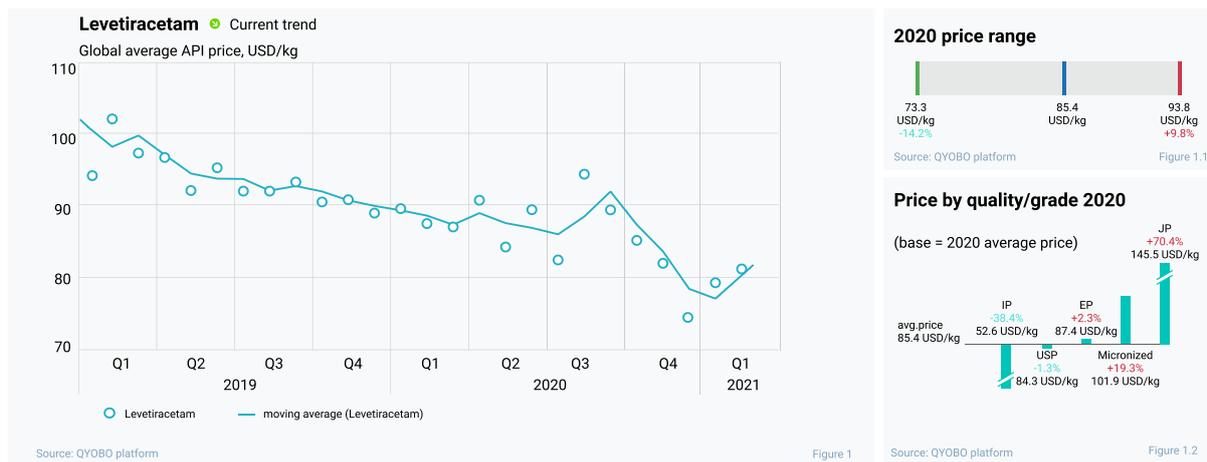


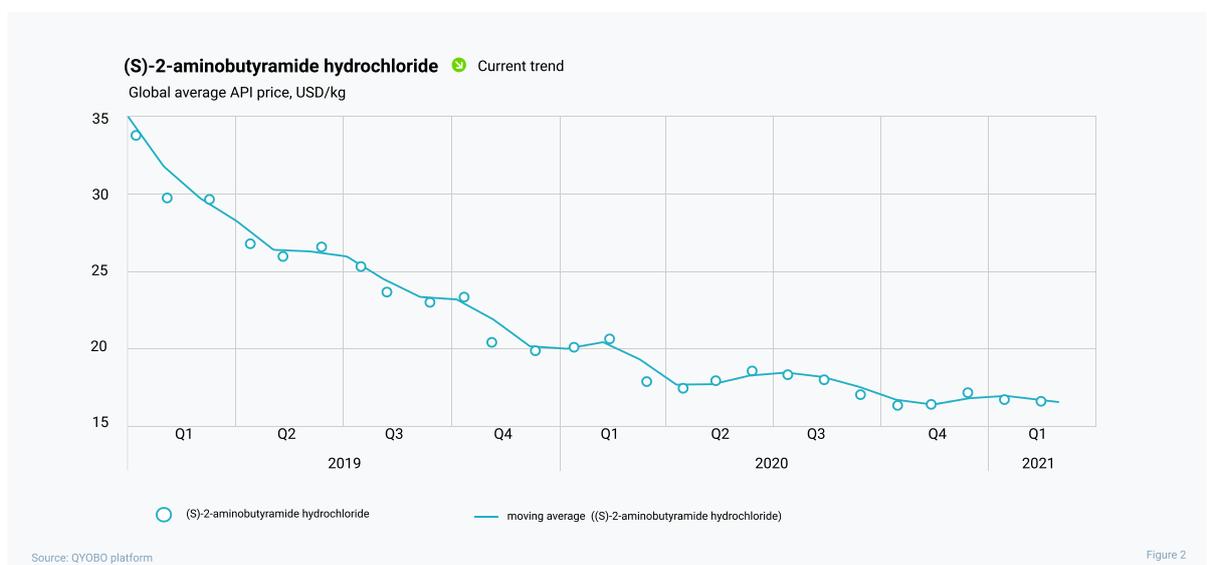
## Levetiracetam - its manufacturing landscape and evolving supply chain

Epilepsy is one of the most common serious neurological disorders with around 50 million people living with this diagnosis.<sup>1</sup> One key medication to treat epilepsy is levetiracetam, which was developed by the Belgian company UCB S.A. and marketed under the trade name Keppra. After being approved by the US FDA in 1999, it has become one of the most popular anti-epileptic remedies.<sup>2</sup>

In 2011, generic versions of Keppra became available after a key UCB patent had expired.<sup>3</sup> In general, generic drugs are more affordable and thus lead to broader availability of essential medicines worldwide. In 2021, 10 years after the first generics entered the market, prices for the drugs ingredients are still decreasing significantly – both for the API itself (levetiracetam) as well as the key intermediate (s)-2-aminobutyramide hydrochloride used to manufacture it.



Over the past two years, levetiracetam prices decreased by 22% - from 93.6 USD/kg in January 2019 to 73.0 USD/kg in December 2020, while prices for (s)-2-aminobutyramide hydrochloride dropped by 49% - from 34.4 USD/kg to 17.6 USD/kg - in the same period. In the beginning of this year prices for (s)-2-aminobutyramide hydrochloride started to stabilize while the levetiracetam API price continued its recent upwards trends since December 2020.



By pharmacopeia, in 2020 levetiracetam conforming with the Japanese Pharmacopeia (JP) was most expensive (+70.4% compared to the average price across all trades), whereas the lowest price was observed for levetiracetam conforming with the Indian Pharmacopeia (IP, -38.4 %, see figure 1.2). Prices for micronized levetiracetam are 19.3% higher than the average market price.

**Offshore manufacturing**

Levetiracetam for the Keppra drug was initially manufactured exclusively in Europe (UCB S.A. - with manufacturing sites in Switzerland and Belgium) and the United States (Ampac Fine Chemicals LLC, subcontractor of UCB S.A. with a manufacturing site in California). As the demand for the API increased and other API manufacturers entered the market, production shifted to Asia. Nowadays, drug manufacturers can choose from dozens of levetiracetam manufacturers, most of them are based in India (17), China (8) and two sites in Puerto Rico and Mexico (see figure 3).

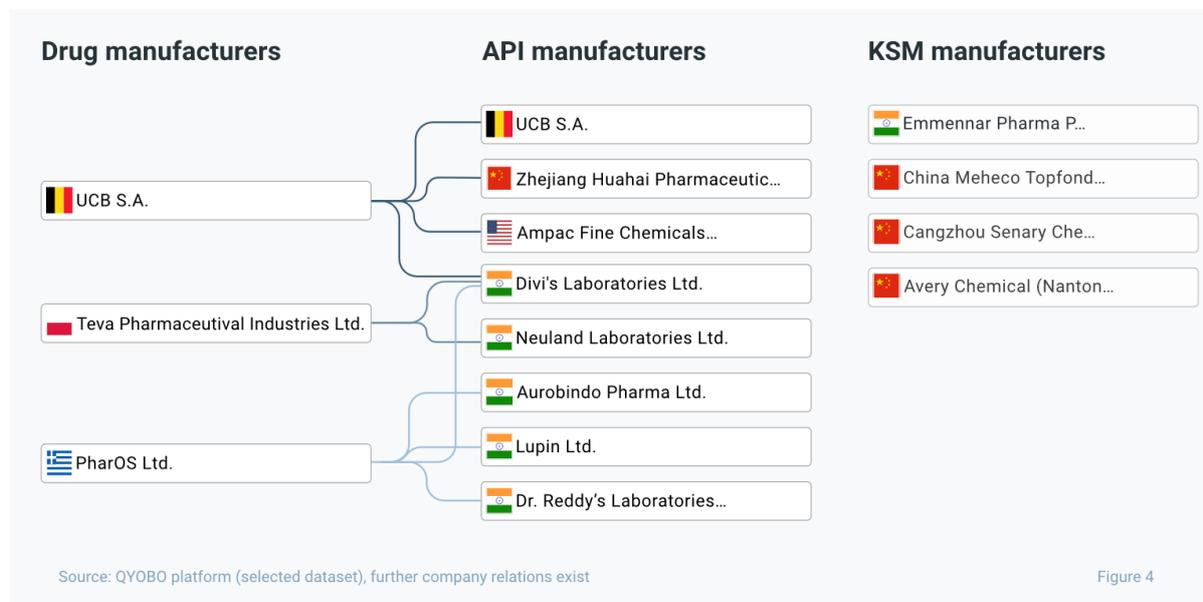
	Drug manufacturers	API manufacturers	KSM manufacturers
	6 4 2 1	17	1
Asia	5 3 1	8	3
	5 3 1		
	10 3 1 1	1	
	7 3 1 1		
	7 2 1		
Europe	6 1 1		
	5 1 1		
	5 1 1		
	5 1 1		
	11 2 1 1	1	
North/Latin America	6 1 1	1	
	5 1 1	1	
Africa	8 1 1 1		
Middle East	12 3 2 1		
	5 2 1 1		

Source: QYOBO platform

Figure 3

While this leaves many alternatives to select an API manufacturer, only four major manufacturers for the key intermediate (s)-2-aminobutyramide hydrochloride are globally active. Three of those are based in China, while the most prominent manufacturer (the only one with a valid USDMF filing) is Emmennar Pharma based in India. With this in mind, QYOBO helps its clients understand global supply chains (see figure 4) and identify potential risks along the entire value chain from the base chemicals or

intermediates to the API and finally the finished drugs. As such, the QYOBO platform gives pharmaceutical and chemical companies unprecedented opportunities to build and monitor robust global supply chains.



#### Glossary:

API Active Pharmaceutical Ingredients

KSM Key Starting Material

EP European Pharmacopeia

IP Indian Pharmacopeia

JP Japanese Pharmacopoeia

USP United States Pharmacopeia

#### About QYOBO GmbH:

QYOBO's mission is to improve access to essential medication for everyone by contributing to a more transparent, efficient and robust supply of pharmaceutical and chemical raw materials.

For this purpose, we've developed the QYOBO market analytics platform for APIs, intermediates and chemicals. From millions of trade, regulatory and financial datasets scattered around the world, our big data algorithms derive unique, actionable insights on market prices and trends, suggest suitable partners for your business and automate data-heavy workflows in procurement, supply chain and business development.

Founded in June 2019 and based in Munich, our company is pursuing its mission collaboratively with its international clients and has been recognized with numerous awards including the BASF market challenge and the Digital Innovation award 2020 by the German Federal Ministry for Economic Affairs & Energy (BMWi).

#### For further information please contact:

Ms. Thuy Linh Nguyen, Corporate Communications

communication@qyobo.com

www.qyobo.com

#### Disclaimer:

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<sup>1</sup>World Health Organization, 20 June 2019. [Epilepsy](#)

<sup>2</sup>National Center for Biotechnology Information, February 2010. [Levetiracetam: a comprehensive review](#)

<sup>3</sup>Pharma Times, 01 August 2011. [UCB stays afloat despite patent expiry storm](#)