

Approved Cancer Drugs for Children

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Frequent Criticism: Too few drugs approved for pediatric cancer

“Since 1980, only **4 drugs** have been approved for the first instance for use in children.” - Coalition Against Childhood Cancer

“In the last 20 years, only **two new drugs** have been approved that were specifically developed to treat children with cancer.” – St. Baldricks

“Over the past 20 years, the FDA has approved about 190 new cancer treatments for adults but only **three for children.**”
USA Today

“Since 1980, **fewer than 10 drugs** have been developed for use in children with cancer. **Only three drugs** have been approved for use in children. Only four additional new drugs have been approved for use by both adults and children.” - National Pediatric Cancer Foundation

“**15 oncology drugs** were approved by the FDA for pediatric use between 1948 and 2003.” – Managed Care

“From 1980 to 2017, only **11 drugs** (already approved in adults) have been approved to use in children with cancer” - Coalition Against Childhood Cancer

Question: How many drugs are FDA approved to treat pediatric cancer?

- A: 11
- B: 34
- C: 4
- D: 15

“There’s no tragedy in life like the death of a child.”

- Dwight D. Eisenhower

Antitoxin Contamination

- Early 1900s
 - Animal anti-sera given to patients with cholera, typhoid, etc.
- A Horse named “Jim”
 - Contaminated serum
 - Anti-toxin resulted in deaths of 13 children
- Second incident
 - Contaminated smallpox vaccine killed 9 children



Laws Enacted

- ❑ 1902 – Biologics Control Act
- ❑ 1906 – Pure Food and Drug Act

Elixir Sulfanilamide Tragedy

ONE PINT ELIXIR ONE PINT
SULFANILAMIDE

Each fluidounce represents:
Sulfanilamide. 40 gra.

SUGGESTED FOR THE TREATMENT OF ALL CONDITIONS
 IN WHICH THE HEMOLYTIC STREPTOCOCCI APPEAR

Dose, begin with 2 to 3 teaspoonfuls in water
 every four hours. Decrease in twenty-four
 to forty-eight hours to 1 or 2 teaspoonfuls
 and continue at this dose until recovery.

[Trade-mark]

THE S. E. MASSENGILL COMPANY
 Manufacturing Pharmacists
 BRISTOL, TENN.-VA.



Law Enacted

- ❑ The Food, Drug and Cosmetic (FDC) Act of 1938

Thalidomide



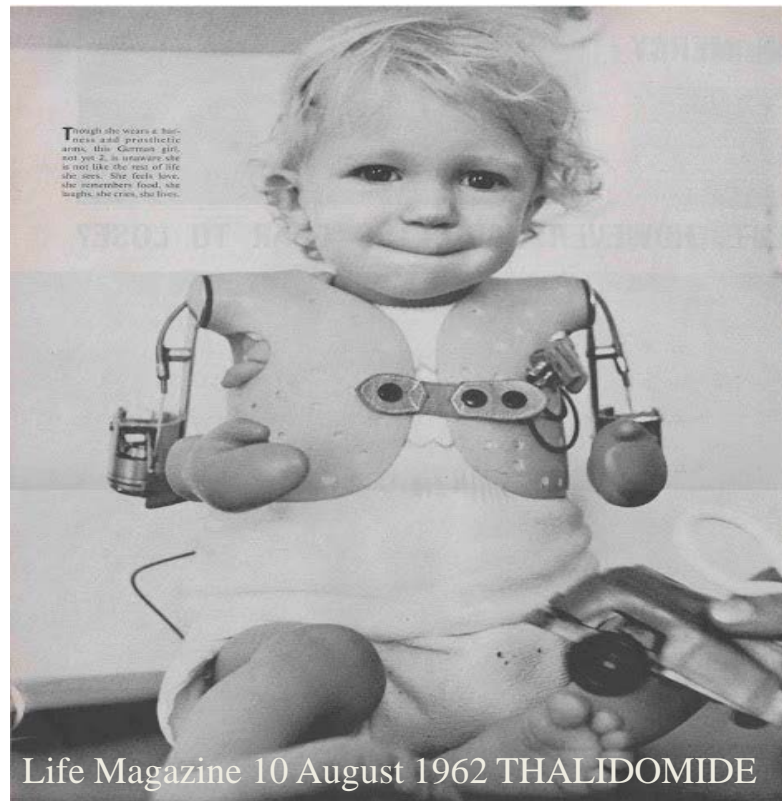
A complete sedative and hypnotic range – *in a single preparation.* That is 'Distaval' . . . the safe day-time sedative which is equally safe in hypnotic doses by night. 'Distaval' is especially suitable for infants, the aged, and patients under severe emotional stress.

'DISTAVAL' TRADE MARK

THALIDOMIDE

sedative and hypnotic

tablets of 25 mg.



Life Magazine 10 August 1962 THALIDOMIDE

Law Enacted

- ❑ Kefauver-Harris amendment, 1962

Summary

Legislation

- Pure Food and Drug Act (1906)
- 1938 Food, Drug and Cosmetic Act
- Kefauver-Harris Amendment (1962)

Impact

SAY WHAT IT IS

SAFE

EFFECTIVE

Next 35 Years (1962-1997)

- First drugs to induce remission in children with ALL (1948)
- National Cancer Chemotherapy Service Center (NCCSC)- 1955
- Pediatric Cooperative Groups
- Combination Chemotherapy- 1965

1997: Food and Drug Administration

Modernization Act (FDAMA)



- Amended the Food, Drug and Cosmetic Act
- Provided marketing incentives (6 months of exclusivity) to manufactures who conduct studies of drugs in children.
- Exclusivity was reauthorized as the Best Pharmaceutical Act for Children BPCA (2003)- *next talk*

Drugs approved prior to FDAMA (1997)

- Approval was based primarily on pediatric clinical trial results
- 16 Drugs
- New molecular entities: L-asparaginase, teniposide, peg-asparaginase

Drugs approved prior to FDAMA for which labeling includes pediatric indications

Drug	Original Approval	Indication
Mercaptopurine	9/11/1953	ALL
Methotrexate	8/10/1959	ALL, meningeal leukemia, osteosarcoma, non-Hodgkin lymphoma
Cyclophosphamide	11/16/1959	Leukemia, lymphoma, NBL, retinoblastoma
Vincristine	7/10/1963	ALL, lymphomas, Wilms, rhabdomyosarcoma, NBL
Dactinomycin	12/10/1964	Ewing Sarcoma, sarcoma botryoides
Vinblastine	11/5/1965	Histiocytosis, testicular germ cell carcinoma, Hodgkin lymphoma
Thioguanine	1/18/1966	Acute non-lymphocytic leukemia
Cytarabine	6/17/1969	Acute non-lymphocytic leukemia
Procarbazine	7/22/1969	Hodgkin lymphoma
Doxorubicin	8/7/1974	Wilms tumor, NBL, soft tissue sarcoma, Hodgkin lymphoma, other lymphomas, ALL, AML
Lomustine	8/4/1976	Brian tumors, Hodgkin
L-Asparaginase	1/10/1978	Leukemia
Daunorubicin	12/19/1979	ALL
Teniposide	7/14/1992 (Pediatric Approval) 10/1/2002	Refractory ALL
PEG-Asparaginase	2/1/1994	ALL
Tretinoin	11/22/1995	APML

Drugs approved post-FDAMA (1997-2018)

- 18 Drugs, 22 indications
- 9 NMEs, where approval was based primarily on pediatric data

Drugs approved post FDAMA with pediatric specific indications (1997-2018)			
Drug	Original Approval	Pediatric Approval	Indication
Gemtuzumab	5/17/2000	9/1/2017	Relapsed or refractory CD33+ AML
Arsenic trioxide	9/5/2000	same	APML
Clofarabine	12/28/2004	same	Refractory ALL
Nelarabine	10/28/2005	same	T-cell ALL
Dasatinib	6/28/2006	11/9/2017	Ph+ CML in the chronic phase,
		12/21/18	Ph+ ALL
Imatinib	9/27/2006	11/9/2017	Ph+ ALL and Ph+ CML
Nilotinib	10/29/2007	3/22/2018	Ph+ CML in the chronic phase
Ipilimumab	3/25/2010	7/21/2017	Unresectable or metastatic melanoma (12 years and older)
Denosumab	6/1/2010	6/13/2013	Giant cell tumor of the bone
Everolimus	10/29/2010	9/25/2012	SEGA
Erwinia asparaginase	11/18/2011	same	ALL
6-MP oral solution	4/28/2014	same	ALL (Liquid formulation approved)
Pembrolizumab	9/4/2014	3/14/2017	refractory classical cHL
		5/23/2017	Microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumor
		6/13/2018	Adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma
		12/19/2018	Metastatic Merkel cell carcinoma (≥ 12 years)
Dinutuximab	3/10/2015	Same	High risk NBL
Avelumab	3/23/2017	same	Metastatic Merkel cell carcinoma (≥ 12 years)
Tisagenlecleucel	8/30/2017	same	Relapsed or refractory ALL
Emapalumab	11/20/2018	Same	Relapsed or refractory primary HLD 15
Lorotrectinib	11/26/2018	Same	Solid tumor with NTRK gene fusion

Supportive Care Oncology Drugs

- 6 Drugs
- Rasburicase was an NME approved primarily on pediatric data
- Tocilizumab also based solely on pediatric data

<i>Supportive care oncology drugs with pediatric indications</i>			
Pegfilgrastim	1/31/2002	11/13/2015	Decrease the incidence of infection®, increase survival in patients acutely exposed to myelosuppressive doses of radiation
Rasburicase	7/12/2002	same	Management of plasma uric acid levels in patients at risk for tumor lysis syndrome
Palifermin	12/15/2004	5/30/2013	Decreased the incidence and duration of severe oral mucositis
Levoleucovorin	3/07/2008	same	Rescue after HD-MTX
Tocilizumab	1/8/2010	8/30/2017	Treatment of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome
Voraxaze	1/17/2012	same	Treatment of toxic plasma methotrexate concentration based on delayed MTX clearance

Summary

- **34 drugs are FDA approved** to treat a childhood cancer, **38 indications**
- An additional **6 drugs** are approved to treat pediatric patients with toxicity associated with cancer treatment
- In the last 25 years, FDA has received 30 new drug applications for pediatric-specific oncology indications
- 29 were approved (23 to treat, 6 to prevent or mitigate therapy-related toxicity)
- **12 were new molecular entities** intended to treat cancer seen primarily in children

Progress....still room for more improvement!!!

Questions?

