blinded outcome of 50 consecutive patients with moderate-to-severe stroke treated with Cerebrolysin alongside MT (30 ml iv for 21 days, first cycle) and during the recovery phase (between 69-90 days, second cycle) compared to 50 historical controls matched by propensity scores. Key outcomes included functional independence (mRS 0 – 2 at 90 days), safety endpoints, and neurological recovery (NIHSS at 24h and 7 day post MT).

Results: Patients receiving Cerebrolysin had higher odds for functional independence (68% vs. 44%, p=0.016, OR 2.7, 95%CI 1.2 – 6.1; NNT: 4.2) at 90-days, and 360-days (OR 3.3, 95%CI 1.4 – 7.7), had lower risk of early secondary ICH (14% vs 40%, p=0.02; RR 0.37; 0.14 – 0.954), and greater neurological improvement at 24 hours (mean ΔNIHSS 8.2 vs 5.1, p=0.01) and at 7 days (10.4 vs. 6.9, p=<0.01). Multivariate analysis identified Cerebrolysin as an independent predictor of favorable outcomes (OR 7.5; 1.8 – 30.9) at 90-days, particularly in patients with diabetes (interaction OR 10.7; 1.07 – 107). The overall mortality rates at 30- and 90- and 360-days were similar in both groups (2% vs 6% and 8% vs 12%, and 18% vs 18%; p>0.1).

Conclusion: Cerebrolysin improved functional outcomes at 90 and 360 days, accelerated neurological recovery, and reduced complications post-MT in patients with good collateral circulation and effective recanalization.

SUMMARY OF THE PRESENTATION

Despite the efficacy of MT, real-world registries like the Hermes trial often do not show efficacy data as pronounced as those from clinical trials. Observational data, such as from the German Stroke Registry, indicate approximately 10% lower rates of functional independence and higher mortality in routine practice. Furthermore, even among functionally independent patients, residual deficits such as aphasia, neglect and cognitive impairment remain common.

Dr. Staszewski emphasized the unmet need to bridge the gap between trial efficacy and everyday effectiveness to improve overall outcomes. He noted, "There is no good neurological outcome without successful recanalization." While recent results show high rates of effective recanalization in everyday practice, these do not always translate to good outcomes due to futile recanalization (30–40% of cases).

The key mechanisms contributing to futile recanalization include:

- No Reflow
- Non-Rescue Ischemic Injury
- Reperfusion Injury

These mechanisms are interconnected and lead to disruption of the blood-brain barrier (BBB). Currently, only supportive measures are available to manage these complications. Since preventative and targeted treatments are not yet well-known, the development of cerebroprotective therapies is critical.

The perfect setting for effective cerebroprotection includes:

- Presence of a penumbra
- Optimal therapeutic time window for salvaging the neurovascular unit (NVU)
- Enhanced drug delivery via successful reperfusion and collateral circulation

MT mimics a transient ischemia model used in preclinical studies where cytoprotective agents have demonstrated efficacy. Experts therefore recommend considering the differential vulnerability within the NVU and adopting pleiotropic drugs delivered at optimal time points to target both primary and secondary stroke-related injuries.

The ideal drugs should be administered during the hyperacute phase to suppress hypoxia, cytotoxic edema, and cell death. They should be initiated within 6 hours to prevent neuroinflammation and reperfusion injury and be continued for days or even weeks to support neurorecovery processes. *(Figure 6)*

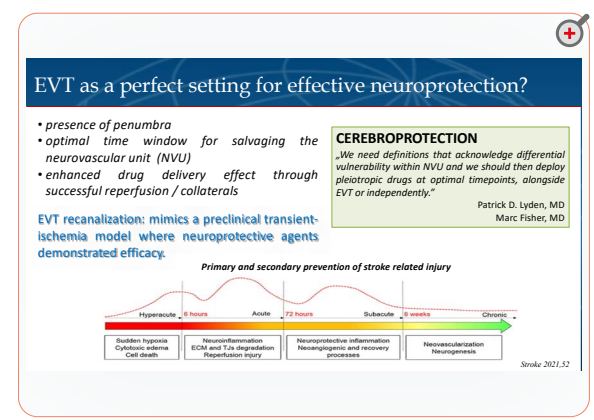

Figure 6

Dr. Staszewski presented the findings from his single-center, prospective, open-label study investigating Cerebrolysin as an adjunctive cerebroprotective therapy to EVT in acute ischemic stroke.

The study successfully reached its primary endpoint, showing a strong and favorable shift toward better functional outcomes at 3 months, with 68% of patients receiving Cerebrolysin achieving functional independence compared to 44% in the control group. Subgroup analyses revealed even more pronounced benefits. The cumulative 3-month mortality rate did not differ between the groups. *(Figure 7, 8 & 9)*

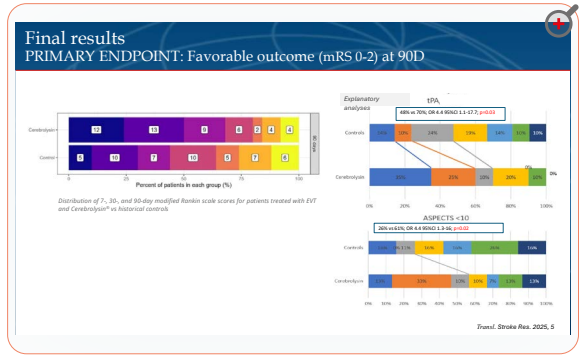

Figure 7

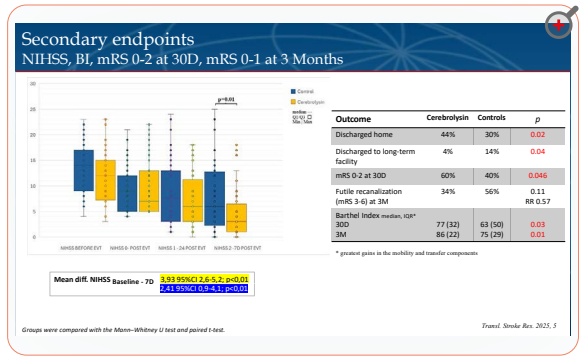

Figure 8

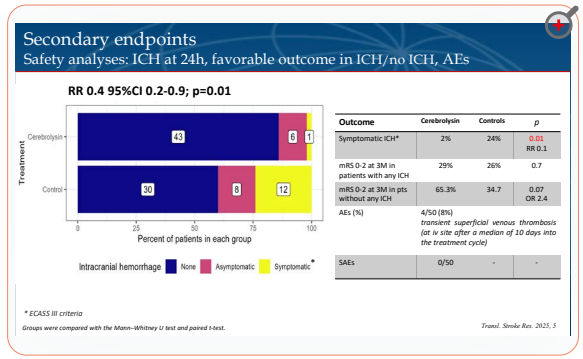

Figure 9

Cerebrolysin appears to be a safe and effective adjunct to EVT in selected patients. It improved both short- and long-term functional outcomes and significantly reduced hemorrhagic complications. These findings align with prior studies and support the concept of cerebroprotective combination therapy in the hyperacute stroke phase.

Cerebrolysin was most effective when administered early (<8h) and following Thrombolysis in Cerebral Infarction (TICI) 2b-3 recanalization.

Dr. Staszewski concluded that stroke care should move beyond recanalization alone, integrating targeted cerebroprotection strategies such as Cerebrolysin to optimize recovery and functional outcomes. *(Figure 10)*

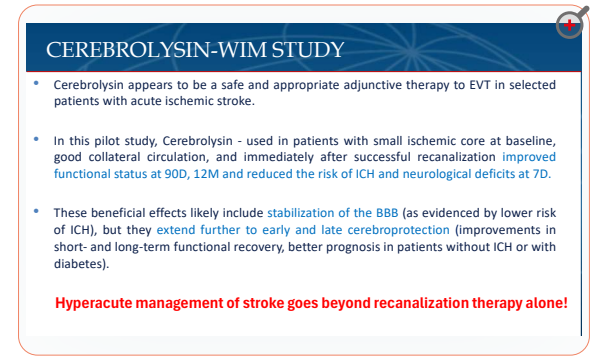

Figure 10

Michael Brainin

Univ.-Prof. Dr. Dr. h.c. mult.
Department for Clinical Neurosciences and Preventive Medicine,
Danube University Krems, Krems, Austria

Can we identify the optimal patient population that benefits most from cerebroprotective treatment?

Promising results in AIS and rehabilitation studies

ABSTRACT

Background and Aims: The C-REGS2 study evaluated the effectiveness of Cerebrolysin in patients with moderate to severe neurological deficits following acute ischemic stroke (AIS) in a real-world clinical setting. The ESCAS trial investigated the combined use of speech therapy and Cerebrolysin in patients with non-fluent aphasia after AIS. Both studies aim to address the need for effective post-acute interventions beyond the recanalization window. Both studies address the need for effective stroke treatment from post-acute phase to rehabilitation.

Methods: C-REGS2 was a large Phase 4 trial conducted according to high-quality comparative effectiveness research standards, ensuring clinical relevance and methodological rigor. Treatment regimens and concomitant medications reflected local practice across multiple centers. Outcomes were assessed on days 21 and 90 post-stroke using validated functional scales. To minimize bias and maintain data quality, rigorous pre-specified analytical procedures and risk-based centralized monitoring were applied.
The recently published ESCAS study was a randomized, double-blind, placebo-controlled phase 4 study focused on language recovery in a non-fluent aphasia population.

Results: C-REGS2 demonstrated strong data integrity, with 90.9% valid data for the primary day-90 modified Rankin Scale endpoint after multilevel case-mix standardization, and a low dropout rate of 5.7% through the final visit. Final results are expected in October 2025, with preliminary findings presented during this symposium.
ESCAS showed that combining speech therapy with Cerebrolysin led to a significant improvement in Western Aphasia Battery scores versus placebo, suggesting a promising synergistic effect for post-stroke language recovery.

Conclusion: C-REGS2 and ESCAS provide valuable insights into multimodal pharmacological and rehabilitative strategies for AIS.

SUMMARY OF THE PRESENTATION

Dr. Michael Brainin presented results from two Cerebrolysin studies:

ESCAS Randomized Pilot Study

Aphasia is a frequent, often underrecognized and undertreated consequence of stroke. Up to 40% of all stroke patients suffer from aphasia, which leads to significant impairments in speaking, reading, writing and often results in depression. These challenges have a substantial impact on quality of life. *(Figure 11)*

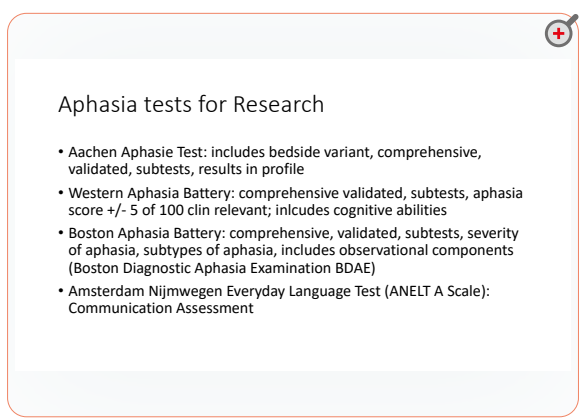

Figure 11

The ESCAS study is an exploratory, prospective, randomized, controlled, academic trial investigating the efficacy and safety of Cerebrolysin in combination with speech therapy versus placebo (saline solution) with speech therapy in patients suffering from non-fluent aphasia following acute ischemic stroke (AIS).

Participants started treatment on day 3–5 post-stroke, receiving three 10-day treatment cycles of Cerebrolysin (30 ml/day) administered in two-week intervals, along with daily one-hour speech therapy.

The primary endpoint was the Western Aphasia Battery (WAB). Patients treated with Cerebrolysin showed significant improvement in modified Rankin Scale (mRS) on day 90 and clinically meaningful improvements in language function compared to placebo, accompanied with better scores on secondary measures like the NIH Stroke Scale (NIHSS) and functional language assessments. The study demonstrated a graded and sustained treatment effect. Cerebrolysin significantly improves recovery from post-stroke aphasia when combined with speech therapy and is well tolerated. *(Figure 12, 13 & 14)*

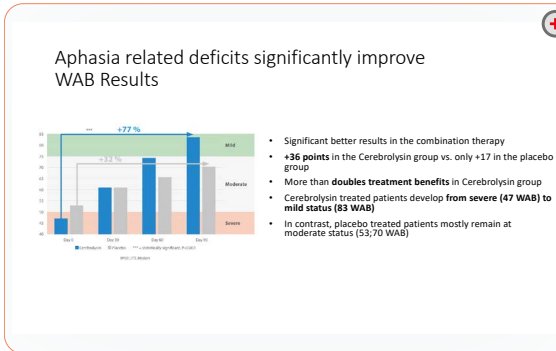

Figure 12

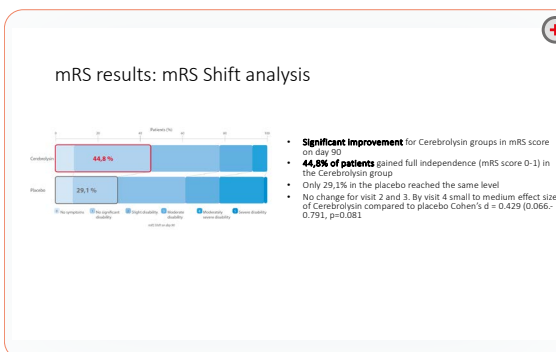

Figure 13

Figure 14

C-REGS2

Prof. Michael Brainin also presented the preliminary findings from a prospective, multinational comparative effectiveness trial investigating the impact of Cerebrolysin on moderate ischemic stroke patients.

C-REGS2 includes both Cerebrolysin treated and untreated patients, with stroke outcomes measured using the NIHSS, the mRS, and the Montreal Cognitive Assessment (MoCA) for cognitive function.

Following the GRACE principles for real-world effectiveness research, the study recruited 1,865 patients presenting with moderate ischemic stroke (NIHSS scores of 8–15), with controls in place for confounding factors such as age, diabetes and pre-existing small vessel disease. *(Figure 15)*

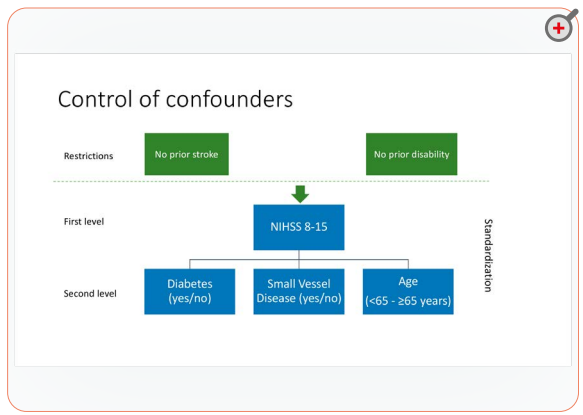

Figure 15

The results were evaluated at various intervals up to three months post-stroke. Fixed-effects and random effects models were used to assess the efficacy of Cerebrolysin under real-world treatment conditions. The study design allows for an objective assessment of treatment effects in different patient populations.

Present data revealed that patients receiving Cerebrolysin achieved significant improvements indicating functional and cognitive gains over the untreated cohort. The final results have been submitted for publication very recently.

Summary

Cerebrolysin studies and real-world data from C-REGS2 – presented at the ESOC 2025 symposium – demonstrate the following benefits in ischemic stroke patients:

- **Improved functional recovery**
- **Reduced risk of hemorrhagic transformation after recanalization**
- **Lower mortality rates following MT**
- **Enhanced cognitive outcomes**
- **Significant language improvements in post-stroke aphasia**

Ongoing research continues to strengthen the role of Cerebrolysin, offering new hope for better stroke recovery worldwide.

ABBREVIATED PRESCRIBING INFORMATION. Name of the medicinal product: Cerebrolysin - Solution for injection. Qualitative and quantitative composition: One ml contains 215.2 mg of Cerebrolysin concentrate in aqueous solution. List of excipients: Sodium hydroxide and water for injection. Therapeutic indications: For treatment of cerebrovascular disorders. Especially in the following indications: Senile dementia of Alzheimer's type. Vascular dementia. Stroke. Craniocerebral trauma (commotio and contusio). Contraindications: Hypersensitivity to one of the components of the drug, epilepsy, severe renal impairment. Marketing Authorisation Holder: EVER Neuro Pharma GmbH, A-4866 Unterach. Only available on prescription and in pharmacies. More information about pharmaceutical form, posology and method of administration, special warnings and precautions for use, interaction with other medicinal products and other forms of interaction, fertility, pregnancy and lactation, effects on ability to drive and use machines, undesirable effects, overdose, pharmacodynamics properties, pharmacokinetic properties, preclinical safety data, incompatibilities, shelf life, special precautions for storage, nature and contents of the container and special precautions for disposal is available in the summary of product characteristics.

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