**July 2017 ENCALS statement on edaravone**

ENCALS

European Network for the Cure of ALS

June 2017

# ENCALS statement on Edaravone (marketed as Radicava®)

Neurologists of the ENCALS centres throughout Europe have discussed the potential of Radicava® as new therapeutic option in ALS/ MND during the ENCALS meeting 18-20th of May in Ljubljana, Slovenia. May 2017, the Food and Drug Administration (FDA) has granted a license for the drug known as a Edaravone (to be marketed as Radicava®) for the treatment of ALS/ MND in the United States (licensed in Japan in 2015 as Radicut®). Currently, there is no official request of pharmaceutical company Mitsubishi Tanabe Pharma (MT Pharma) to the European Medicine Agency (EMA) to register Radicava for use in ALS/MND in Europe. However, some online pharmacies import Radicava® from Japan for several thousands of euro's per patient per month.

**What is Edaravone?**
Edaravone is a free radical scavenger and originally developed for treatment of stroke.
The drug is administered intra-venously (IV). ALS patients would receive the drug every day for two weeks, then take a break('drug holiday') for two weeks. The first two-week sessions should be administered in a hospital because of potential side effects or potential reactions to the drug.

**What is known about the effectiveness of Edaravone?**
Japanese clinicians working with Mitsubishi Tanabe Pharma (MT Pharma) ran a 9 month study of Edaravone. The trial involved over 200 ALS/ MND patients (half taking the drug, half on placebo). The trial, however, did not show any statistically significant benefit, although there was a trend towards slower disease progression with the drug. This hint of an effect led the investigators to analyse the data more thoroughly and they identified a subgroup of patients that appeared to obtain some benefit.

Subsequently, they carried out an additional smaller study focused on the particular subgroup of patients with symptoms in 3 out of 4 body regions (arms, legs, bulbar and thorax), within 2 years from symptom onset and with normal respiratory function. Over 130 participants took part in this trial, receiving intravenous infusion of Edaravone. The results showed a statistically significant slowing of disease progression (assessed using the Revised ALS Functional Rating Scale) over the 24-week treatment period in this small subgroup of ALS patients.

**The facts about Radicava**

- **The treatment with Radicava is intense with daily infusions during 2 weeks every month continuously.**
- **Radicava, requires a PICC line or Port-A-Cath for daily intravenous (IV) injection and can take up to an hour for the daily infusion to be completed. Peripherally Inserted Central Catheter (PICC) is a soft flexible tube inserted into the arm.**
- **At least the first two 2-week periods of infusions need to be administered in a hospital because of safety and possible side effects**

- **A moderate slowdown of disease progression was only shown for a subgroup of ALS patients, representing not more than 7% of ALS patients based on the inclusion criteria of the last trial.**
- **No shown effect on survival**
- **Effects after 6 months unknown. More long term data is needed (at least a year).**
- **Trials were conducted in Japan. There are no data on Edaravone in patients of European background**
- **Radicava is not approved for use in ALS in Europe (European Medicine Agency, EMA)**
- **The costs of Radicava are a several thousands of euro's per month plus the expenses of the infusion. As there is no reimbursement in place, these costs are for the patient.**
- **A trial in Europe is needed.**

**The opinion of ENCALS**

The consensus among the neurologists connected to ENCALS is that based on the studies conducted there is not enough evidence yet that Radicava® substantially alters the disease progression in ALS. Even if neurologists could select the small subgroup of 7% of ALS patients, there is insufficient evidence for substantial beneficial effects: We don't know whether it prolongs survival and we don't know whether it really slows down disease progression as the follow-up was only 24 weeks.

**ENCALS invites MT Pharma for a trial in Europe**

ENCALS would like to invite Mitsubishi Tanabe Pharma to conduct a trial in Europe, with a follow-up of at least a year and with the time of survival as one of the outcome measures. The ENCALS centres are willing to help MT Pharma to set up this trial. Within the TRICALS network we have more than 600 patients throughout Europe who wish to participate in a clinical trial.

For more information on the results of the trials of Edaravone:

**https://mndresearch.wordpress.com/2017/05/06/edaravone-radicava-approved-to-treat-mnd-in-usa-what-does-this-mean-for-people-with-mnd-in-the-uk/**