DRUG TREATMENT SINCE 1989

In the 20–year period between 1989 and 2009, 13 major antiepileptic drugs have been licensed and introduced into clinical practice. Several have now largely disappeared from routine practice due to serious toxicity discovered after marketing (felbamate and vigabatrin) or perceived ordinariness (gabapentin, tiagabine) but the others are now established in practice. Furthermore, 20 other drugs are in stages of clinical testing and seldom has there been a period of greater activity, which was perhaps matched only by the developments in the 15 years after 1938. In 2009, we are now firmly in the molecular age. The early waves of interest, first in GABAergic mechanisms (in the 1970s and 1980s) and then glutaminergic mechanisms (in the 1980s and 1990s), and in sodium and calcium channel blockade, which are the traditional drug targets, have partly given way to a still limited but more diverse list of potential drug mechanisms. Currently, research targets not only these three classical mechanisms but also blockade of potassium channels, gap junctions, synaptic vesicle proteins, and neuronal adenosine, nicotinic acetylcholine and serotonin receptors. In addition, much more is known about the chemistry, structure, and functioning of channels and receptors, and their regional cerebral and microscopic distribution. Drugs can now be targeted at specific isoforms and genetic variants – this at least is the theory, but it has to be admitted that progress has been limited. Despite this explosion of research into the mechanisms of action of antiepileptic drugs, almost all of the currently licensed drugs have been discovered either by pure chance, the manipulation of the structure of existing compounds (with resulting 'me–too drugs') or by random screening. The full promise of the molecular age at the dawn of the second ILAE century has yet to be delivered.

Drugs licensed in Europe and the United States since 1989

Year of 1st licence	Proprietary name	Country of 1st licence	Manufacturer
1989	**Vigabatrin**	UK	Marion Merrill Dow
1990	**Lamotrigine**	Ireland	Burroughs–Wellcome
1990	**Oxcarbazepine**	Denmark	Novartis
1993	**Felbamate**	USA	Carter Wallace
1994	**Gabapentin**	USA, UK	Parke–Davis
1995	**Topiramate**	UK	Johnson and Johnson
1996	**Tiagabine**	France	Novo–Nordisk
1999	**Levetiracetam**	USA	UCB Pharma
2000	**Zonisamide**	USA (Japan in 1989)	Elan Pharmaceuticals
2004	**Pregabalin**	European Union	Pfizer
2007	**Stiripentol**	European Union	Laboratoires Biocodex
2007	**Rufinamide**	European Union	Eisai
2008	**Lacosamide**	European Union	UCB Pharma