LIST OF ORPHAN MEDICINES FOR RARE AND DIFFICULT TO TREAT DISEASES IN ETHIOPIA

ETHIOPIAN FOOD, MEDICINE AND HEALTHCARE ADMINISTRATION AND CONTROL AUTHORITY (EFMHACA)

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1. Introduction

A pharmaceutical product is called “orphan drug” when, although promising or clearly valid from a Scientific and therapeutic point of view, but it is not profit – bearing and therefore, not interesting for the pharmaceutical industry.

Orphan medicines are designated for broad medical conditions where development is possible for many therapeutic indications targeting specific groups of patients. The orphan indication refers to the potential use for diagnosis, prevention or treatment of the designated condition.

What is different about rare disease and orphan drugs?

- Diseases are usually poorly or incompletely understood: Generally, the lower the prevalence, the less well we tend to understand them.
- Small populations: Limited opportunity for study and replication.
- Highly heterogeneous group of disorders: 7,000 different diseases with often high phenotypic diversity within individual disorders.
- Usually little precedent for drug development within individual disorders: often requires more (and more careful) planning than non-Orphan and need a solid scientific base upon which to build an overall program.

2. Orphan medicine designation criteria

Different countries have orphan medicine designation criteria, for instance the European Medicines Agency press office (EMEA) & Japan Minister of Health, Labor and welfare have settled a criteria for designation of pharmaceuticals as orphan medicines.

According to European Medicines Agency press office (EMEA): Medicines intended for the treatment, prevention or diagnosis of rare diseases (defined as those that affect fewer than five in 10,000 persons in the European Union) may be awarded an ‘orphan designation’ by the European Commission on the basis of a positive opinion from the European Medicines Agency’s (EMEA) Committee for Orphan Medicinal Products (COMP).

According to Japan Minister of Health, Labor and welfare, may designate drugs satisfying the following criteria as orphan drugs:

1. **Number of patients:** The number of patients who may use the drug should be less than 50,000 in Japan. The number of patients could be estimated based on the report of Health and Science Research or the data published by reliable scientific societies. The number of patients with a difficult-to-treat disease is sometimes difficult to estimate accurately due to lack of research on the patient population. Therefore, estimates from a variety of statistical data are generally used to indicate that the number of those patients is less than 50,000 in Japan.
2. **Medical Needs:** The drugs should be indicated for the treatment of serious diseases, including difficult-to-treat diseases. In addition, they must be drugs for which there are high medical needs where there is no appropriate alternative drug or treatment and high efficacy or safety is expected compared with existing products
3. **Possibility of development:** There should be a theoretical rationale for the use of the product for the target disease, and the development plan should be appropriate. For example, in the case of application of an orphan drug, the possibility of development should be explained based on existing non-clinical and clinical data in the latter half of the phase I study or in the first half of the phase II study except when the product has already been approved overseas or sufficient clinical study data are available.

The orphan drug designation may be withdrawn if the requirement for the number of patients is not satisfied; the requirement for medical needs is not satisfied because of approval for other similar medical products or other reasons; any false statement is found in the application for designation.

Since Ethiopia has no criteria for orphan designation, the following are lists of medicines are of orphan-designated authorized medicines European Medicine Agency and US Food and Drug Administration based on Community marketing authorization and public assessment report. Therefore this list of medicine could serve as a base line to set criteria for designation of orphan

medicines in Ethiopia and to prepare list of orphan medicines depending on public health assessment report.

3. Orphan-designated List of Drugs for Ethiopia

S.N.	BRAND NAME	GENERIC NAME	DESIGNATED ORPHAN MEDICINE INDICATION	THERAPEUTIC GROUP
1	Vidaza	Azacitidine	Treatment of myelodysplastic syndromes (MDS)	Hematology/Oncology
2	Atriance	Nelarabine	Treatment of acute lymphoblastic leukaemia	Hematology/ Oncology
3	Evoltra	Clofarabine	Treatment of acute lymphoblastic leukaemia	Hematology/ Oncology
4	Sutent	Sunitinib	Treatment of malignant gastrointestinal stromal tumours and treatment of renal cell carcinoma	Hematology/ Oncology
5	Nexavar	Sorafenib tosylate	Treatment of renal cell carcinoma	Oncology/Hematology
6	Sprycel	Dasatinib	Treatment of acute lymphoblastic leukaemia (AL) and treatment of chronic myeloid leukaemia (CML)	Hematology/ Oncology
7	Litak	Cladribine	Treatment of indolent non-Hodgkin's lymphoma and Hair cell leukaemia	Hematology/ Oncology
8	Lysodren	Mitotane	Treatment of adrenal cortical carcinoma	Oncology/Hematology
9	Trisenox	Arsenic trioxide	Treatment of acute promyelocytic leukaemia (APL)	Hematology/ Oncology
10	Iclusig	Ponatinib	Treatment of chronic myeloid leukaemia (CML) and Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL).	Hematology/ Oncology

11	Dacogen	Decitabine	Treatment of myelodysplastic syndromes (MDS)	Hematology/ Oncology
12	Sprycel	Dasatinib	Treatment of Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML); Ph+ acute lymphoblastic leukaemia (ALL).	Hematology/ Oncology
13	Tobi Podhaler	Tobramycin	Suppressive therapy of chronic pulmonary infection due to Pseudomonas aeruginosa	Oncology/Hematology
14	Gliolan	5-aminolevulinic hydrochloride	Intra-operative photodynamic diagnosis of residual glioma	Oncology
15	Yondelis	Ecteinascidin	Treatment of soft tissue sarcoma	Oncology
16	Torisel	Temsirolimus	Treatment of renal cell carcinoma	Oncology
17	Torisel	Temsirolimus	Treatment of advanced renal cell carcinoma (RCC); Treatment of adult patients with relapsed and / or refractory mantle cell lymphoma (MCL)	Oncology
18	Yondelis	Trabectedin	Advanced Ovarian Cell Cancer	Oncology
19	Mepact	Mifamurtide	Treatment of high-grade resectable non-metastatic osteosarcoma	Oncology
20	Savene	Dexrazoxane	Treatment of anthracycline extravasations	Oncology
21	Jakafi/Jakavi	Ruxolitinib	Treatment of primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythaemia-vera myelofibrosis or post-essential-thrombocythaemia myelofibrosis	Hematology
22	Xagrid	Anagrelide hydrochloride	Treatment of essential thrombocythaemia	Hematology
23	Imnovid	Pomalidomide	Treatment of relapsed and refractory multiple myeloma	Hematology

24	Thalidomide	Thalidomide	Treatment of multiple myeloma, Myelofibrosis and Treatment of myelodysplastic syndromes (MDS)	Hematology
25	Kogenate	Antihemophilic factor (recombinant): Factor VIII and Factor IX	Prophylaxis and treatment of bleeding in individuals with hemophilia A or for prophylaxis when surgery is required in individuals with hemophilia A.	Hematology
26	Revlimid	Lenalidomide	Treatment of multiple myeloma, Treatment of myelodysplastic syndromes (MDS), Resistance Lymphoma	Hematology
27	Nplate	Romiplostim	Treatment of immune (idiopathic) thrombocytopenic purpura (ITP) in splenectomised patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).	Hematology
28	Somavert	Pegvisomant	Treatment of acromegaly	Endocrinology and metabolism
29	Signifor	Pasireotide	Treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed	Endocrinology and metabolism
30	Soliris	Eculizumab	Treatment of paroxysmal nocturnal haemoglobinuria (PNH); atypical haemolytic uraemic syndrome (aHUS).	Endocrinology and metabolism
31	Cabergolin	CABERGOLIN	Dopamine agonist for prolactinone	Endocrinology and metabolism
32	Thelin	Sitaxentan sodium	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	Cardiovascular and Respiratory

34	Tracleer	Bosentan	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	Cardiovascular and respiratory
35	Ventavis	Iloprost	Treatment of primary and of the following forms of secondary pulmonary hypertension: connective tissue disease pulmonary hypertension, drug-induced pulmonary hypertension, portopulmonary hypertension, pulmonary hypertension associated with congenital heart disease and chronic thromboembolic pulmonary hypertension	Cardiovascular and respiratory
36	Firazyr	Icatibant acetate	Symptomatic treatment of acute attacks of hereditary angioedema (HAE)	Cardiovascular
37	Volibris	Ambrisentan	Treatment of pulmonary arterial hypertension & chronic thromboembolic pulmonary hypertension.	Cardiovascular and Respiratory
38	Esbriet	Pirfenidone	Treatment of mild to moderate Idiopathic Pulmonary Fibrosis (IPF)	Respiratory
39	Diacomit	Stiripentol	Treatment of severe myoclonic epilepsy in infancy	Nervous system
40	Prialt	Ziconotide	Treatment of chronic pain requiring intraspinal analgesia	Nervous system
41	Onsenal	Celecoxib	Treatment of familial adenomatous polyposis (FAP)	Gastro-enterology
42	Revestive	Teduglutide	Treatment of adult patients with Short Bowel Syndrome	Gastro-enterology
43	Betaseron	Interferon beta-1b	Treatment of multiple sclerosis.	Neurology

44	Procysbi	Mercaptamine bitartrate	Treatment of proven nephropathic cystinosis.	Nephrology

4. Successful classification of Rare Disease and Orphan Drugs

US Food and Drug Administration proposed some prerequisite for successful classification of Rare Disease and Orphan Drugs for the year 2013-2018: this are:

- Increased Rare Diseases Staffing CDER & CBER
- "Breakthrough" for serious diseases and unmet needs
- Increased opportunities for interaction between FDA and patients, e.g.: patient-focused drug development and benefit-risk assessment framework
- Staff training
- Regulatory science development
- Rare disease evaluation tool

This experience could be shared depending on our situation and might be helpful to develop orphan drug designation criteria and list of orphan drug.

5. Conclusion

- Ethiopian Ministry of health should develop criteria for designation of orphan drug depending on the public health assessment result.
- Different countries experience for successful classification of orphan medicines could be taken as a bench mark to develop Ethiopian orphan medicine list.

6. References:

1. Journal of Palliative medicine. Volume 7 Number 1 2004.

2. List of orphan-designated authorized medicines; European Medicines Agency, London, 6 November 2008.
3. Lists of medicinal Products for Rare diseases in Europe; Orphan Drugs Collection, January 2014.
4. Orphan Drug Designations and Approvals List as of 03- 03-2014 Governs April 1, 2014-Jun 30, 2014.
5. Orphan Medicine Designation Criteria in Japan.
6. Rare diseases, Orphan drugs and Innovation: Center for Drug Evaluation and Research US Food and Drug Administration Perspective.