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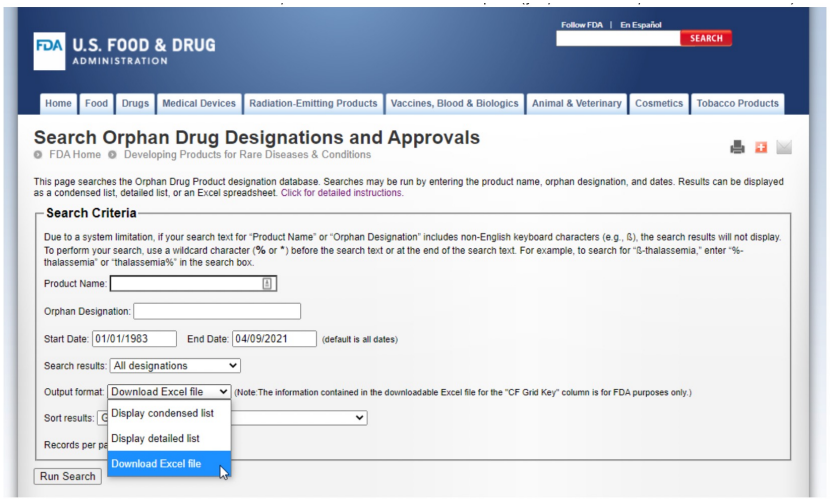
FDA Orphan Drug Data Analysis

05-06-2021

Background

- Obtain data from FDA Orphan Drug Designations and Approvals and processed them into MyChem.info and MyDisease.info
- Source:
  - https://www.accessdata.fda.gov/scripts/opdlisting/oopd



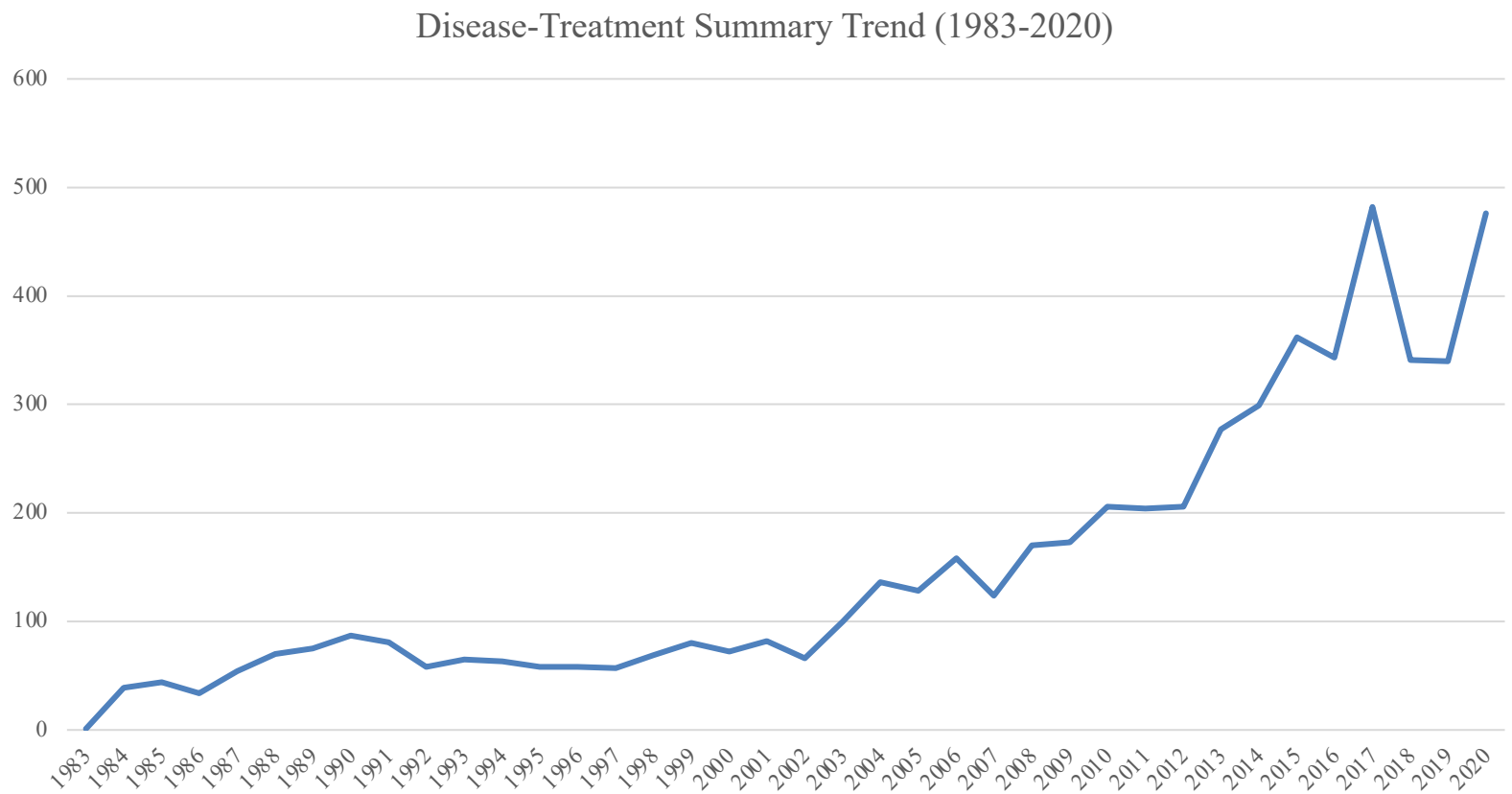
Data Set (1/2)

A	B	C	D	E	F
Generic Name	**Trade Name**	**Date Designated**	**Orphan Designation**	**Orphan Designation Status**	**FDA Orphan Approval Status**
(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-(pyridin-2-yl)hepta-2,4-dien-2-yl]oxacyclododec-4-en-6-yl 4-methylpiperazine-1-carboxylate		6/22/17	Treatment of chronic myelomonocytic leukemia (CMML)	Designated	Not FDA Approved for Orphan Indication
(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide		11/2/17	Treatment of paroxysmal nocturnal hemoglobinuria	Designated	Not FDA Approved for Orphan Indication
(2-chloro-4-phenoxyphenyl)(4-(((3R,6S)-6-(hydroxymethyl)tetrahydro-2H-pyran-3-yl)amino)-7H-pyrrolo[2,3-d]pyrimidin-5- yl)methanone		12/8/20	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Designated	Not FDA Approved for Orphan Indication
1-(2-Nitro-imidazolyl)-3-[18F]fluoro-2-propanol;1H-1-(3-[18F]fluoro-2-hydroxypropyl)-2-nitroimidazole		1/6/16	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Designated	Not FDA Approved for Orphan Indication
2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride		6/17/19	Treatment of beta-thalassemia	Designated	Not FDA Approved for Orphan Indication
3?,6?,7?,12?-tetrahydroxy-5?-cholan-24-oic acid		10/22/20	treatment of progressive familial intrahepatic cholestasis	Designated	Not FDA Approved for Orphan Indication
4-{4-[[6-(4-Chlorophenyl)-spiro[3.5]non-6-en-7-yl]methyl}-piperazin-1-yl}-N-{[3-nitro-4-[((2S)-1,4-dioxan-2-ylmethyl)amino]phenyl}sulfonyl}-2-(1H- pyrrolo[2,3-b]pyridin-5-yloxy)benzamide		8/28/20	Treatment of Chronic Lymphocytic Leukemia	Designated	Not FDA Approved for Orphan Indication
a non-replicating, recombinant adeno-associated virus serotype 9 (AAV9) containing the human Methyl CpG Binding Protein 2B (MECP2B) cDNA under the control of a segment of the murine MECP2 promoter.		4/17/19	Treatment of Rett Syndrome (RTT)	Designated	Not FDA Approved for Orphan Indication
A recombinant plasmid-derived DNA-based vaccine targeting the E6 and E7 antigens of both HPV6 and HPV11		7/28/20	Treatment of recurrent respiratory papillomatosis	Designated	Not FDA Approved for Orphan Indication
a self-complementary adeno-associated virus serotype 9 (AAV9) vector expressing codon-optimized human SURF1 DNA coding sequence		10/20/20	Treatment of Leigh Syndrome.	Designated	Not FDA Approved for Orphan Indication
allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting CD19 antigen		2/16/21	Treatment of acute lymphoblastic leukemia	Designated	Not FDA Approved for Orphan Indication
antibody drug conjugate comprised of an anti-B cell maturation (BCMA) IgG1 humanized antibody conjugated covalently to the dibenzocyclooctyne (DBCO) noncleavable linker maytansinoid warhead		2/23/21	Treatment of multiple myeloma	Designated	Not FDA Approved for Orphan Indication
apadamtase alfa		9/28/20	Treatment of Sickle Cell Disease	Designated	Not FDA Approved for Orphan Indication
ascorbic acid		5/11/09	Treatment of Charcot-Marie-Tooth disease type 1A.	Designated	Not FDA Approved for Orphan Indication

Data Set (2/2)

- Total: 5,849 records (treatment-disease)
- Generic Name (Column A)
  - Chemicals (substance and compound)
  - Medication, gene therapy or other therapies
    - Processed with mychem, pubchem and Google search
- Orphan Designation (Column D)
    - Processed with Medical NLP algorithms

Data Trend


Disease-Treatment Summary Trend (1983-2020)
600
500
400
300
200
100
0
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
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2007
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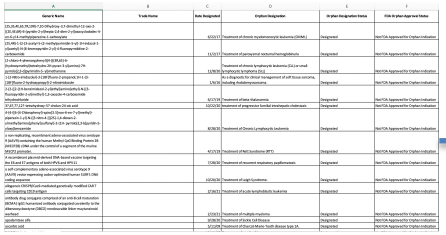
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020

Process Flow



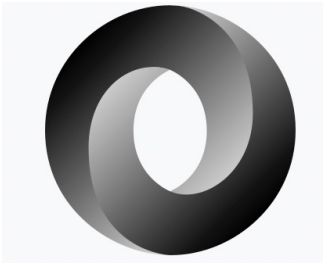
Original Excel File

PubChem

Medical NLP Algorithms

Semi-automation data review

Processed Excel File



JSON objects

Data Clean and Normalization (1/3) (column D)

- Example 1:
  - Treatment of paroxysmal nocturnal hemoglobinuria

  paroxysmal nocturnal hemoglobinuria (C0024790; Neoplastic Process)

- Example 2:
  - For immune reconstitution and prevention of graft versus host disease following allogeneic hematopoietic stem cell transplantation.

  graft versus host disease (C0018133;Disease or Syndrome)

Data Clean and Normalization (2/3) (column D)

- Example 3:
  - Intravenous treatment of patients presenting with moderate to severe acetaminophen overdose

  Acetaminophen overdose (C0572025; injury or poisoning)

- Example 4:
  - For use in post-exposure prophylaxis for occupational exposure to human immunodeficiency virus

  Exposure to Human immunodeficiency virus (C1096519; injury or poisoning)

Data Clean and Normalization (3/3) (column D)

- Processing Types:

Disease or Syndrome
Neoplastic Process
Pathologic Function
Injury or Poisoning
Gene or Genome
Congenital Abnormality
Finding
Sign or Symptom
Intellectual Product
Anatomical Abnormality
Bacterium
Virus
Body Space or Junction
Mental or Behavioral Dysfunction
Cell Component
Eukaryote

Result – Column A

- Group 1 (51.92%; 3,037 records): PubChem, MyChem and Google search
  - Key: InChl Key or Substance ID

- Group 2 (48.08%; 2812 records): Not directly related to chemicals or did not find any match

Result – Column D

- Group 1 (96.6%; 5,650 records): Processed with type support

Record Id	Original text	Parsed Text	Text Type
1	Treatment of chronic myelomonocytic leukemia (CMML)	Chronic Myelomonocytic Leukemia	Neoplastic Process
2	Treatment of paroxysmal nocturnal hemoglobinuria	Paroxysmal nocturnal hemoglobinuria	Disease or Syndrome
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Chronic Lymphocytic Leukemia	Neoplastic Process
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Small Lymphocytic Lymphoma	Neoplastic Process
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	SLL	Gene or Genome
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Rhabdomyosarcoma	Neoplastic Process
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Soft tissue sarcoma	Neoplastic Process
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Diagnostic	Diagnostic Procedure
5	Treatment of beta-thalassemia	BETA-THALASSEMIA	Disease or Syndrome

- Group 2 (3.4%; 199 records): Not directly related to disease or did not find any match

2247	For promotion of cutaneous wound healing in extreme burn treatment protocols.	For promotion of cutaneous wound healing in extreme burn treatment protocols.
2321	Prevention of graft rejection following solid organ transplantation	Prevention of graft rejection following solid organ transplantation
2611	Mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent transplant	Mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent transplant
3006	Prevention of graft rejection following solid organ transplantation	Prevention of graft rejection following solid organ transplantation
3090	For the promotion of early engraftment in bone marrow transplantation.	For the promotion of early engraftment in bone marrow transplantation.

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Result

- Since some generic names do not have compound/substance ids in PubChem and MyChem.info, so we only included 3,149 records (3149/5849=53.8%) in the final data set.
- JSON objects use inchikey as _id for MyChem and UMLS or MONDO as _id for MyDisease

Discussion

- Data Presentation on FDA's website:

Search Orphan Drug Designations and Approvals

FDA Home › Developing Products for Rare Diseases & Conditions

Generic Name:	(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-(pyridin-2-yl)hepta-2,4-dien-2-yl]oxacyclododec-4-en-6-yl 4-methylpiperazine-1-carboxylate
Date Designated:	06/22/2017
Orphan Designation:	Treatment of chronic myelomonocytic leukemia (CMML)
Orphan Designation Status:	Designated
FDA Orphan Approval Status:	Not FDA Approved for Orphan Indication
Sponsor:	H3 Biomedicine Inc. (US Research Subsidiary of Eisai Co., Ltd.) 300 Technology Square Floor 5 Cambridge, Massachusetts 02139 United States *The sponsor address listed is the last reported by the sponsor to OOPD.*

Discussion

- JSON Examples (MyChem):


```
{
    "_id": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",
    "fda_orphan_drug": [
        {
            "pubchem_cid": 118323590,
            "pubchem_sid": "381128152, 439581800",
            "inchikey": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",
            "generic_name": "(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide",
            "designated_date": "2017-11-02",
            "designation_status": "Designated",
            "approval_status": "Not FDA Approved for Orphan Indication",
            "sponsor": "Alexion Pharmaceuticals, Inc|300 George Street|New Haven|Connecticut|6511|United States",
            "orphan_designation": {
                "original_text": "Treatment of paroxysmal nocturnal hemoglobinuria",
                "umls": "C0024790",
                "parsed_text": "Paroxysmal nocturnal hemoglobinuria"
            }
        },
        {
            "pubchem_cid": 118323590,
            "pubchem_sid": "381128152, 439581800",
            "inchikey": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",
            "generic_name": "(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide",
            "designated_date": "2017-12-14",
            "designation_status": "Designated",
            "approval_status": "Not FDA Approved for Orphan Indication",
            "sponsor": "Alexion Pharmaceuticals, Inc|300 George Street|New Haven|Connecticut|6511|United States",
            "orphan_designation": {
                "original_text": "Treatment of C3 glomerulopathy (C3G)",
                "umls": "C4521256",
                "parsed_text": "Glomerulopathy"
            }
        }
    ]
},
```

Discussion

- JSON Examples (MyDisease):


```
{
    "_id": "MONDO:0008380",
    "fda_orphan_drug": [
        {
            "pubchem_cid": 11455910,
            "pubchem_sid": "252157732",
            "inchikey": "PQAPVTKIEGUPRN-UHFFFAOYSA-N",
            "generic_name": "N-[4-[[2-(1,1-Dimethylethyl)phenyl]sulfonyl]phenyl]-2,3,4-trihydroxy-5-[[2-(1-methylethyl)phenyl]methyl]benzamide",
            "designated_date": "2020-09-14",
            "designation_status": "Designated",
            "approval_status": "Not FDA Approved for Orphan Indication",
            "sponsor": "Oxular Ltd|Magadalen Centre|1 Robert Robinson Avenue|Oxford|OX4 4GA|United Kingdom",
            "orphan_designation": {
                "original_text": "Treatment of retinoblastoma",
                "umls": "C0035335",
                "parsed_text": "Retinoblastoma"
            }
        },
        {
            "pubchem_cid": 437740,
            "pubchem_sid": "172650142, 319221596, 347829146, 404717883, 319392766",
            "inchikey": "PRDJGNVQBVXXEO-UHFFFAOYSA-N",
            "generic_name": "thioureidobutyronitrile",
            "designated_date": "2015-11-17",
            "designation_status": "Designated",
            "approval_status": "Not FDA Approved for Orphan Indication",
            "sponsor": "Innovation Pharmaceuticals, Inc.|100 Cummings Center|Suite 151-B|Beverly|Massachusetts|1915|United States",
            "orphan_designation": {
                "original_text": "Treatment of retinoblastoma.",
                "umls": "C0035335",
                "parsed_text": "Retinoblastoma"
            }
        },
```

Thank you