Nutricia is the **UK’s leader** in Medical Nutrition

At Nutricia we believe medical nutrition is an integral part of healthcare.

- Our focus is on supplying high quality products, systems and support services to patients and healthcare professionals.
- Nutricia is the largest provider of specialist medical nutrition in Europe and the market leader in the UK and Ireland.
- Nutricia has a heritage of innovation spanning more than 100 years. Souvenaid is supported by over 10 years of research.

Examples of our products and services.

We have the largest range of Medical Nutrition in the UK with over 200 products specifically targeted for the very young, the old and the sick.

Souvenaid® is a Food for Special Medical Purposes for the dietary management of early Alzheimer's disease and must be used under medical supervision.
Souvenaid®, a unique nutrient combination, has been shown to improve memory in mild Alzheimer’s disease
Alternative avenue of research addressing the root cause of AD – loss of synapse and inability to regenerate synapse due to diminished uptake of nutrients: as opposed to research into Amyloid plaques & Tau.

Rational behind ‘brain health & nutrition’
The importance of the ‘Fortasyn Connect’ formulation (precursors required for formation of neuronal membranes, cofactors enhance bioavailability of nutritional precursors
Synapse loss is an early event in the clinical course of AD\textsuperscript{1}

Synapse Loss in the Course of AD

- Normal
- Preclinical
- MCI
- Dementia

- Abnormal

- Amyloid-B accumulation
- Tau-mediated neuronal injury
- Synaptic dysfunction
- Brain structure
- Cognition
- Clinical function

Adapted from Sperling et al. 2011

- Synapse loss occurs early in the course of AD and is associated with a decline in memory performance\textsuperscript{1,2}


Souvenaid\textsuperscript{®} is a Food for Special Medical Purposes for the dietary management of early Alzheimer’s disease and must be used under medical supervision.
The loss of synapses increases with disease progression.

Reduced number of synapses in mild cognitive impairment (MCI) and Alzheimer’s disease (AD) compared with control\(^1,2\)

![Bar chart showing number of synapses in Healthy control, MCI, and AD](chart.png)


Souvenaid\(^\circledast\) is a Food for Special Medical Purposes for the dietary management of early Alzheimer’s disease and must be used under medical supervision.
The biochemical pathway for synthesising new neuronal membranes

The Kennedy Pathway is the biochemical process for synthesising new neuronal membranes

- Choline & Phospholipids
  - Uridine
  - Phosphocholine
  - CDP-choline
  - Phosphatidylycerol
  - New neuronal membrane

- B-vitamins
- anti-oxidants
- Cofactors
- Omega-3 fatty acids

These are the key nutrients required to form new neuronal membranes


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In AD, specific nutrients may not be available to sustain the pathway supporting synapse formation. Levels of certain nutrients (e.g., omega-3 fatty acids and B vitamins) are lower in patients with AD than in age-matched individuals without the disease. Impairments in metabolic pathways reduce the bioavailability of some of these nutrients. Uridine Monophosphate (UMP) cannot be obtained through a normal diet.

For references please see slide 19.
Souvenaid® contains a unique, patented combination of nutrients designed to support synapse formation.

- **DHA and EPA**
- **Uridine Monophosphate (UMP)**
- **B vitamins and other cofactors**
- **Choline & Phospholipids**

Nutritional precursors are required to form neuronal membranes. Cofactors enhance the bioavailability of nutritional precursors.

DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid. (DHA and EPA are Omega-3 fatty acids)

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Souvenaid is based on over 10 years of research.

- **Start of research into nutrition & Alzheimer's at Nutricia Research**: 1998
- **Final product concept developed**: 2001
- **Start first clinical trial**: 2002
- **Proof of concept. Results first trial**: 2004
- **Results 2nd and 3rd trials**: 2007

**Various national and international preclinical research consortia including 'Dementia' and 'Neuronutrients'**

**Continued research and involvement of Professor Wurtman, MIT, Boston USA**

**30 Preclinical research papers**

**Souvenir I**
Prof Scheltens
VUMc, NL

**Souvenir II**
Prof Scheltens
VUMc, NL

**LiPiDiDiet**
Prof Soininen
UEF, Finland

Souvenir I received funding from Stichting Technische Wetenschappen
Souvenir II received funding from the NL Food and Nutrition Delta project, FND #10003
LiPiDiDiet: Funded by the EU FP7 project LiPiDiDiet grant Agreement #211696

Souvenaid® is a Food for Special Medical Purposes for the dietary management of early Alzheimer's disease and must be used under medical supervision.
## Overview

<table>
<thead>
<tr>
<th>Journal</th>
<th>Trial</th>
<th>n</th>
<th>AD type</th>
<th>Mean MMSE</th>
<th>AD drugs</th>
<th>Duration</th>
<th>Primary endpoint</th>
<th>Primary endpoint results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Dementia 2010</td>
<td>225</td>
<td>Mid</td>
<td></td>
<td>23.9</td>
<td>No</td>
<td>12 weeks</td>
<td>WMS-r (delayed verbal recall) ADAS-Cog (13 item)</td>
<td>Significantly improved memory No improvement on ADAS-Cog Souvenaid was well tolerated</td>
</tr>
<tr>
<td>J. Alzheimer's Dis 2012</td>
<td>259</td>
<td>Mid</td>
<td></td>
<td>25.0</td>
<td>No</td>
<td>24 weeks</td>
<td>Memory domain of the NTB (z-score)</td>
<td>Significantly improved memory</td>
</tr>
<tr>
<td>J. Alzheimer's Dis 2015</td>
<td>201</td>
<td>Mid</td>
<td>Allowed</td>
<td>-</td>
<td>Allowed</td>
<td>24 week extension study</td>
<td>Safety, adherance and blood nutritional markers</td>
<td>Souvenaid was well tolerated with a high intake adherence A significant increase in exploratory memory outcome in both active – active and control active arm</td>
</tr>
</tbody>
</table>

ADAS-Cog = Alzheimer Disease Assessment Scale on Cognition; NTB = Neuropsychological Test Battery; WMS-r = Wechsler Memory Scale-revised

Souvenaid® has been shown to improve memory over 12, 24 and 48 weeks¹⁻³


Souvenaid® is a Food for Special Medical Purposes for the dietary management of early Alzheimer’s disease and must be used under medical supervision.
Memory continues to improve up to 48 weeks\textsuperscript{1}

Significant increase in memory from week 24 to week 48 in both groups:\textsuperscript{1}

\begin{itemize}
\item ITT, Mixed Model for Repeated Measures, 2 degrees of freedom contrast (trajectory of change, mean ± SE).
\item NTB = Neuropsychological Test Battery.
\item Souvenir II OLE was a 24 week extension study offered to all Souvenir II completers. All patients received Souvenaid\textsuperscript{*} and AD medication was allowed as representative of clinical practice.
\end{itemize}


Souvenaid\textsuperscript{*} is a Food for Special Medical Purposes for the dietary management of early Alzheimer's disease and must be used under medical supervision.
Souvenaid® is very well tolerated with an adherence of >90%¹-³

There was also no significant difference between Souvenaid® and control groups in adverse events¹,²

Souvenaid®: an innovative nutritional product for your patients with mild Alzheimer’s disease

- Souvenaid® is the first medical nutrition product designed to support synapse formation
- Souvenaid® has been shown to improve memory over 12, 24 and 48 weeks\(^1,2,3\)
- Souvenaid® is extremely well tolerated with a lack of significant adverse events\(^1,2,3\)
- Can be taken with concomitant drug therapy for Alzheimer’s disease - no drug interactions seen in clinical trials

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Souvenaid® is a Food for Special Medical Purposes for the dietary management of early Alzheimer’s disease and must be used under medical supervision.
Describing Souvenaid® to your patients with mild Alzheimer’s disease

- Once a day, every day in addition to their normal diet
- Small volume (125ml)
- Available in two flavours (strawberry and vanilla)
- Available directly from Nutricia or over-the-counter in pharmacies

Why not include Souvenaid® in your conversations with mild Alzheimer’s disease patients?

Allergy information:
Contains ingredients obtained from milk, fish and soy.
Lactose and gluten free.
Not suitable for patients with galactosaemia

Souvenaid® is a Food for Special Medical Purposes for the dietary management of early Alzheimer’s disease and must be used under medical supervision.
References for Slide 9. Availability of nutrients needed to support synapse formation in AD patients