



NEWS RELEASE

FDA Approves Merck's JUVISYNC™ (sitagliptin and simvastatin) Tablets, a Once-Daily Therapy for Patients with Type 2 Diabetes Who Need to Lower Blood Sugar and Cholesterol, Known Risk Factors for Cardiovascular Disease

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Multiple National Guidelines Recommend that Patients with Type 2 Diabetes be Treated for Cholesterol

Merck (NYSE:MRK), known as MSD outside the United States and Canada, announced today that the U.S. Food and Drug Administration (FDA) has approved JUVISYNC™(sitagliptin and simvastatin), a new treatment for type 2 diabetes that combines the glucose-lowering medication sitagliptin, the active component of JANUVIA® (sitagliptin), with the cholesterol-lowering medication ZOCOR® (simvastatin). JUVISYNC is the first treatment option for healthcare providers to help patients who need the blood sugar-lowering benefits of a DPP-4 inhibitor and the cholesterol-lowering benefits of simvastatin, with the convenience of a single tablet once daily. "Although clinical guidelines put people with type 2 diabetes who need glycemic and lipid therapy at the same risk level as those with coronary heart disease, nearly 40 percent of eligible patients do not receive statin treatment," said Barry J. Goldstein, M.D., Ph.D., vice president, Diabetes and Endocrinology, Merck. "We are proud to bring forward a treatment option that can help these patients who need both glycemic and lipid therapy."

Indications and usage for JUVISYNC

JUVISYNC is indicated in patients for whom treatment with both sitagliptin and simvastatin is appropriate. Sitagliptin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.



Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Drug therapy is indicated as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate. In patients with coronary heart disease (CHD) or at high risk of CHD, simvastatin can be started simultaneously with diet.

In patients at high risk of coronary events because of existing coronary heart disease, diabetes, peripheral vessel disease, history of stroke or other cerebrovascular disease, simvastatin is indicated to reduce the risk of total mortality by reducing CHD deaths, reduce the risk of non-fatal myocardial infarction and stroke, and reduce the need for coronary and non-coronary revascularization procedures. Simvastatin is indicated to: reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and triglycerides (TG); to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary hyperlipidemia (Fredrickson type IIa, heterozygous familial and nonfamilial) or mixed dyslipidemia (Fredrickson type IIb); to reduce elevated TG in patients with hypertriglyceridemia (Fredrickson type IV hyperlipidemia); to reduce elevated TG and VLDL-C in patients with primary dysbetalipoproteinemia (Fredrickson type III hyperlipidemia); and to reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable.

JUVISYNC should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. JUVISYNC has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis while taking JUVISYNC. JUVISYNC has not been studied in conditions where the major abnormality is elevation of chylomicrons (i.e., hyperlipidemia Fredrickson types I and V). Because doses of JUVISYNC appropriate for patients with moderate or severe renal impairment (CrCl <50 mL/min, approximately corresponding to serum creatinine levels of >1.7 mg/dL in men and >1.5 mg/dL in women) or end-stage renal disease (ESRD) are not available in this combination product, JUVISYNC is not recommended in patients with moderate or severe renal impairment or ESRD.

Type 2 diabetes patients who need glycemic and lipid therapy are at an increased risk of cardiovascular disease

“People with type 2 diabetes who need glycemic and lipid therapy are at increased risk of cardiovascular disease and its complications,” said Helena W. Rodbard, M.D., FACP, MACE, past president of the American College of Endocrinology (ACE), and past president of the American Association of Clinical Endocrinologists (AACE). “I am excited to be able to offer my patients a treatment option such as JUVISYNC that combines two important medications to lower both blood sugar and cholesterol in one tablet.”

The FDA approved JUVISYNC based upon clinical bioequivalence studies in healthy subjects that demonstrated administration of JUVISYNC is equivalent to co-administration of corresponding doses of the two individual medications, sitagliptin and simvastatin, as separate tablets.

Important selected safety information about JUVISYNC

JUVISYNC is contraindicated in patients with a history of a serious hypersensitivity reaction, such as anaphylaxis or angioedema, to any component of this medication; concomitant administration of strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, posaconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin and nefazodone); concomitant administration of gemfibrozil, cyclosporine, or danazol; active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels; women who are pregnant or may become pregnant; and nursing mothers. JUVISYNC should be administered to women of childbearing age only when such patients are highly unlikely to conceive.

There have been postmarketing reports of acute pancreatitis, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis, in patients taking sitagliptin. After initiation of JUVISYNC, patients should be observed carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected, JUVISYNC should be promptly discontinued and appropriate management initiated. It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis while taking JUVISYNC.

The risk of myopathy, including rhabdomyolysis, is dose related. All patients starting therapy with JUVISYNC, or whose dose of simvastatin is being increased, should be advised of the risk of myopathy, including rhabdomyolysis, and told to report promptly any unexplained muscle pain, tenderness or weakness. JUVISYNC therapy should be discontinued immediately if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. JUVISYNC therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis.

Increases in A1C and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including simvastatin.

Persistent increases (to more than 3X the ULN) in serum transaminases have occurred in approximately one percent of patients who received simvastatin in clinical studies. It is recommended that liver function tests be performed before the initiation of treatment, and thereafter when clinically indicated. There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including simvastatin. If serious liver injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs during treatment with JUVISYNC, promptly interrupt therapy.

When sitagliptin was used in combination with a sulfonylurea or with insulin, medications known to cause hypoglycemia, the incidence of hypoglycemia was increased over that of placebo used in combination with a sulfonylurea or with insulin. Therefore, a lower dose of sulfonylurea or insulin may be required to reduce the risk of hypoglycemia.

Assessment of renal function is recommended prior to initiating JUVISYNC and periodically thereafter. JUVISYNC is not recommended for use in patients with moderate or severe renal impairment or end-stage renal disease because doses of JUVISYNC appropriate for patients with moderate or severe renal impairment or ESRD are not available in this combination product.

There have been postmarketing reports of worsening renal function, including acute renal failure, sometimes requiring dialysis, in patients treated with sitagliptin. A subset of these reports involved patients with renal impairment, some of whom were prescribed inappropriate doses of sitagliptin. A return to baseline levels of renal impairment has been observed with supportive treatment and discontinuation of potentially causative agents.

Sitagliptin, a component of JUVISYNC, is comparable to a sulfonylurea (glipizide) in helping patients lower blood sugar

In a clinical trial of patients with inadequate glycemic control on diet, exercise and metformin monotherapy ≥ 1500 mg/day, patients were randomized in a double-blind manner to the addition of sitagliptin 100 mg once daily or the sulfonylurea glipizide 5-20 mg/day (mean daily dose 10 mg daily) for 52 weeks. In this study, sitagliptin achieved the pre-specified bounds for non-inferiority vs. a sulfonylurea (glipizide). After 52 weeks, the mean A1C reduction from baseline was 0.5 percent for sitagliptin (n=576) and 0.6 percent for glipizide (n=559) in the intent-to-treat patient population and 0.7 percent for sitagliptin and 0.7 percent for glipizide in the per protocol analysis, confirming the similar mean A1C reductions of sitagliptin compared to glipizide. At 52 weeks, mean body weight decreased with the addition of sitagliptin (-1.5 kg) and increased with the addition of glipizide (1.1 kg), a significant difference of 2.5 kg (-3.1, -2.0; $p < 0.001$) or 5.5 pounds. Additionally, patients treated with sitagliptin experienced a significantly lower incidence of hypoglycemia than patients treated with glipizide (4.9 percent vs. 32.0 percent, respectively, $p < 0.001$). A conclusion in favor of the non-inferiority of sitagliptin to glipizide may be limited to patients with baseline A1C comparable to those included in the study.

Reductions in risk of CHD mortality and cardiovascular events with simvastatin

The Heart Protection Study (HPS), a large, multi-center, placebo-controlled, double-blind study with a mean duration of 5 years conducted in 20,536 patients, including 5,963 patients with type 2 diabetes (2,978 on simvastatin and 2,985 on placebo) showed that simvastatin 40 mg/day significantly reduced total and CHD mortality; non-fatal MI, stroke, and revascularization procedures (coronary and non-coronary).

Participants in HPS (mean age 64) were at high risk of developing a major coronary event because of existing CHD (65 percent), diabetes (Type 2, 26 percent; Type 1, 3 percent), history of stroke or other cerebrovascular disease (16 percent), peripheral vessel disease (33 percent), or hypertension in males ≥ 65 years (6 percent). Treatment with simvastatin produced significant relative risk reductions for all components of the two composite endpoints, including major coronary events comprised of CHD mortality and non-fatal MI, and major vascular events comprised of stroke and revascularization procedures including coronary, peripheral and other non-coronary procedures (27 percent for major coronary events and 24 percent for major vascular events, $p < 0.0001$).

Diabetic patients showed risk reductions for MCE and MVE (27 percent and 22 percent, respectively; $p < 0.0001$) due to simvastatin treatment regardless of baseline A1C levels or obesity with the greatest effects seen for diabetic patients without CHD.

The Scandinavian Simvastatin Survival Study (4S) assessed the effect of therapy with simvastatin on total mortality in 4,444 patients with CHD and baseline total cholesterol 212-309 mg/dL (5.5-8.0 mmol/L). In this multicenter, randomized, double-blind, placebo-controlled study, patients were treated with standard care, including diet, and either simvastatin 20-40 mg/day ($n=2,221$) or placebo ($n=2,223$) for a median duration of 5.4 years.

In 4S, treatment with simvastatin significantly reduced the risk of mortality by 30 percent ($p=0.0003$), and the risk of CHD mortality by 42 percent ($p=0.00001$). Simvastatin also significantly decreased the risk of major coronary events (CHD mortality plus hospital-verified and silent non-fatal myocardial infarction) by 34 percent ($p < 0.00001$), and the risk of fatal plus non-fatal cerebrovascular events (combined stroke and transient ischemic attacks) by 28 percent ($p=0.033$).

Significant improvements in lipid levels with simvastatin

Simvastatin has been shown to be effective in reducing total cholesterol, low-density lipoprotein cholesterol (LDL-C) in heterozygous familial and non-familial forms of hyperlipidemia and in mixed hyperlipidemia. Maximal to near maximal response is generally achieved within 4-6 weeks and maintained during chronic therapy. Simvastatin consistently and significantly decreased total cholesterol, LDL-C, total-C/HDL-C ratio, and LDL-C/HDL-C ratio; simvastatin also decreased triglycerides and increased high-density lipoprotein cholesterol (HDL-C).

Pricing and availability of JUVISYNC

The price of JUVISYNC will be the same price as JANUVIA alone. JUVISYNC will be broadly available in pharmacies in the near future.

Convenient once-daily JUVISYNC

The dosages for therapy with JUVISYNC are 100/10, 100/20, and 100/40 (mg sitagliptin/mg simvastatin) once daily. JUVISYNC should be taken as a single daily dose in the evening. JUVISYNC should be swallowed whole. The tablets must not be split, crushed, or chewed before swallowing.

The recommended starting dose is 100/40 mg/day. For patients already taking simvastatin (10, 20, or 40 mg daily) with or without sitagliptin 100 mg daily, JUVISYNC may be initiated at the dose of 100 mg sitagliptin and the dose of simvastatin already being taken. After initiation or titration of JUVISYNC, lipid levels may be analyzed after four or more weeks and dosage adjusted, if needed.

Selected risk information for JUVISYNC

There have been postmarketing reports of serious hypersensitivity reactions in patients treated with sitagliptin. These include anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. Onset of these reactions occurred within the first 3 months after initiation of treatment with sitagliptin, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue JUVISYNC, assess for other potential causes for the event, and institute alternative treatment. Angioedema has also been reported with other dipeptidyl peptidase-4 (DPP-4) inhibitors. Use caution in a patient with a history of angioedema with another DPP-4 inhibitor because it is unknown whether such patients will be predisposed to angioedema with JUVISYNC.

In clinical studies, the adverse reactions reported, regardless of investigator assessment of causality, in ≥ 5 percent of patients treated with sitagliptin as monotherapy and in combination therapy and more commonly than in patients treated with placebo, were upper respiratory tract infection (sitagliptin, 15.5%; placebo, 6.2%); nasopharyngitis (11.0%, 9.3%); peripheral edema (8.3%, 5.2%), and headache (5.5%, 4.1%).

Simvastatin occasionally causes myopathy manifested as muscle pain, tenderness, or weakness with creatine phosphokinase (CK) levels above $10 \times$ ULN. Myopathy sometimes takes the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and rare fatalities have occurred. The risk of myopathy is increased by high levels of statin activity in plasma. Predisposing factors for myopathy include advanced age (≥ 65 years), female gender, uncontrolled hypothyroidism, and renal impairment.

Because of the increased risk of myopathy/rhabdomyolysis, particularly at higher doses of simvastatin, concomitant use of JUVISYNC is contraindicated with drugs that are strong CYP3A4 inhibitors or with gemfibrozil, cyclosporine or danazol, and large quantities of grapefruit juice (>1 quart daily) should be avoided. Use caution when prescribing JUVISYNC with other fibrates or colchicine. The dose of JUVISYNC should not exceed 100/10 mg daily in patients receiving concomitant therapy with verapamil or diltiazem, and 100/20 mg daily in patients receiving amiodarone,

amlodipine or ranolazine. The use of simvastatin with these drugs, or with lipid-lowering doses of niacin, should be carefully weighed against the potential risk of myopathy/rhabdomyolysis with these combinations. Caution should be used when treating Chinese patients with JUVISYNC 100 mg/40 mg per day coadministered with lipid-modifying doses of niacin-containing products. It is recommended that adjusting the dose of JUVISYNC be considered during concomitant use with voriconazole to reduce the risk of myopathy/rhabdomyolysis.

It is recommended that liver function tests be performed before the initiation of treatment, and thereafter when clinically indicated. Persistent increases (>3 times ULN) in serum transaminases have occurred in approximately 1 percent of patients who received simvastatin in clinical studies.

In clinical trials of simvastatin, the most commonly reported side effects, regardless of cause, included upper respiratory infections (9.0 percent), headache (7.4 percent), abdominal pain (7.3 percent), constipation (6.6 percent), and nausea (5.4 percent).

Expanding the sitagliptin family of products

Merck is committed to further advancing the medical community's understanding of how to better manage type 2 diabetes, and to providing novel treatment options to people with type 2 diabetes who need them. With JANUVIA, JANUMET, and now JUVISYNC, Merck has a growing family of products that provides physicians with important treatment options for patients with type 2 diabetes.

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#) and [YouTube](#).

Merck Forward-Looking Statement

This news release includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Such statements may include, but are not limited to, statements about the benefits of the merger between Merck and Schering-Plough, including future financial and operating results, the combined company's plans, objectives, expectations and intentions and other statements that are not historical facts. Such statements are based upon the current beliefs and expectations of Merck's

management and are subject to significant risks and uncertainties. Actual results may differ from those set forth in the forward-looking statements.

The following factors, among others, could cause actual results to differ from those set forth in the forward-looking statements: the possibility that the expected synergies from the merger of Merck and Schering-Plough will not be realized, or will not be realized within the expected time period; the impact of pharmaceutical industry regulation and health care legislation; the risk that the businesses will not be integrated successfully; disruption from the merger making it more difficult to maintain business and operational relationships; Merck's ability to accurately predict future market conditions; dependence on the effectiveness of Merck's patents and other protections for innovative products; the risk of new and changing regulation and health policies in the United States and internationally and the exposure to litigation and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck's 2010 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Prescribing Information and Medication Guide for JUVISYNC are available at http://www.merck.com/product/usa/pi_circulars/j/juvisync/juvisync_pi.pdf and http://www.merck.com/product/usa/pi_circulars/j/juvisync/juvisync_mg.pdf.

For more information, visit JUVISYNC.com.

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