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Short communication

Regulatory trends in antidiabetic drug approvals between 2016 and 2026

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Introduction

Diabetes mellitus is a chronic metabolic disease characterized by elevated blood sugar levels. Depending on whether insulin is produced in an appropriate or insufficient amount, we differentiate type 1 diabetes where the body's immune system attacks and destroys the beta cells in the pancreas responsible for insulin production or type 2 where the cells in insulin-sensitive tissues do not respond normally to insulin (Sapra & Bhandari, 2023). Diabetes mellitus is a significant global problem with approximately 1 in 9 of the adult population is living with diabetes, with over 4 in 10 unaware that they have this condition (IDF, 2025). In 2024, approximately 589 million adults had diabetes with projections expected to rise up to 853 million by 2050. Nearly 81% of patients diagnosed with diabetes live in low- and middle- income countries. (IDF, 2025). This creates a need for continuous development and evaluation of antidiabetic drugs and treatment of diabetes mellitus. Even though the first line for treatment of diabetes mellitus type 2 for many individuals still continues to be metformin, the newer recommendations focus on a patient-oriented approach. Antidiabetic drugs such as GLP-1 agonists and SGLT-2 inhibitors have been shown to be a better option for treating patients with cardiovascular and renal comorbidities (ADA, 2023).

Materials and methods

This study was conducted through a systematic search and analysis of EMA- and FDA-approved antidiabetic drugs from 2016 to 2026. The main topic of research was information regarding novel drugs, label expansion and new approvals.

Results and discussion

Historically, antidiabetic agent approvals were based mainly on glycemic efficacy, with glycated hemoglobin (HbA1C) as the primary surrogate endpoint for clinical benefit (EMA, 2012; FDA, 2020). However, this approach proved insufficient to capture broader clinical impact of glucose-lowering therapies, particularly given that cardiovascular disease remains the leading cause of morbidity in patients with type 2 diabetes. This was also proven with the emergence of evidence that rosiglitazone was associated with a significant increase in myocardial infarction and with an increase in the risk of death from cardiovascular causes (Nissen & Wolski, 2007). These findings exposed the limitations of relying solely on surrogate endpoints and underscored the need for direct cardiovascular risk evaluation (FDA, 2008; Hiatt et al., 2013). Because of this, the criteria for evaluating new antidiabetic drugs shifted from evaluating only

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glycemic control to prioritizing cardiovascular safety as the primary endpoint (EMA, 2023; Cosentino, F. et al., 2020). Recent updates on the guidance further emphasize cardiovascular risk characterization as a central component of the benefit-risk evaluation. This can be noticed in the trend of approvals. The period from 2016 to 2020 included initial approvals of GLP-1 receptor agonists, oral SGLT2 inhibitors, and several fixed-dose combinations. In this time frame the main regulatory aspect remained demonstration of glucose-lowering efficacy together with exclusion on cardiovascular harm. The trials intended for demonstration of cardiovascular safety showed significant reduction in major adverse cardiovascular events. With the shift towards outcome-driven regulation came the second phase. In this time period from 2021-2023 approval of new molecules was limited. Instead of new approvals there was a shift towards label expansions based on cardiovascular and renal outcomes. The period between 2024-2026 reflects a regulatory environment where clinically meaningful endpoints are translated into highly specific label expansion. The emergence of non-peptide GLP-1 receptor agonists signals a broader trend toward formulation-driven innovation, where improving accessibility and acceptability of therapy becomes a critical component of therapeutic value.

Conclusion

We can conclude that regulatory evaluation of antidiabetic therapies has undergone a significant transformation from glycemic efficacy being the main endpoint for clinical benefit to demonstration of cardiovascular safety. This shift was caused by the limitations of relying exclusively on HbA1c as it was demonstrated with rosiglitazone. Recently regulatory decisions have been adjusted to specific clinical outcomes. The evolution of new antidiabetic drug regulations demonstrate emphasis on clinical outcomes of the patient so that cardiovascular and renal outcomes are ensured.

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