Bristol-Myers Squibb Company

AstraZeneca

This information is not for use by US/UK media.

Medical and Lay Media Fact Sheet

Kidney Fact Sheet

The role of the kidney in the reabsorption of glucose	The kidneys filter, reabsorb, and excrete water, sodium, electrolytes, and other substances to control the composition of essential body fluids.[1] In addition, they play an important role in the handling of blood glucose—with renal glucose reabsorption from the urine being the primary mechanism by which filtered glucose is actively returned to the blood.[2,3] In healthy individuals, the kidney filters ~180 grams of glucose each day, with virtually all glucose being reabsorbed back into the body's circulation.[4,5] In the glomerulus, glucose is filtered out of the blood. It then travels into the proximal tubule[4], where sodium-glucose cotransporters (SGLTs)—mainly SGLT2—transport glucose into the cells of the proximal tubule, followed by transport back into the blood via facilitative glucose transporters. [4] SGLT2 is the major sodium-glucose transporter in the kidney and is responsible for the majority of total renal glucose reabsorption.[4]
The impact of type 2 diabetes on the kidneys	Patients with type 2 diabetes have elevated blood glucose levels (hyperglycaemia). Even in the presence of hyperglycaemia, SGLT2 continues to reabsorb excess glucose and its associated calories in the kidney. This reabsorption continues independently of plasma insulin levels and further exacerbates hyperglycaemia.[5-7]
How does SGLT2 inhibition work?	SGLT2 inhibition causes less glucose with its associated calories to be reabsorbed back into the bloodstream. The amount of glucose removed depends on blood glucose concentration and glomerular filtration rate.[8]
Dapagliflozin — The first and only SGLT2 inhibitor	Dapagliflozin is the first and only SGLT2 inhibitor approved for the treatment of type 2

	diabetes. SGLT2, the target of dapagliflozin, is selectively expressed in the kidney.[8]

References

1. Guyton AC, Hall JE. Urine formation by the kidneys: glomerular filtration, renal blood flow, and their control. In: Schmitt W, Gruliow R, eds. *Textbook of Medical Physiology.* 11th ed. Philadelphia, PA: Elsevier Saunders; 2006:307-326.
2. Bailey CJ. Renal glucose reabsorption inhibitors to treat diabetes. *Trends Pharmacol Sci*. 2011;32(2):63-71.
3. Wright EM, Hirayama BA, Loo DF. Active sugar transport in health and disease. *J Intern Med*. 2007;261(1):32-43.
4. Gerich JE. Role of the kidney in normal glucose homeostasis and in the hyperglycaemia of diabetes mellitus: therapeutic implications. *Diabet Med*. 2010;27(2):136-142.
5. Marsenic O. Glucose control by the kidney: an emerging target in diabetes. *Am J Kidney Dis*. 2009;53(5):875-883.
6. Chao EC, Henry RR. SGLT2 inhibition—a novel strategy for diabetes treatment. *Nat Rev Drug Discov*. 2010;9(7):551-559.
7. Rahmoune H, Thompson PW, Ward JM, Smith CD, Hong G, Brown J. Glucose transporters in human renal proximal tubular cells isolated from the urine of patients with non–insulin-dependent diabetes. *Diabetes*. 2005;54(12):3427-3434.
8. Dapagliflozin SPC, Bristol-Myers Squibb/AstraZeneca, 12.11.2012

732HQ12NP041
05/12