

REGULATORY AND MARKET ACCESS LANDSCAPE FOR CYSTIC FIBROSIS

PRO84

Jaiswal H¹; Rubinstein J²; Zacarelli C²; Guill EW²

¹ Decision Resources Group, Gurugram, Haryana, HR, India
² Context Matters (A Decision Resources Group Company), New York, NY, USA

International Society for Pharmacoeconomics and Outcomes Research (ISPOR), 22nd Annual European Congress, 2 – 6 November 2019, Copenhagen, Denmark

BACKGROUND

Cystic fibrosis is a rare, inherited, and life-threatening disorder that requires treatment to improve patients’ quality of life (QoL). Although most treatments for cystic fibrosis are symptomatic, some newer drugs are aimed at correcting the protein irregularities that cause the disease. These drugs are classified as cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies. This poster captures insights around the regulatory and reimbursement decisions for drugs used for the treatment of cystic fibrosis.

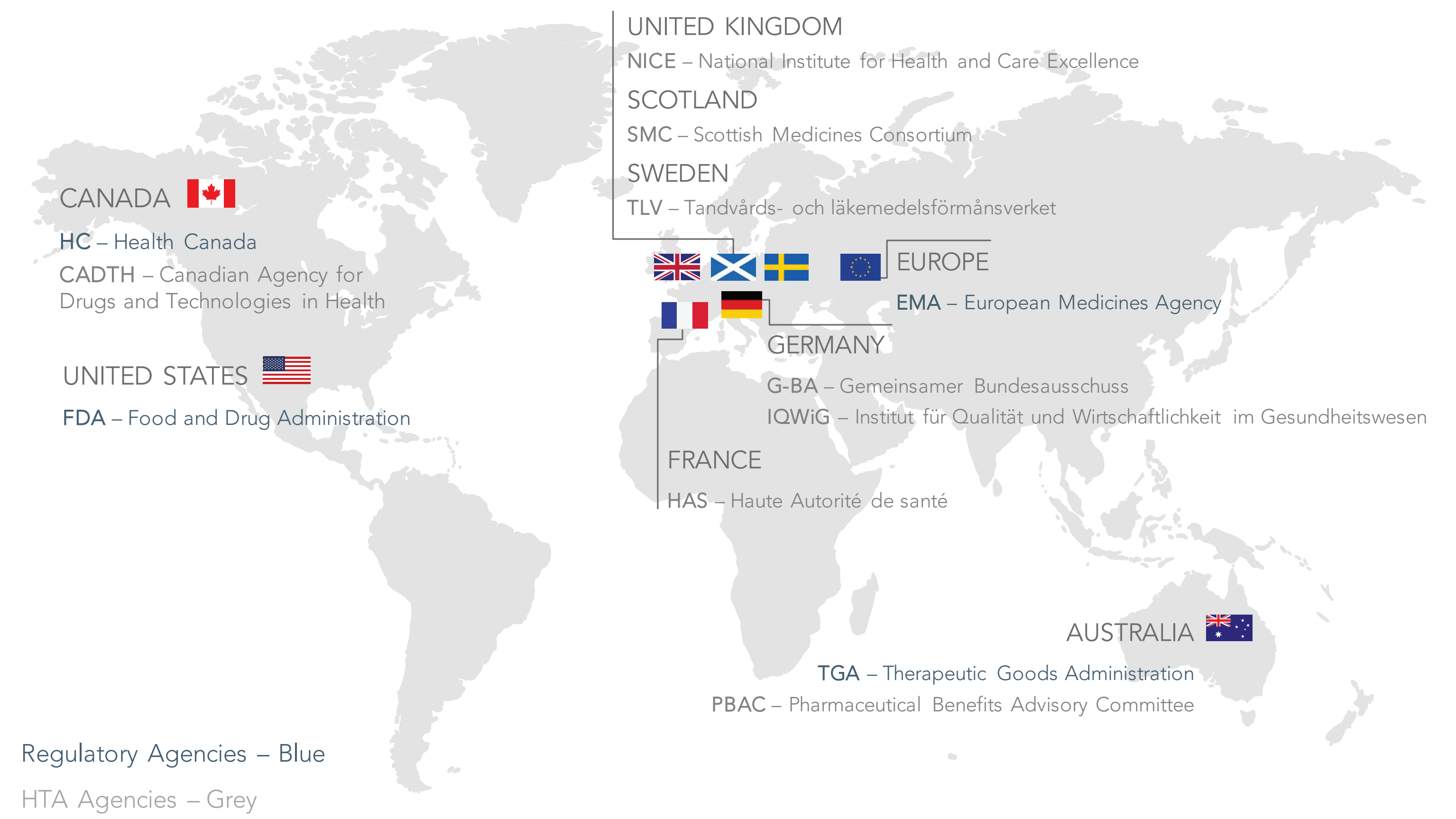
OBJECTIVE

To track the orphan drug status, marketing authorization, and market access of drug products available for the treatment of cystic fibrosis.

METHODS

Data on the orphan drug status and regulatory drug approvals for nine brands were collected from 1993 to August 2019 from the Food and Drug Administration (FDA), European Medicines Agency (EMA), Health Canada (HC), and Therapeutic Goods Administration (TGA) websites. Data were collected for the following drugs: aztreonam, dornase alfa, ivacaftor, lumacaftor-ivacaftor, levofloxacin, tobramycin (two brands), tezacaftor-ivacaftor, and tezacaftor-ivacaftor + ivacaftor. Health technology assessments (HTAs) for eight drugs from CADTH (Canada), G-BA and IQWiG (Germany), HAS (France), NICE (UK), PBAC (Australia), SMC (Scotland), and TLV (Sweden) were evaluated. Data were collected for the following drugs: aztreonam, dornase alfa, ivacaftor, lumacaftor-ivacaftor, levofloxacin, tobramycin, tezacaftor-ivacaftor, and tezacaftor-ivacaftor + ivacaftor.

FIGURE 1: REGULATORY AND HTA AGENCIES COVERED



RESULTS

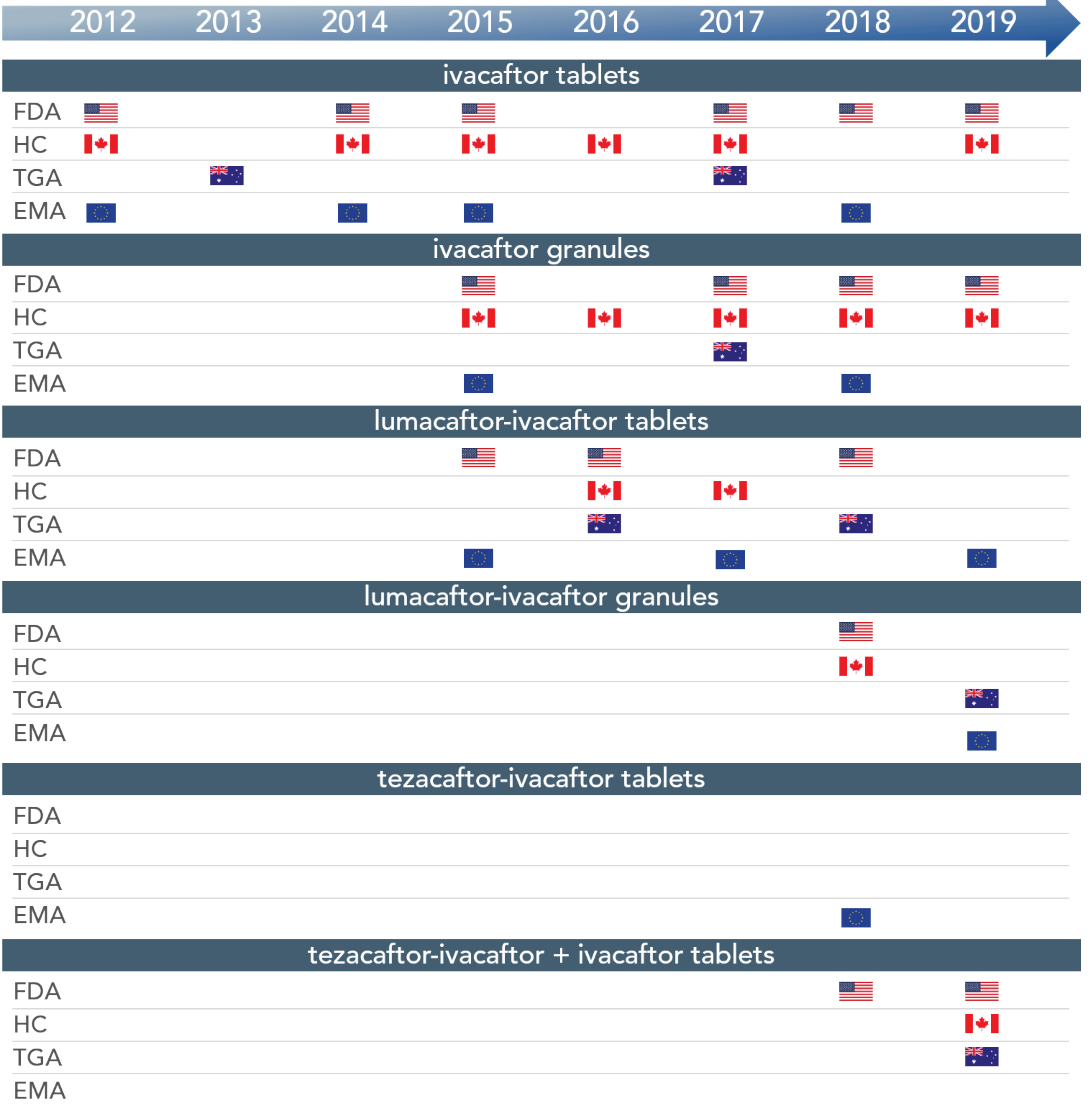
Regulatory Approval: The first drug to treat cystic fibrosis was approved in 1993. This drug improved lung function and reduced the risk of respiratory infections but did not treat the underlying disease. The first disease-modifying drug, ivacaftor, was approved in 2012 and lumacaftor-ivacaftor, tezacaftor-ivacaftor, and tezacaftor-ivacaftor + ivacaftor were approved in the next several years.

FIGURE 2: REGULATORY APPROVAL DATES AND ORPHAN DRUG STATUS

DRUG NAME	REGULATORY APPROVAL DATES			
	FDA	EMA	HC ¹	TGA
aztreonam	22/02/2010	21/09/2009	11/09/2009	02/02/2010
dornase alfa	30/12/1993	10/03/1994 ²	08/09/1994	29/11/1994
ivacaftor	31/01/2012	22/07/2012	26/11/2012	29/11/2013
lumacaftor-ivacaftor	02/07/2015	18/11/2015 ³	26/01/2016	08/03/2016
levofloxacin	N/A	25/03/2015 ⁴	09/06/2015	N/A
tobramycin-1*	22/12/1997	N/A	16/02/1999	N/A
tobramycin-2*	22/03/2013	20/07/2011	01/04/2011	26/10/2012
tezacaftor-ivacaftor	N/A	31/10/2018	N/A	N/A
tezacaftor-ivacaftor + ivacaftor	12/02/2018	N/A	27/06/2019	05/03/2019

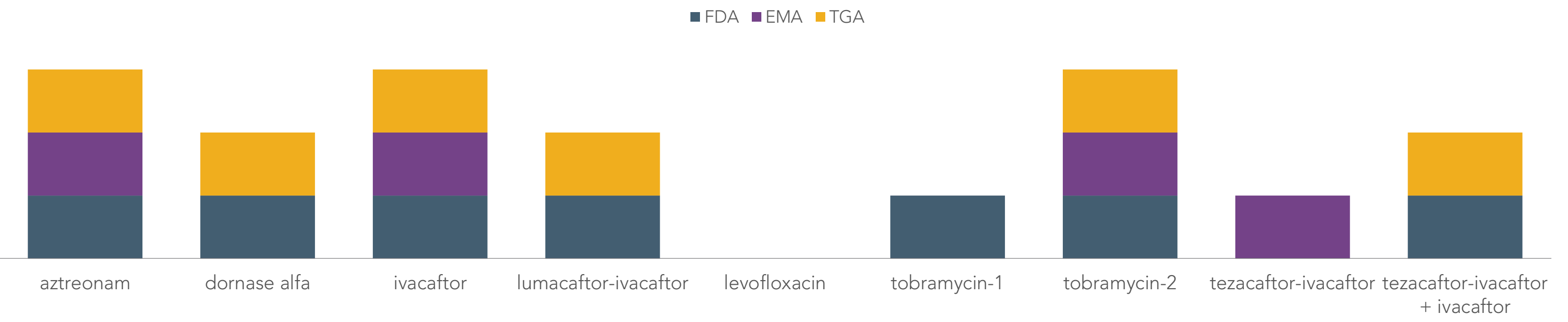
N/A – Not available
Blue Text – Orphan drug
Red Text – Not an orphan drug
*There are two brand names for the same generic drug (tobramycin).
¹ To communicate when HC approves a drug that is considered to be an orphan drug by either the United States FDA or EMA, HC identifies them in its New Drug Authorizations Highlights report. HC does not provide clear information on orphan drug designation for the drugs mentioned in this table.
² This drug was approved through the national procedure. The data captured here are only for France.
³ This product is no longer an orphan medicine. It was originally designated an orphan medicine on 20 September 2010 and withdrawn from the Community register of orphan medicinal products in October 2015 upon request of the marketing authorisation holder.
⁴ This product is no longer an orphan medicine. It was originally designated an orphan medicine on 23 September 2009 and withdrawn from the Community register of orphan medicinal products in February 2015 upon request of the marketing authorisation holder.

FIGURE 3: REGULATORY TIMELINES FOR CFTR MODULATOR THERAPIES



First approval and label updates by regulatory agencies are represented by flags.
Sources: The FDA, HC, TGA, and EMA websites.

FIGURE 4: ORPHAN DRUG STATUS ACROSS THE FDA, EMA, AND TGA



Each block represents the orphan drug designation for the color-coded agency (FDA/EMA/TGA).
Sources: The FDA, EMA, and TGA websites.

Market Access: The base-case incremental cost-effectiveness ratio (ICER) of £214,772 (lumacaftor-ivacaftor), £473,071 (ivacaftor), £421,173 (tezacaftor-ivacaftor; homozygous population), £360,499 (tezacaftor-ivacaftor; heterozygous population), or > \$200,000 (aztreonam) per quality-adjusted life year (QALY) resulted in Do not recommend decisions. Current market access shows that G-BA (n = 3/3), HAS (n = 4/5), and TLV (n = 4/5) recommend more drugs without restrictions for the treatment of cystic fibrosis than CADTH (n = 0/6), NICE (n = 0/2), PBAC (n = 2/6), and SMC (n = 1/6). IQWiG provides non-binding recommendations to G-BA. CADTH, NICE, PBAC, and SMC tend to apply restrictions or give Do not recommend decisions mainly due to uncertain efficacy/effectiveness or uncertain/low cost-effectiveness.

FIGURE 5: CURRENT MARKET ACCESS

aztreonam			dornase alfa			ivacaftor			levofloxacin		
Agency	Date	Decision	Agency	Date	Decision	Agency	Date	Decision	Agency	Date	Decision
SMC	12/2014	Recommend with restrictions	SMC	-	-	SMC	11/2016	Do not recommend	SMC	08/2016	Recommend with restrictions
PBAC	11/2010	Do not recommend	PBAC	07/2009	Recommend	PBAC	03/2019	Recommend	PBAC	-	-
G-BA	-	-	G-BA	-	-	G-BA	06/2016	Recommend	G-BA	-	-
HAS	04/2018	Recommend	HAS	02/2011	Recommend	HAS	07/2019	Recommend	HAS	-	-
CADTH	07/2011	Recommend	CADTH	06/2013	No decision	CADTH	11/2015	Recommend	CADTH	11/2016	Recommend
NICE	-	-	NICE	-	-	NICE	-	-	NICE	-	-
TLV	03/2012	Recommend	TLV	-	-	TLV	-	-	TLV	05/2016	Recommend
IQWiG	-	-	IQWiG	-	-	IQWiG	03/2016	No decision	IQWiG	-	-

lumacaftor-ivacaftor			tezacaftor-ivacaftor			tezacaftor-ivacaftor + ivacaftor			tobramycin		
Agency	Date	Decision	Agency	Date	Decision	Agency	Date	Decision	Agency	Date	Decision
SMC	07/2019	Do not recommend	SMC	07/2019	Do not recommend	SMC	-	-	SMC	05/2012	Recommend
PBAC	07/2018	Recommend with restrictions	PBAC	-	-	PBAC	03/2019	Recommend	PBAC	11/2013	Recommend with restrictions
G-BA	08/2019	Recommend	G-BA	05/2019	Recommend	G-BA	-	-	G-BA	-	-
HAS	12/2018	Recommend	HAS	-	-	HAS	-	-	HAS	11/2011	Recommend
CADTH	09/2018	Do not recommend	CADTH	-	-	CADTH	-	-	CADTH	07/2013	No decision
NICE	07/2016	Do not recommend	NICE	-	-	NICE	-	-	NICE	03/2013	Recommend with restrictions
TLV	03/2019	Recommend	TLV	05/2019	Do not recommend	TLV	-	-	TLV	12/2011	Recommend
IQWiG	05/2019	No decision	IQWiG	-	-	IQWiG	-	-	IQWiG	-	-

CONCLUSION

Novel CFTR modulator therapies have been approved by the FDA, EMA, HC, and TGA in recent years, with the goal of improving patients’ life expectancy and QoL. High base-case ICERs, high costs, uncertain or lower cost-effectiveness, and/or uncertain efficacy/effectiveness are obstacles in the path to gaining market access for CF therapies, even when the drugs treat the underlying disease.