

Medicine essays example

[Health & Medicine](#), [Drugs](#)



Orphan Drug

Introduction

The main purpose for the enactment of the U. S. Orphan Drug Act (ODA) of 1983 is to conduct a research on some of the rare diseases whose medical needs remain to be unresolved.

The law has given incentives to various sponsors who have tried to develop therapies for some of the rare medical conditions that can affect at least 200, 000 individuals on a yearly basis (Premiere Research 1). For this study, the objective is to create a regulatory strategy or path for Orphan Drug development, particularly on the oral iron chelator, one of the subsets of thalassemia or any other subsets of anemia.

Based on the study of Algren, acute iron poisoning and chronic iron overload can cause global morbidity and mortality (Algren 2). Hence, a treatment should be formulated to cure acute iron poisoning and chronic iron overload. Although such treatment is difficult to formulate and can be very challenging especially to care providers, it is highly recommended to create a cure for chronic iron overload in order to solve the management dilemmas of care provided. The oral iron supplements are generally prescribed by physicians to patients suffering from iron deficiency anemia (Algren 2). At present, access to iron supplements and iron-containing multivitamins is available in drug stores to accommodate the needs of adults and children. Due to the accessibility of these iron supplements and multi-vitamins containing iron, there are instances when patients suffer from overdose of iron. Thus, the approach for the treatment of acute iron toxicity must include adequate supportive care, optimize the hemodynamic status and antidotal therapy

along with IV deferoxamine, provided that the same was prescribed by a physician (Algren 2). One of the ways to cure overdose of iron is by an acute ingestion gastrointestinal (GI) decontamination, which shows to possess beneficial effects according to doctors (Algren 2).

The condition of chronic iron overload in relation to red cell disorders shall include sickle cell anemia and thalassemia, which can affect a number of individuals. Since the human body is incapable to produce enough iron, there are persons who are prone to sickle cell anemia and thalassemia, and iron deficiency. To be able to treat these patients who are in need of several iron transfusions of iron, there is a possibility that iron may accumulate and deposited into the various organ systems of a patient. In fact, some of the long term effects of chronic iron overload may result to multiple organ dysfunctions that can affect the failure or malfunction of the liver, endocrine and the heart, liver, and endocrine (Algren 2). The purpose of iron chelation is to prevent the possibility of organ failure and to lower the incidents of mortality.

Regulatory strategy or path for Orphan Drug development for Oral Iron Chelator, Thalassemia or other subsets of anemia An “ orphan drug” based on the definition of United States, Orphan Drug Act of January 1983 shall refer to those products that have been formulated and intended to provide treatment for rare types of diseases. These products have been developed for those patients suffering from very serious diseases that are left with no treatment, since no cure is currently available in the market (Premiere Research 2).

For this study, the diseases that will be cured by the orphan drug shall be

used for oral iron chelator, thalassemia or other subsets of anemia. Although only a few people are affected by these rare diseases which may start at birth, or infancy, it is imperative for the government to develop and create a cure for these rare diseases (Sharma, et al. 291). Studies revealed that some products have been withdrawn from the market due to economic or therapeutic reasons. Some of these drugs were withdrawn for a multitude of reasons, such as “thalidomide”, which had been used as a hypnotic drug, but was banned in the market due to its high teratogenic risk and it triggers fetal malformations (Sharma, et al. 291).

These diseases such as “thalassemia”, anemia and over dose of iron will require oral iron chelator. However, for the past years, there had been no satisfactory treatment that can be accessed in the present market. Thus, the drug development and marketing of Orphan Drug to be used for the three enumerated diseases is not expected to be recovered right away. However, there are four key incentives provided under the ODA which will include seven (7) years of market exclusivity, protocol assistance, tax credits of up to 50 percent, FDA fee waivers and research grants (Premiere Research 2). To be able to receive such benefits, the law requires that a sponsor to file an application for orphan drug designation, and to be able to demonstrate the medical plausibility for the expected benefit of the drug formulation to cure the rare disease.

U. S. Orphan Drug Act

After the ODA was enacted into law, there were at least 360 orphan drugs have been approved and about 2, 500 compounds which have been given orphan designations (Premiere Research 2). This particular study will focus

on finding a drug or cure for oral iron chelator, thalassemia or any other subsets of anemia, which will then be submitted for approval to the U. S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

As part of the application, there should be a single annual report that will include separate agency reports providing information to agencies that are in charge with the development of orphan medical products. Along with the application, is the review and status of ongoing clinical studies that give a description of the investigation plan for the succeeding year, and the projection of current problems in the process that can cause an impact in its designation as an orphan drug product. The annual report must be submitted to all regulatory agencies and shall only be made applicable to sponsors after having achieved an orphan designation status product from the two agencies, namely, the U. S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) (Sharma, et al. 296).

Thalassemia major (TM) without iron chelation therapy and iron-mediated free radical damage can result to liver, endocrine, and myocardial toxicities (Uygun and Kurtoglu 50). Thus, deferoxamine has been the widely-recognized and accepted standard therapeutic option for iron chelation therapy (Uygun and Kurtoglu 50). However, the use iron chelation therapy has been troublesome for patients that it has led to suboptimal patient compliance. Deferoxamine has been accepted as the universal standard as the therapeutic option for iron chelation therapy. However, since the procedure is very troublesome and causes the suboptimal patient compliance due to the discomfort, there has to be a new regimen created in

order to lessen the burden of the patients (Uygun and Kurtoglu 50). To be able to maximize the effectiveness of iron chelation therapy, the important developments of the procedure include oral iron chelators deferiprone and deferasirox in order to improve the regimen (Uygun and Kurtoglu 50). These two oral drugs are effective but both can cause different pharmacokinetics and side-effects (Uygun and Kurtoglu 50).

Treatment of the condition associated with the treatment of the disease: blood transfusion

The process of splenectomy will be performed for the patients with deteriorating hypersplenism or when the annual packed red blood cells transfusion requirements have increased above 200 ml/kg on a yearly basis. Based on the study of Uygun and Kurtoglu, the patients who participated in their study had received one dose of deferiprone, deferasirox, and combination therapy involving deferiprone and deferoxamine that were made in the following doses or quantities of 40–75, 10–40, and 50–75 mg/kg/day + 40–50 mg/kg, for a period of three to five days in one whole week (Uygun and Kurtoglu 51). The results of the patients were taken from the previous medical records that contained demographic data, the percentage or dosage of chelators, hepatic enzymes, levels of ferritin, serum, and the time and cause why the drug was discontinued (Uygun and Kurtoglu 51).

A new chemical entity/drug to treat the condition

Based on recent studies, there are current complications that are connected with iron overload in thalassemia major or TM. Thus, patients who suffer from TM have to endure the long-term iron chelation therapy since it is a mandatory regimen to ensure their health. At present, the rate of use of oral

chelator had doubled due to the compliance issues for deferoxamine (Uygun and Kurtoglu 50). There had been many identified advantages and disadvantages of oral chelators, but there is very limited data available for comparative studies.

The retrospective evaluation of TM patients who had been using oral chelators showed that oral chelators are effective to lower the iron overload that will apply to ferritin level and to the cardiac T2* value. Due to the side effects the chelators, several physicians discontinued the procedure due to the high rates and recommended that TM patients who use oral chelators should take the necessary precautions when using the procedure. The high rate of side effects and drug discontinuation of oral chelators suggests that spleen may be affected on the pharmacokinetics of serum ferritin levels due to the inflammatory processes (Uygun and Kurtoglu 51). The results will show that the spleen is the second largest organ in the body after the liver being the first. Since the spleen stores the most iron aggregates in the body, it is predicted that splenectomy may lead to a diverse effect on iron balance and influence the pharmacokinetic profiles of chelators among the patients. Thus, after the study of simple use of oral chelators, it can be concluded that is the appropriate choice in iron overload. However, due to the serious side effects it can bring, the use of blood transfusion needs to be further analyzed. The side effects of oral chelators and the impact of splenectomy on the patients are the considerations to make before the drug is sent for approval (Uygun and Kurtoglu 51).

Developing the New Chemical Entity (NCE) involves phase advanced development

The drug that will be used for prevent iron overdose is deferiprone.

Deferiprone is available as a 500mg tablet and an oral solution that should be administered for 100mg/ 0. 4ml) (Tamilselvan, et al. 1132). Many doctors prescribe 75 mg/kg per day which should be divided into three doses. The deferiprone monotherapy is the recent therapy that was introduced and requires further studies. In the recent study of Maggio and colleagues made an assessment on the efficiency of deferiprone as opposed to combination therapy in a randomized trial that was participated by 213 thalassemia patients, and majority of them were at least 23 years (Tamilselvan, et al. 1132). These patients had been studied for the past five (5) years. The results showed that the combination of deferiprone with subcutaneous deferoxamine carried more effective results if it contained lower serum ferritin (Tamilselvan, et al. 1132).

Unlike the other drug, deferasirox which is a tablet that can be dissolved in water or juice and taken on an empty stomach, the studies will show that the periodic serum ferritin has several adverse effects, particularly agranulocytosis (Tamilselvan, et al. 1133).

During blood transfusion, monitoring of white blood cell counts is recommended in order to avoid deferiprone in patients with myeloproliferative disorders. Other side effects that should be avoided are gastrointestinal symptoms that may show signs of nausea, vomiting, and abdominal pain, as shown in at least 33% of patients (Tamilselvan, et al. 1132). However, these side effects are common and the doctors have not prescribed discontinued use of the drug (Tamilselvan, et al. 1132). Other

predicted side effects include elevations of liver transaminases during the deferiprone treatment. Some studies suggest that deferiprone was associated with progressive liver fibrosis, but this findings are still to be confirmed. ROW US, Europe, U. K., localities and related local regulatory requirements

In the Europe Union, the Orphan Drug Regulation that was enacted in the year 2000 was allowed to find a cure for a disease or disorder that can affect 5 in 10, 000 citizens, to qualify as “ rare” on the basis of the definition provided under the law (Sharma, et al. 291). Although it may appear to be a small number, such definition of rare diseases affects as much as 30 million of European citizens. Based on the study of the EURORDIS or the European Organization for Rare Diseases, the number of rare diseases numbers of 6, 000 to 8, 000, have identified genetic conditions (Sharma, et al. 293). The medical literature has provided a description of five new rare conditions per week and at least 25 to 30 million persons had been reported to be affected by these rare diseases in Europe.

In U. K., there is no orphan drug policy in place. However, there are government research funds which had been allocated for the development of drugs for rare diseases. It will be difficult to pass an orphan drug policy since there are some practitioners who have the ability to procure unapproved drugs which may be given to individual patients based on clinical judgment (Sharma, et al. 294). Although there had been application for orphan drug that had been submitted under exceptional circumstances, there is insufficient information on the safety, quality, and efficacy of the product. Thus, it is unethical to collect such information about the components of the

orphan drug. Thus, the manufacturers should provide a report in detail as part of the post-marketing surveillance to study the particular drug. At the same time, there should be a provision that will allow that abating fees for new drug application that will involve small market drugs under cost recovery (Sharma, et al. 294).

Time of IND, Orphan Drug Designation application

The sponsor should submit the initial pediatric study plan (PSP) before the date on which the sponsor submits the required to make an assessments, which should be later than 60 calendar days after the date of the end-of-phase 2 meeting. If the by end-of-phase 2 meeting deadline is not observed, the sponsor should submit the initial PSP before the initiation of any phase 3 studies, or a combination of the phase 2 and phase 3 study, of the drug which is the main subject of the initial PSP. In the event that phase 3 study or a combined phase 2 and phase 3 study had not been conducted, the sponsor should submit the initial PSP not later than 210 calendar days before a marketing application or supplement is submitted. At the same time, the sponsor must submit the initial PSP for investigational new drug (IND) application of the proposed drug.

Orphan Drug Treatment

There are many patients all over the world that have encountered red cell disorders and myelodysplasia. Thus, there is a possibility that after undergoing through series of the blood transfusion, it may result to chronic iron overload. The morbidity and mortality is closely associated with iron overload (Tamilselvan, et al. 1132). Although, there is very little information

about oral iron chelators being studied among humans, the acute iron poisoning is not highly recommended. At present, the deferoxamine was the only iron chelator that is provided in the market. Since deferoxamine therapy is time-consuming, troublesome and carries undesirable adverse effects, many patients have failed to comply with the regimen. For the last two decades, there had been significant evidence that promoted the use of the oral iron chelators deferiprone and deferasirox (Tamilselvan, et al. 1132). Thus, for future research and long-term follow studies, oral chelators must be analyzed on detail. The proposed that defriprone should be the main choice for patients using oral chelator since it is closely associated to combat chronic iron overload (Tamilselvan, et al. 1132).

Designation application and approved Pediatric plan

The sponsor must be able to submit a marketing application for a drug or biological product that includes a new active ingredient, new dosage form, new dosing regimen, or new administration request. These data should be submitted before an amendment is made based on the agreement made upon initial PSP. Any changes to the submission dates, planned requests for a deferral should be specified in the application.

Works Cited:

Algren, D. Adam. “ Review of Oral Iron Chelators for the Treatment of Iron Overload in Pediatric Patients.” Web. Retrieved on 13 December 2014.

Haberle, Johannes, and Shawn E. McCandless. “ Orphan Drugs In Development For Urea Cycle

Disorders: Current Perspectives.” Orphan Drugs: Research & Reviews 4. (2014): 63-

70. Academic Search Complete. Web. 13 Dec. 2014.

Premiere Research. “ The Science of Hope: The need, the challenges and three proven strategies for successful orphan drug development”. Web. Retrieved on 13 December 2014.

Sharma, Aarti, et al. “ Orphan Drug: Development Trends And Strategies.” Journal of Pharmacy & Bioallied Sciences 2. 4 (2010): 290-299. Academic Search Complete. Web. 13 Dec. 2014.

Sprecher, Franziska. “ Orphan Drugs and Paediatric Medicinal Products.” Pharmaceuticals Policy & Law 15. 3/4 (2013): 173-194.

Tamilselvan, T., and Abhay Dharamsi. “ Management Of Iron Overload In B-Thalassemia Major With Oral Iron Chelator: A Review.” Journal of Pharmacy Research 5. 2 (2012): 1132-1135.

Uygun, Vedat, and Erdal Kurtoglu. “ Iron-Chelation Therapy with Oral Chelators In Patients with Thalassemia Major.” Hematology 18. 1 (2013): 50-55.