ALS EMERGENCY TREATMENT FUND

The Role of Expanded Access in Clinical Drug Development

FDA regulations for Expanded Access clinical trials were first written in the 1980s during the AIDS crisis. The new regulatory mechanism defined permissible "*Treatment Use*" of investigational drugs under a Treatment IND or Treatment Protocol for cohorts of patients who were not candidates for ongoing research trials; or –in exceptional cases- for individual patients under an Individual / Emergency IND or Protocol.

Expanded Access programs are clinical trials for patients who are not eligible to take part in research trials. Last revised in 2009, the current regulations can be found in 21 CFR 312, Subpart I. They are logically written and easy to understand. In 2013, FDA released a Guidance on the Treatment IND and another on cost recovery in investigational treatment programs.

Four essential requirements must be met for authorization of an Expanded Access program:

1. The drug is intended to treat a serious or life-threatening condition, and there is no satisfactory alternative treatment available.
2. The potential benefit to the patients outweighs the additional risk to patients, in consideration of the seriousness of the disease.
3. The access program must not interfere with continued clinical development of the drug.
4. The primary intent of the access program is treatment; research objectives are secondary.

FDA encouraged drug companies to consider these programs as a way to engage otherwise disenfranchised physicians and patients and –secondarily- as a way to gather additional safety data on their products.

Over 100,000 AIDS sufferers gained early access to new antiretroviral drugs, including the first protease inhibitors through FDA-authorized Expanded Access programs.

Brand	Name	Indication	EAP Start	EAP End	EAP Enrolled	FDA Approved
Epivir	3TC / lamivudine	AIDS / ARC	1993	1995	**29,430**	Yes
Videx	ddI / didanosine	AIDS / ARC	1989	1991	**21,000**	Yes
Zerit	d4T / stavudine	AIDS / ARC	1992	1994	**12,551**	Yes
Hivid	ddC / zalcitabine	AIDS / ARC	1990	1992	**6,705**	Yes
Retrovir	AZT / zidovudine	AIDS / ARC	1986	1987	**4,804**	Yes
Mycobutin	rifabutin	AIDS / ARC	1992	1993	**2,506**	Yes
Invirase	saquinavir	AIDS / ARC	1995	1995	**2,200**	Yes
Crixivan	indinavir	AIDS / ARC	1995	1995	**1,500**	Yes

Most of the breakthrough receptor inhibitor drugs in the late 1990s and early 2000s were available to patients through Expanded Access prior to marketing approval.

Brand	Name	Indication	EAP Start	EAP End	EAP Enrolled	FDA Approved
Herceptiin	trastuzumab	ErbB2+ B.C.	1996	1998	**300**	Yes, Accelerated
Gleevec	imatinib	CML	2000	2001	**7,400**	Yes, Accelerated
Eloxatin	oxaliplatin	colon cancer	2000	2002	**8,600**	Yes, Accelerated
Alimta	permetrexed	Non-s.c. lung	2002	2004	**3,200**	Yes
Tarceva	erlotinib	Non-s.c. lung	2003	2005	**1,140**	Yes, Accelerated
Nexavar	sorafenib	kidney cancer	2004	2005	**2,500**	Yes
Sutent	sunitinib	kidney cancer	2005	2007	**4,500**	Yes, Accelerated
Tykerb	lapatinib	ErbB2+ B.C.	2006	2007	**4,300**	Yes, Accelerated
Kyprolis	carfilzomib	mult. myeloma	2011	2012	**350**	Yes, Accelerated

Additional examples of Expanded Access for investigational drugs include the following:

Brand	Name	Indication	EAP Start	EAP End	EAP Enrolled	FDA Approved
Rilutek	riluzole	ALS	1995	1995	**8,000**	Yes
Myotrophin	mecasermine	ALS	1996	1999	**250**	No
Voraxaze	glucarpidase	mtx toxicity	2007	2012	**150**	Yes
CP-675,206	tremelimumab	melanoma	2008	2009	**unknown**	No
VPRIV	velaglucerase alfa	Gaucher Type-1	2009	2012	**210**	Yes
Elelyso	taliglucerase alfa	Gaucher Type-1	2009	2013	**unknown**	Yes

All above examples are from ALS-ETF's database of over 50 FDA-authorized Expanded Access programs that were conducted over the last twenty five years.

Not every drug that is made available through Expanded Access ultimately wins marketing approval. By intent, these programs are initiated when the particular treatment is still investigational, before the determination of efficacy is complete. If Expanded Access programs have had any impact on the outcomes of development efforts, the case history suggests it has been exclusively favorable. Several program sponsors collected efficacy data as well as safety during Expanded Access, and the generated data informed the continued research of the study drug. According to FDA, there are no cases of unexpected adverse reaction during an Expanded Access program that resulted in a delay of eventual marketing approval.