Case Study

EpiVue® Sickle Cell Disease

Epidemiology and Patient Population Analysis

How REACH Market Research combined systematic literature review, secondary and primary market research, and rare disease expertise to size the G6 sickle cell disease (SCD) patient population and uncover market-relevant population dynamics.

Overview

Company X has several clinical programs for rare hematology conditions and wanted to better understand the epidemiology of SCD. Despite having demonstrated clinical proof of concept in SCD, company X had limited understanding of how many people are affected by SCD across their target geographies. The new product planning team requested an **EpiVue®** epidemiology analysis for SCD to understand not only disease prevalence but to get a better handle on key population dynamics to inform their internal market sizing efforts.

Approach

Comprehensive review of the published literature

Our team reviewed over three dozen publications evaluating the merits of each resource based on sample size, study design and methodology, and evidence of sample or study bias.

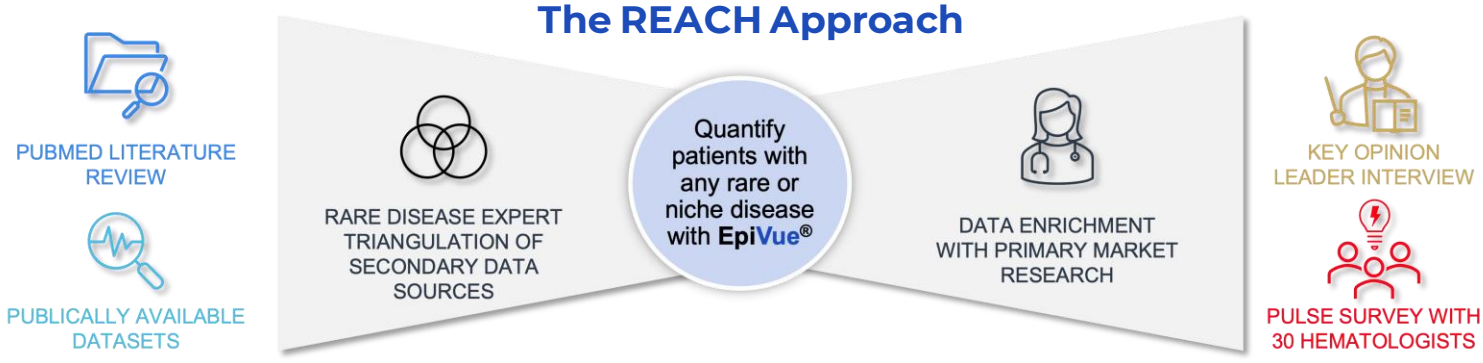
Primary market research with hematologists

We interviewed three and surveyed 30 U.S. hematologists to better understand drug-treatment rates, representation of key subpopulations, and other key population dynamics that influence the market.

Analyzed and integrated and multisource data

We reconciled different prevalence data sources to estimate the population size with the strongest available evidence and combined that with registry data and physician insights on drug-treatment rates and market segmentation.

The REACH Approach



Results

See the results on the following pages

Sickle Cell Disease EPIDEMIOLOGY

United States and EU5

DISEASE OVERVIEW

Sickle cell disease (SCD) is an inherited genetic disorder that affects red blood cell (RBC) shape, function, and lifespan. The underlying cause of the disease is a single mutation in the hemoglobin gene (*HBB)* that leads to the production of abnormal hemoglobin (HbS). HbS carries less oxygen than normal hemoglobin and forms long polymers that cause RBCs to misshapen. These deformed RBCs stick together, block blood flow to major organs, and carry less oxygen than healthy RBCs. As a result, SCD patients experience chronic oxygen depravation of end organs that only worsens with time causing organ failure and death. These patients live in chronic pain, with sporadic episodes of severe, debilitating pain attacks among other complications (e.g., infection, anemia).

DISEASE DEFINITION

For this analysis, we define cases of SCD as individuals with one of the following genotypes– Hb SS, SC, SD, SE, Sβ0 thalassemia, or Sβ+ thalassemia.

Figure 1. G6 diagnosed prevalent cases of sickle cell disease by region

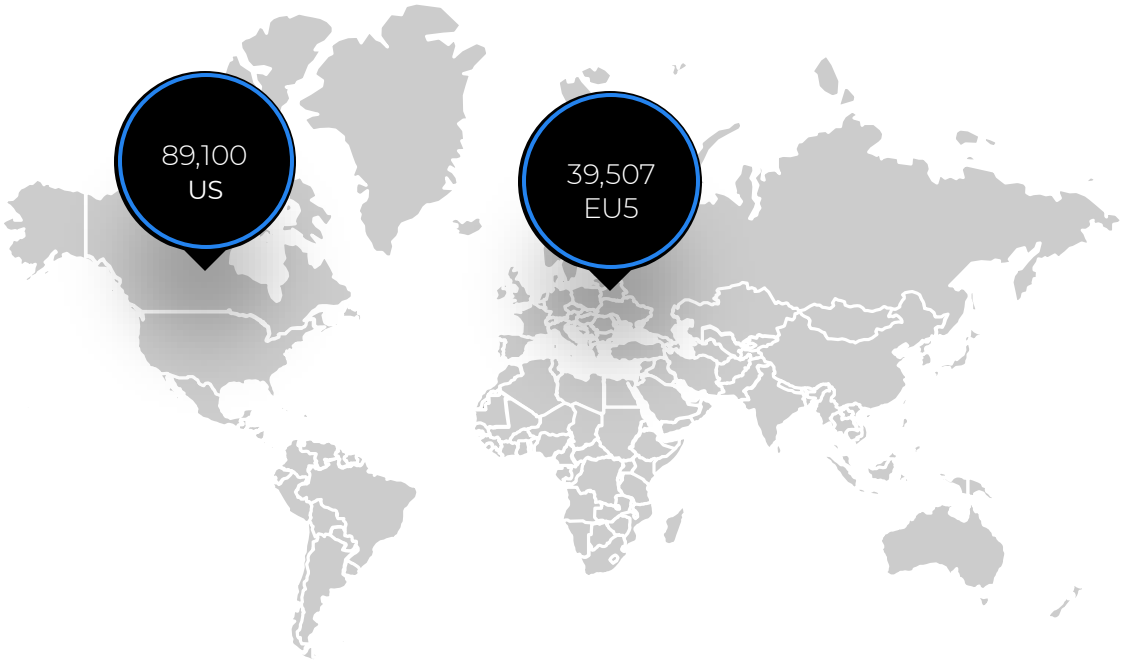


Table 1. Diagnosed prevalent and drug-treated patients in the G6[1]

	US	France	UK	Germany	Italy	Spain	Total
Diagnosed prevalence (per 100k)	27	29.7	22	3.6	2.11	1.76	**n/a**
Diagnosed prevalent cases	89,100	19,917	14,489	3,000	1,275	826	**128,607**
Drug-treated rate	56%	56%	56%	56%	56%	56%	**56%**
Drug-treated patients	49,896	11,154	8,114	1,680	714	463	**72,021**

1. See appendix for epidemiology references and methodology

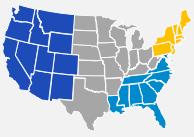
KEY POPULATION DYNAMICS – SICKLE CELL DISEASE

Diagnosis. Nearly all SCD patients in the G6 are diagnosed at birth thanks to national newborn screening programs in all 50 U.S. states as well as Germany, France, Spain, and the United Kingdom; Italy, however does not have NBS for SCD although calls for such screening have been made by the Italian Association of Pediatric Hematology Oncology and the Italian Society of Thalassemia and Hemoglobinopathies.

Subtypes. There are seven subtypes of SCD; two account for most patients. HbSS is the most severe and most prevalent form of the disease; patients carry two mutated *HBB* genes. HbSC patients carry one abnormal and one healthy *HBB* gene and have a mild form of SCD. Other forms of SCD including HbS beta thalassemia, HbSD, HbSE, an HbSO.

SCD Subtype[3]	% of SCD Patients
HbSS	75%
HbSC	18%

Patient phenotypes. The SCD population can be segmented by Hb levels or by the frequency of annual VOCs (pain crises). The predominant patient phenotype – low Hb level or pain crises – is a key determinant in treatment selection (Figure 2.1 and 2.2).



U.S. geographic distribution. In the United states, 85% of SCD patients live in 18 states:[4]

- **Northeast:** NY, NJ, PA
- **Central:** TX, MI, IL, OH
- **South**: FL, GA, NC, SC, AL, TN, VA, MS, LA, MA
- **West**: CA

1. See appendix on methodology
2. REACH primary market research; see appendix on methodology
3. Saraf SL, Molokie RE, Nouraie M, et al. Differences in the clinical and genotypic presentation of sickle cell disease around the world. Paediatr Respir Rev. 2014;15(1):4-12.
4. Wilson-Frederick SM, Hulihan M, Anderson KK. Prevalence of Sickle Cell Disease among Medicaid Beneficiaries in 2012. CMS Office of Minority Health Data Highlight, No. 16. Baltimore, MD. 2019.

Distinct phenotypes demarcate two market-relevant subpopulations

A patient's predominant phenotype (high frequency of VOCs versus low hemoglobin levels) has added a key decision point in the treatment algorithm for SCD. This change is driven by the recent availability of Novartis's Adakveo (crizanlizumab) and Global Blood Therapeutics' Oxbryta (voxelotor). Adakveo has shown its effectiveness at reducing VOCs while Oxbryta has demonstrated efficacy for increasing hemoglobin levels in SCD patients. The availability of Adakveo and Oxbryta not only give physicians much needed treatment options, but they have also split the market into two segments based on the predominant patient phenotype.

The clinical manifestations of SCD occur along a spectrum. The frequency of VOCs is a clinical manifestation that is highly variable with nearly one-third of patients being VOC-free or having only one crisis a year. Indeed, surveyed U.S. hematologists (adult and pediatric) report that the largest share (40%) of their SCD patients have two to five VOCs a year. With regards to how the SCD patient population segments based on hemoglobin levels, patients are evenly split between having hemoglobin levels that are in the range of 8.5-10.5g/dL and less than 8.5g/dL.

Figure 2. SCD Population Segmented Annual VOC Frequency[1]

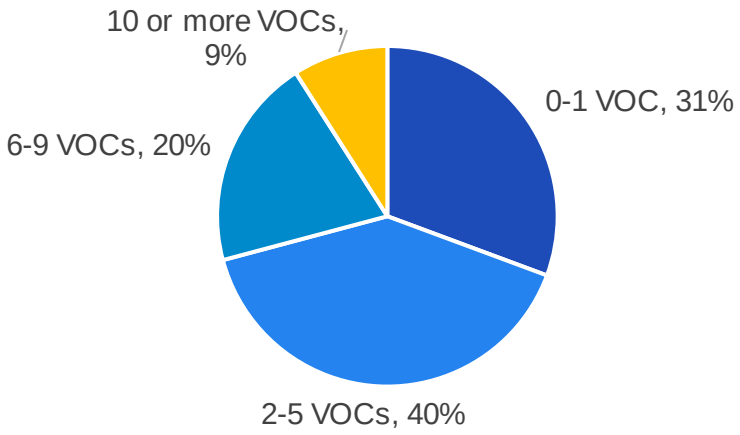
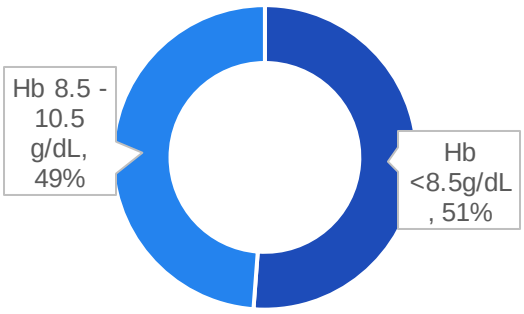


Table 2. Hb levels in healthy and SCD adults[2]

Patient type	Hb level
Health adult, male	13.8-17.2 g/dL
Healthy adult, female	12.1 to 15.1 g/dL
SCD, HbSS	8.5 g/dL (mean)
SCD, HbSC	11 g/dL (mean)

Figure 3. SCD Population Segmented by Hb Levels[1]



1. REACH primary market research; see appendix on methodology
2. Piel FB, Steinberg MH, Rees DC. Sickle cell disease. *N Engl J Med.* 2017;376(16):1561-1573.