**INDICATION**

Nascobal® (Cyanocobalamin, USP) Nasal Spray is indicated for the maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin $B_{12}$ therapy and who have no nervous system involvement. Nascobal Nasal Spray is also indicated as a supplement for other vitamin $B_{12}$ deficiencies including: dietary deficiency of vitamin $B_{12}$ occurring in strict vegetarian diets; malabsorption of vitamin $B_{12}$ resulting from conditions including HIV infection, AIDS, and Crohn’s disease; inadequate secretion of intrinsic factor resulting from lesions that destroy the gastric mucosa and other conditions associated with gastric atrophy including multiple sclerosis, HIV infection, AIDS, certain endocrine disorders, iron deficiency, and subtotal gastrectomy; total gastrectomy; competition for vitamin $B_{12}$ by intestinal parasites or bacteria; and inadequate utilization of vitamin $B_{12}$ that may occur if antimetabolites for the vitamin are employed in the treatment of neoplasia.

**IMPORTANT SAFETY INFORMATION**

Nascobal® (Cyanocobalamin, USP) Nasal Spray is contraindicated in patients with sensitivity to cobalt and/or vitamin $B_{12}$ or any component of the medication. If a patient is not properly maintained with Nascobal Nasal Spray, intramuscular vitamin $B_{12}$ is necessary. Vitamin $B_{12}$ concentrations must be monitored.

Patients with pernicious anemia should be instructed that they will require weekly administration of Nascobal Nasal Spray for the remainder of their lives. Failure to do so will result in return of the anemia and in development of incapacitating and irreversible damage to the nerves of the spinal cord. Patients with early Leber’s disease (hereditary optic nerve atrophy) who were treated with vitamin $B_{12}$ suffered severe and swift optic atrophy. Vitamin $B_{12}$ deficiency may suppress the signs of polycythemia vera. Treatment with vitamin $B_{12}$ may unmask this condition. Hypokalemia and sudden death may occur in severe megaloblastic anemia which is treated intensely with vitamin $B_{12}$.

Side effects thought to be related to Nascobal use are usually mild and include headache, nausea, and rhinitis.

Please see adjacent brief summary of prescribing information.

*In a separate study Nascobal nasal spray and Nascobal nasal gel were bioequivalent.*

References:
**ADVERSE REACTIONS**

The incidence of adverse experiences described in the Table below are based on data from a short-term clinical trial in vitamin B12 deficient patients in hematologic remission receiving Nascobal Nasal Gel for Intranasal Administration (500 mcg) and intramuscular vitamin B12 (N=25). In the pharmacokinetic study comparing Nascobal Nasal Spray and Nascobal Nasal Gel, the incidence of adverse events was similar.

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Experience</th>
<th>Number of Patients (Occurrences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin B12</td>
<td>Nasal Gel</td>
<td>500 mcg</td>
</tr>
<tr>
<td>B</td>
<td>Asthma</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Back Pain</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Sensitized Skin</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>1 (1)*</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular System</td>
<td>Peripheral Vascular Disorder</td>
</tr>
<tr>
<td></td>
<td>Digestive System</td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Anaphylaxis</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Mucocutaneous System</td>
<td>Arthritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pruritus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucous Membranes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemorrhagic</td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myopathy</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anesthesia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anxiety</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tinnitus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypersensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemoptysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Incontinence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parasthesia</td>
</tr>
<tr>
<td></td>
<td>Respiratory System</td>
<td>Dyspnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rhinitis</td>
</tr>
</tbody>
</table>

* Sore throat, common cold: There may be a possible relationship between these adverse experiences and the study drugs. These adverse experiences could have also been produced by the patient's clinical state or underlying serious medical condition.

The intensity of the reported adverse experiences following the administration of Nascobal Nasal Gel for Intranasal Administration and intramuscular vitamin B12 were judged to be not to be of intramuscular dosing. Similarly, a few adverse experiences of moderate intensity were reported following intranasal dosing involving hypertension, nystagmus, headache and dizziness, and of Nascobal Nasal Gel for Intranasal Administration (headache, nausea, and pruritus) were reported following dosing with Nascobal Nasal Gel Intramuscular Administration.

The following adverse reactions have been reported with parental vitamin B12:

- **General:** Anaphylactic shock and death have been reported after parental vitamin B12 administration. No such reactions have been reported in clinical trials with Nascobal Nasal Spray or Nascobal Nasal Spray (Cyanocobalamine, USP) Nasal Gel. Blurred vision and other ocular reactions to vitamin B12 may be due to such conditions as infection, tumor, drugs having bone marrow suppressor properties such as chlorambucil, and congenital or folic acid deficiencies.

**PRECAUTIONS**

**GENERAL:** An intradoseal test dose of pernicious anemia is recommended before Nascobal Nasal Spray is administered to patients suspected to have pernicious anemia. Deficiency that is allowed to progress for more than three months may produce permanent degenerative lesions of the spinal cord. Doses of folic acid greater than recommended in patients with vitamin B12 deficiency may produce deficiency in patients with vitamin B12 deficiency. Neurologic manifestations will not be prevented with folic acid, and if not treated with vitamin B12 will result. Doses of vitamin B12, exceeding 10 mcg daily may produce hematologic response in patients with folate deficiency. The serum response to vitamin B12 therapy, therefore, serum potassium levels and the platelet count should be monitored carefully during therapy. Vitamin B12 deficiency may be associated with megaloblastic anemia. Ingestion of vitamin B12 results in true diabetes. Hypokalemic and thrombocytosis could occur as a consequence of severe megaloblastic to normal erythropoiesis with vitamin B12 therapy. Therefore, serum potassium levels and the platelet count should be monitored carefully during therapy. Vitamin B12 deficiency may suppress the signs of polymya vera. Treatment with vitamin B12 may unmask this condition. If a patient is not properly maintained with Nascobal Nasal Spray, intramuscular vitamin B12 is necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. The effectiveness of Nascobal Nasal Spray in patients with coexistent iron deficiency anemia has not been determined. Treatment with Nascobal Nasal Spray should be deferred until symptoms have subsided.

**LABORATORY TESTS**

Hematologic, biochemical, and urine count, vitamin B12 levels should be obtained prior to treatment. If folate levels are low, folate acid should also be administered. All hematology parameters should be normal when beginning therapy with Nascobal Nasal Spray. Vitamin B12, blood levels and peripheral blood counts should be monitored initially at one month after the start of treatment with Nascobal Nasal Spray, and then at intervals of 3 to 6 months. A decline in the serum levels of B12 after one month of treatment with Nascobal Spray may indicate that the dose may need to be adjusted upward. Patients should be seen one month after each dose adjustment; continued low levels of serum B12 would indicate that the patient is not a candidate for this mode of administration.

Patients with pernicious anemia have about 3 times the incidence of carcinoma of the stomach as that in the general population, so appropriate tests for this condition should be carried out when indicated.

**DRUG-LABORATORY TEST INTERACTIONS**

Persons taking methotrexate, methotrexate or pyrimethamine invalidate folic acid and vitamin B12 diagnostic assays. Hot foods may cause nasal secretions and a resulting loss of medication; therefore, patients should be told to avoid eating hot foods immediately before each administration of doses 2 through 4.

**LABORATORY TESTS**

Hematologic, biochemical, and urinalysis should be obtained prior to treatment. If folic acid levels are low, folic acid should also be administered. All hematology parameters should be normal when beginning therapy with Nascobal Nasal Spray. Vitamin B12 levels and peripheral blood counts should be monitored initially at one month after the start of treatment with Nascobal Nasal Spray, and then at intervals of 3 to 6 months. A decline in the serum levels of B12 after one month of treatment with Nascobal Spray may indicate that the dose may need to be adjusted upward. Patients should be seen one month after each dose adjustment; continued low levels of serum B12 would indicate that the patient is not a candidate for this mode of administration.

Patients with pernicious anemia have about 3 times the incidence of carcinoma of the stomach as that in the general population, so appropriate tests for this condition should be carried out when indicated.

**DRUG-INDICATED TEST INTERACTIONS**

Persons taking methotrexate, methotrexate or pyrimethamine invalidate folic acid and vitamin B12 diagnostic assays. Hot foods may cause nasal secretions and a resulting loss of medication; therefore, patients should be told to avoid eating hot foods immediately before each administration of doses 2 through 4.

**INFORMATION FOR PATIENTS**

Patients with pernicious anemia should be instructed that they will require weekly intranasal administration of Nascobal Nasal Spray for the remainder of their lives. Failure to do so will result in return of the anemia and in development of incapacitating and irreversible damage to the nerves of the spinal cord. Also, patients should be warned about the danger of taking folic acid in place of vitamin B12 because the former may prevent anemia but allow progression of subacute combined degeneration of the spinal cord.

(For food may cause nasal secretions and a resulting loss of medication; therefore, patients should be told to administer Nascobal Nasal Spray at least one hour before or one hour after ingestion of hot foods or liquids.)

A vegetarian diet which contains no animal products (including milk products or eggs) does not supply any vitamin B12. Therefore, patients following such a diet should be advised to take Nascobal Nasal Spray weekly. The need for vitamin B12 is increased by pregnancy and lactation. Deficiency has been recognized in infants of vegetarian mothers who were breast fed, even though the mothers had no symptoms of deficiency at the time. Because the nasal dosage forms of Vitamin B12 have a lower absorption than intramuscular dosage, nasal dosage forms are administered weekly, rather than the monthly intramuscular dosage. As shown in the Figure above, at the end of a month, weekly nasal administration results in significantly higher serum Vitamin B12 levels than after intramuscular administration. The patient should also understand the importance of returning for follow-up blood tests every 3 to 6 months to confirm adequacy of the therapy.

Careful instructions on the actuator assembly, removal of safety clip, priming of the actuator and nasal administration of Nascobal Nasal Spray should be given to the patient. Although instructions for patients are supplied with individual bottles, procedures for use should be demonstrated to each patient.

To report suspected adverse reactions, contact Par Pharmaceutical Companies, Inc. at 1-800-826-9393.

**DOSAGE AND ADMINISTRATION**

The recommended initial dose of Nascobal Nasal Spray is one spray (100 mcg) administered in one nostril once weekly. Nascobal Nasal Spray should be administered at least one hour before or one hour after ingestion of hot foods or liquids. A vegetarian diet which contains no animal products (including milk products or eggs) does not supply any vitamin B12. Therefore, patients following such a diet should be advised to take Nascobal Nasal Spray weekly. The need for vitamin B12 is increased by pregnancy and lactation. Deficiency has been recognized in infants of vegetarian mothers who were breast fed, even though the mothers had no symptoms of deficiency at the time. Because the nasal dosage forms of Vitamin B12 have a lower absorption than intramuscular dosage, nasal dosage forms are administered weekly, rather than the monthly intramuscular dosage. As shown in the Figure above, at the end of a month, weekly nasal administration results in significantly higher serum Vitamin B12 levels than after intramuscular administration. The patient should also understand the importance of returning for follow-up blood tests every 3 to 6 months to confirm adequacy of the therapy.

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don’t be fooled...

Is it the common cold, the flu, or something else? An accurate diagnosis can be a challenge which is why a rapid influenza test that enables the early recognition of patients with influenza has many advantages*. The OSOM® Influenza A&B Test is affordable, fast, and objective. It can assist you in determining proper treatment and in helping to reduce overall healthcare costs... awesome, yes OSOM®.

osom®

For more information call 800 332 1042 or visit us at www.seksuldiagnostics.com

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A Letter to Henry Schein’s Valued Customers

As we enter the winter season, the prevention, diagnosis, and treatment of diseases are top of mind. This issue of the BioTherapeutics Quarterly journal will address these topics on two major disease states, diabetes and influenza. November is National Diabetes Awareness Month. You’ll find a special report on diabetes enclosed in this issue, beginning on page 8. We have published a selection from the CDC’s 2011 National Diabetes Fact Sheet. Diabetes affects 25.8 million people in the United States, 8.3% of the population. Prevention, diagnosis and treatment are all critical in the fight against this disease.

Influenza is a deadly disease that kills on average 36,000 Americans annually. Immunization is the most effective way to prevent infection. We are featuring an MMWR article that discusses the latest recommendations for vaccination against the disease. The FDA has also issued an alert, featured in this issue, regarding Tamiflu suspension, which is used in the treatment of influenza.

Be sure to check out our New Drug Approvals section and featured product announcements as well as our Generically Speaking section. We are highlighting TEVA Pharmaceuticals, the top U.S. generic company.

As we move into the end of 2011, we would like to say a special Thank You to our Valued Customers and hope that you have enjoyed your complimentary issue of the journal this year. We look forward to serving you in 2012 and bringing you an additional four issues of our journal.

Sincerely,

Louis Ferraro
Vice President & General Manager
BioTherapeutics, Henry Schein Medical

OUR Mission

To provide health care professionals with a practical and relevant source of information regarding diagnostics, pharmaceuticals, and vaccines in a quick and easy-to-read publication that provides educational updates and insight to assist you in prevention, diagnosis, and treatment of disease.
Performance & Savings

Give your patients a TRUE EDGE in diabetes testing with these high performing, no coding meters.

TRUEresult® and TRUE2go®
Blood Glucose Monitoring Systems
- Results in as fast as 4 seconds
- Tiny, 0.5 microliter blood sample

Both systems utilize TRUEtest™ Strips featuring Quad-Electrode™ Laser Accuracy.

TRUEbalance™
Blood Glucose Monitoring System
- Accurate results in 10 seconds
- Small, 1.0 microliter blood sample

Utilizes TRUEbalance™ Test Strips featuring patented TRUEfill® technology.

Clinically Proven Accuracy.
TRUEresult® performs as well as leading brands.

Recommend these no coding systems to your patients with confidence, today!
National Diabetes Fact Sheet, 2011

FAST FACTS ON DIABETES

Diabetes affects 25.8 million people
8.3% of the U.S. population

DIAGNOSED
18.8 million people

UNDIAGNOSED
7.0 million people

All ages, 2010

- Among U.S. residents aged 65 years and older, 10.9 million, or 26.9%, had diabetes in 2010.
- About 215,000 people younger than 20 years had diabetes (type 1 or type 2) in the United States in 2010.
- About 1.9 million people aged 20 years or older were newly diagnosed with diabetes in 2010 in the United States.
- In 2005–2008, based on fasting glucose or hemoglobin A1c levels, 35% of U.S. adults aged 20 years or older had prediabetes (50% of adults aged 65 years or older). Applying this percentage to the entire U.S. population in 2010 yields an estimated 79 million American adults aged 20 years or older with prediabetes.
- Diabetes is the leading cause of kidney failure, nontraumatic lower-limb amputations, and new cases of blindness among adults in the United States.
- Diabetes is a major cause of heart disease and stroke.
- Diabetes is the seventh leading cause of death in the United States.

Citation

National Center for Chronic Disease Prevention and Health Promotion
Division of Diabetes Translation

Diagnostics | Pharmaceuticals | DxRx Solutions | Continuing Education | News
Estimation methods

The estimates in this fact sheet were derived from various data systems of the Centers for Disease Control and Prevention (CDC), the Indian Health Service’s (IHS) National Patient Information Reporting System (NPIRS), the U.S. Renal Data System of the National Institutes of Health (NIH), the U.S. Census Bureau, and published studies. The estimated percentages and the total number of people with diabetes and prediabetes were derived from 2005–2008 National Health and Nutrition Examination Survey (NHANES), 2007–2009 National Health Interview Survey (NHIS), 2009 IHS data, and 2010 U.S. resident population estimates. The diabetes and prediabetes estimates from NHANES were applied to the 2010 U.S. resident population estimates to derive the estimated number of adults with diabetes or prediabetes. The methods used to generate the estimates for the fact sheet may vary over time and need to be considered before comparing fact sheets. In contrast to the 2007 National Diabetes Fact Sheet, which used fasting glucose data to estimate undiagnosed diabetes and prediabetes, the 2011 National Diabetes Fact Sheet uses both fasting glucose and hemoglobin A1c (A1c) levels to derive estimates for undiagnosed diabetes and prediabetes. These tests were chosen because they are most frequently used in clinical practice. Detailed information about the data sources, methods, and references are available at http://www.cdc.gov/diabetes/pubs/references11.htm.

Diagnosed and undiagnosed diabetes among people aged 20 years or older, United States, 2010

<table>
<thead>
<tr>
<th>Group</th>
<th>Number or percentage who have diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥20 years</td>
<td>25.6 million or 11.3% of all people in this age group</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>10.9 million or 26.9% of all people in this age group</td>
</tr>
<tr>
<td>Men</td>
<td>13.0 million or 11.8% of all men aged 20 years or older</td>
</tr>
<tr>
<td>Women</td>
<td>12.6 million or 10.8% of all women aged 20 years or older</td>
</tr>
<tr>
<td>Non-Hispanic whites</td>
<td>15.7 million or 10.2% of all non-Hispanic whites aged 20 years or older</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>4.9 million or 18.7% of all non-Hispanic blacks aged 20 years or older</td>
</tr>
</tbody>
</table>

Sufficient data are not available to estimate the total prevalence of diabetes (diagnosed and undiagnosed) for other U.S. racial/ethnic minority populations.
Diagnosed and undiagnosed diabetes

Estimated percentage of people aged 20 years or older with diagnosed and undiagnosed diabetes, by age group, United States, 2005–2008

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–44</td>
<td>3.7%</td>
</tr>
<tr>
<td>45–64</td>
<td>13.7%</td>
</tr>
<tr>
<td>≥65</td>
<td>26.9%</td>
</tr>
</tbody>
</table>


Diagnosed diabetes among people younger than 20 years of age, United States, 2010

About 215,000 people younger than 20 years have diabetes (type 1 or type 2). This represents 0.26% of all people in this age group. Estimates of undiagnosed diabetes are unavailable for this age group.

Racial and ethnic differences in diagnosed diabetes

National estimates of diagnosed diabetes for some but not all minority groups are available from national survey data and from the IHS NPIRS, which includes data for approximately 1.9 million American Indians and Alaska Natives in the United States who receive health care from the IHS. Differences in diabetes prevalence by race/ethnicity are partially attributable to age differences. Adjustment for age makes results from racial/ethnic groups more comparable.

Data from the 2009 IHS NPIRS indicate that 14.2% of American Indians and Alaska Natives aged 20 years or older who received care from IHS had diagnosed diabetes. After adjusting for population age differences, 16.1% of the total adult population served by IHS had diagnosed diabetes, with rates varying by region from 5.5% among Alaska Native adults to 33.5% among American Indian adults in southern Arizona.

After adjusting for population age differences, 2007–2009 national survey data for people aged 20 years or older indicate that 7.1% of non-Hispanic whites, 8.4% of Asian Americans, 11.8% of Hispanics, and 12.6% of non-Hispanic blacks had diagnosed diabetes. Among Hispanics, rates were 7.6% for both Cubans and for Central and South Americans, 13.3% for Mexican Americans, and 13.8% for Puerto Ricans.

Compared to non-Hispanic white adults, the risk of diagnosed diabetes was 18% higher among Asian Americans, 66% higher among Hispanics, and 77% higher among non-Hispanic blacks. Among Hispanics compared to non-Hispanic white adults, the risk of diagnosed diabetes was about the same for Cubans and for Central and South Americans, 87% higher for Mexican Americans, and 94% higher for Puerto Ricans.
New cases of diagnosed diabetes

Estimated number of new cases of diagnosed diabetes among people aged 20 years or older, by age group, United States, 2010

About 1.9 million people aged 20 years or older were newly diagnosed with diabetes in 2010.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–44</td>
<td>465,000</td>
</tr>
<tr>
<td>45–64</td>
<td>1,052,000</td>
</tr>
<tr>
<td>≥65</td>
<td>390,000</td>
</tr>
</tbody>
</table>

Source: 2007–2009 National Health Interview Survey estimates projected to the year 2010

New cases of diagnosed diabetes among people younger than 20 years of age, United States, 2002–2005

SEARCH for Diabetes in Youth is a multicenter study funded by CDC and NIH to examine diabetes (type 1 and type 2) among children and adolescents in the United States. SEARCH findings for the communities studied include the following:

- During 2002–2005, 15,600 youth were newly diagnosed with type 1 diabetes annually, and 3,600 youth were newly diagnosed with type 2 diabetes annually.
- Among youth aged <10 years, the rate of new cases was 19.7 per 100,000 each year for type 1 diabetes and 0.4 per 100,000 for type 2 diabetes. Among youth aged 10 years or older, the rate of new cases was 18.6 per 100,000 each year for type 1 diabetes and 8.5 per 100,000 for type 2 diabetes.
- Non-Hispanic white youth had the highest rate of new cases of type 1 diabetes (24.8 per 100,000 per year among those younger than 10 years and 22.6 per 100,000 per year among those aged 10–19 years).
- Type 2 diabetes was extremely rare among youth aged <10 years. While still infrequent, rates were greater among youth aged 10–19 years than in younger children, with higher rates among U.S. minority populations than in non-Hispanic whites.
- Among non-Hispanic white youth aged 10–19 years, the rate of new cases was higher for type 1 than for type 2 diabetes. For Asian/Pacific Islander and American Indian youth aged 10–19 years, the opposite was true—the rate of new cases was greater for type 2 than for type 1 diabetes. Among non-Hispanic black and Hispanic youth aged 10–19 years, the rates of new cases of type 1 and type 2 diabetes were similar.
New cases of diagnosed diabetes (continued)

Rate of new cases of type 1 and type 2 diabetes among youth aged <20 years, by race/ethnicity, 2002–2005

Source: SEARCH for Diabetes in Youth Study
NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

Prediabetes

Prediabetes among people aged 20 years or older, United States, 2010

- Prediabetes is a condition in which individuals have blood glucose or A1c levels higher than normal but not high enough to be classified as diabetes. People with prediabetes have an increased risk of developing type 2 diabetes, heart disease, and stroke.
- Studies have shown that people with prediabetes who lose weight and increase their physical activity can prevent or delay type 2 diabetes and in some cases return their blood glucose levels to normal.
- In 2005–2008, based on fasting glucose or A1c levels, 35% of U.S. adults aged 20 years or older had prediabetes (50% of those aged 65 years or older). Applying this percentage to the entire U.S. population in 2010 yields an estimated 79 million Americans aged 20 years or older with prediabetes.
- On the basis of fasting glucose or A1c levels, and after adjusting for population age differences, the percentage of U.S. adults aged 20 years or older with prediabetes in 2005–2008 was similar for non-Hispanic whites (35%), non-Hispanic blacks (35%), and Mexican Americans (36%).
- Using a different data source than for other race/ethnicity groups, a different age group, and a different definition on the basis of fasting glucose levels only, and after adjusting for population age differences, 20% of American Indians aged 15 years or older had prediabetes in 2001–2004.
Deaths among people with diabetes, United States, 2007

- Diabetes was the seventh leading cause of death based on U.S. death certificates in 2007. This ranking is based on the 71,382 death certificates in 2007 in which diabetes was the underlying cause of death. Diabetes was a contributing cause of death in an additional 160,022 death certificates for a total of 231,404 certificates in 2007 in which diabetes appeared as any-listed cause of death.
- Diabetes is likely to be underreported as a cause of death. Studies have found that about 35% to 40% of decedents with diabetes had it listed anywhere on the death certificate and about 10% to 15% had it listed as the underlying cause of death.
- Overall, the risk for death among people with diabetes is about twice that of people of similar age but without diabetes.

Overall, the risk for death among people with diabetes is about twice that of people of similar age but without diabetes.

Estimated diabetes costs in the United States, 2007

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (direct and indirect)</td>
<td>$174 billion</td>
</tr>
<tr>
<td>Direct medical costs</td>
<td>$116 billion</td>
</tr>
<tr>
<td></td>
<td>After adjusting for population age and sex differences, average medical expenditures among people with diagnosed diabetes were 2.3 times higher than what expenditures would be in the absence of diabetes.</td>
</tr>
<tr>
<td>Indirect costs</td>
<td>$58 billion (disability, work loss, premature mortality)</td>
</tr>
</tbody>
</table>

Medical expenses for people with diabetes are more than two times higher than for people without diabetes.
Preventing diabetes complications

Glucose control

- Studies in the United States and abroad have found that improved glycemic control benefits people with either type 1 or type 2 diabetes. In general, every percentage point drop in A1c blood test results (e.g., from 8.0% to 7.0%) can reduce the risk of microvascular complications (eye, kidney, and nerve diseases) by 40%. The absolute difference in risk may vary for certain subgroups of people.
- In patients with type 1 diabetes, intensive insulin therapy has long-term beneficial effects on the risk of cardiovascular disease.

Blood pressure control

- Blood pressure control reduces the risk of cardiovascular disease (heart disease or stroke) among people with diabetes by 33% to 50%, and the risk of microvascular complications (eye, kidney, and nerve diseases) by approximately 33%.
- In general, for every 10 mmHg reduction in systolic blood pressure, the risk for any complication related to diabetes is reduced by 12%.
- No benefit of reducing systolic blood pressure below 140 mmHg has been demonstrated in randomized clinical trials.
- Reducing diastolic blood pressure from 90 mmHg to 80 mmHg in people with diabetes reduces the risk of major cardiovascular events by 50%.

Control of blood lipids

- Improved control of LDL cholesterol can reduce cardiovascular complications by 20% to 50%.

Preventive care practices for eyes, feet, and kidneys

- Detecting and treating diabetic eye disease with laser therapy can reduce the development of severe vision loss by an estimated 50% to 60%.
- About 65% of adults with diabetes and poor vision can be helped by appropriate eyeglasses.
- Comprehensive foot care programs, i.e., that include risk assessment, foot-care education and preventive therapy, treatment of foot problems, and referral to specialists, can reduce amputation rates by 45% to 85%.
- Detecting and treating early diabetic kidney disease by lowering blood pressure can reduce the decline in kidney function by 30% to 70%. Treatment with particular medications for hypertension called angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) is more effective in reducing the decline in kidney function than is treatment with other blood pressure lowering drugs.
- In addition to lowering blood pressure, ARBs and ACEIs reduce proteinuria, a risk factor for developing kidney disease, by about 35%.

Detecting and treating diabetic eye disease with laser therapy can reduce the development of severe vision loss by an estimated 50% to 60%. 
General information

Prevention or delay of type 2 diabetes

- The Diabetes Prevention Program (DPP), a large prevention study of people at high risk for diabetes, showed that lifestyle intervention to lose weight and increase physical activity reduced the development of type 2 diabetes by 58% during a 3-year period. The reduction was even greater, 71%, among adults aged 60 years or older.
- Treatment with the drug metformin reduced the risk by 31% overall and was most effective in younger (aged 25–44 years) and in heavier (body mass index ≥35) adults.
- Prevention or delay of type 2 diabetes with either lifestyle or metformin intervention was effective in all racial and ethnic groups studied and has been shown to persist for at least 10 years.
- Interventions to prevent or delay type 2 diabetes in individuals with prediabetes can be feasible and cost-effective. Research has found that lifestyle interventions are more cost-effective than medications.

Acknowledgements

The following organizations collaborated in compiling the information for this fact sheet:

American Association of Diabetes Educators: http://www.diabeteseducator.org
American Diabetes Association: http://www.diabetes.org
Centers for Medicare & Medicaid Services: http://cms.hhs.gov
U.S. Department of Veterans Affairs: http://www.healthquality.va.gov
U.S. Food and Drug Administration: http://www.fda.gov
Health Resources and Services Administration: http://www.hrsa.gov
Indian Health Service: http://www.hhs.gov/programs/diabetes/index.asp
Juvenile Diabetes Research Foundation International: http://www.jdrf.org
National Diabetes Education Program, a joint program of NIH and CDC: http://www.yourdiabetesinfo.org

* Links to non-Federal organizations are provided solely as a service to our users. Links do not constitute an endorsement of any organization by CDC or the Federal Government, and none should be inferred. The CDC is not responsible for the content of the individual organization Web pages found at this link.

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For other information:
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National Center for Chronic Disease Prevention and Health Promotion
Centers for Disease Control and Prevention
4770 Buford Highway NE, Mailstop K-10, Atlanta, GA 30341-3717
Phone: 770-488-5000, http://www.cdc.gov/diabetes


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New Drug Approvals

August 10, 2011

COMPLERA™ (EMTRICITABINE; RILPIVIRINE; TENOFOVIR DISOPROXIL FUMARATE)

Manufacturer: Gilead

About this product: COMPLERA, a combination of 2 nucleoside analog HIV-1 reverse transcriptase inhibitors (emtricitabine and tenofovir disoproxil fumarate) and 1 non-nucleoside reverse transcriptase inhibitor (rilpivirine), is indicated for use as a complete regimen for the treatment of HIV-1 infection in treatment-naive adults. The following points should be considered when initiating therapy with COMPLERA:

- More rilpivirine-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure compared to subjects with HIV-1 RNA less than 100,000 copies/mL at the start of therapy.
- The observed virologic failure rate in rilpivirine-treated subjects conferred a higher rate of overall treatment resistance and cross-resistance to the NNRTI class compared to efavirenz.
- More subjects treated with rilpivirine developed lamivudine/emtricitabine associated resistance compared to efavirenz.
- COMPLERA is not recommended for patients less than 18 years of age.

August 17, 2011

ZELBORAF™ (VEMURAFENIB)

Manufacturer: HOFFMAN-LA ROCHE

About this product: ZELBORAF™ is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAFV600E mutation as detected by an FDA-approved test.

Limitation of Use: ZELBORAF is not recommended for use in patients with wild-type BRAF melanoma.

August 25, 2011

FIRAZYR® (ICATIBANT ACETATE)

Manufacturer: SHIRE ORPHAN THERAPIES

About this product: FIRAZYR is a bradykinin B2 receptor antagonist indicated for treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older.

August 26, 2011

XALKORI® (CRIZOTINIB)

Manufacturer: Pfizer

About this product: XALKORI is a kinase inhibitor indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. This indication is based on response rate. There is no data available demonstrating improvement in patient reported outcomes or survival with XALKORI.
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Prescribe Denavir — your patients can be prepared for their next outbreak.

Convenience of a 5-gram tube.
Potentially only one patient co-pay for multiple outbreaks.

Efficacy at your patient’s fingertips.
Patients apply steroid-free Denavir directly to the cold sore, providing relief from the discomfort, dryness and cracking.

Reduction in the duration of the lesion.
Denavir also reduces the duration of pain associated with the lesion.

The same trusted MOA as oral antivirals. Denavir is an effective, topical cream, antiviral medication that is not systemically absorbed.

Eligible patients pay no more than $15 with a coupon (subject to eligibility restrictions and limitations). Visit denavir.com for details.

A favorable safety profile.
Denavir was well tolerated in clinical trials. The most frequently reported adverse events were headache (5.3% vs. 5.8% with placebo) and application site reaction (1.3% vs. 1.8% with placebo).

Dosing every 2 hours during waking hours for a period of 4 days.

New American Therapeutics, Inc. supports physicians and patients with educational materials and coupons (subject to eligibility restrictions and limitations). Please see full restrictions and limitations below. Download both at no cost at Denavir.com or call 1-888-DENAVIR (1-888-336-2847).

Denavir® (penciclovir cream, 1%) is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older.

IMPORTANT SAFETY INFORMATION
Denavir should only be used on herpes labialis on the lips or face. Application to mucous membranes is not recommended. Denavir should not be used in patients with known hypersensitivity to the product or any of its ingredients.

Denavir is available by prescription only. Please see the Full Prescribing Information on the back.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

*The systemic absorption of penciclovir following topical administration has not been evaluated in patients less than 18 years of age.

If a patient’s co-pay or pharmacy bill exceeds $15, they can present the certificate to the pharmacist for an instant rebate of up to a maximum of $45 for each Denavir prescription. If their total out of pocket pharmacy bill exceeds $80 for any single Denavir prescription, they will be responsible for the additional balance. Not valid with any other offer. Subject to eligibility restrictions and limitations. This offer is not valid for prescriptions reimbursed in whole or part by Medicaid, Medicare, or any other federal or state program (including any prescription drug programs). This offer is not valid in Massachusetts except for cash-paying patients, or where otherwise prohibited by law.

References

New American Therapeutics, Inc. holds the exclusive right to market and distribute Denavir in the United States. Denavir® is a registered trademark of New American Therapeutics, Inc.
**Denavir**

**Denavir** is a white to pale yellow solid or crystal with a mp of 25-35°C. It has a solubility of 1 mg/ml in methanol, 13 mg/ml in propylene glycol, and 17 mg/ml in water. It is stable at pH 1-7 for 24 hours and is not affected by heat (up to 100°C).

**Pharmacokinetics**: Denavir contains penicillin, an antibiotic active against herpes viruses. Denavir is excrated for topical administration as a 1% cream. Each gram contains 100 mg of penicillin V potassium and the following inactive ingredients: croscarmellose sodium, 100 mg; cornstarch, 50 mg; lactose, 50 mg; magnesium stearate, 10 mg; polyethylene glycol 400, 2 mg; polyvinyl alcohol 2 mg; purified water to 1 g.

**Microbiology**: Denavir contains penicillin V potassium, an antibiotic active against herpes viruses. Denavir is excrated for topical administration as a 1% cream. Each gram contains 100 mg of penicillin V potassium and the following inactive ingredients: croscarmellose sodium, 100 mg; cornstarch, 50 mg; lactose, 50 mg; magnesium stearate, 10 mg; polyethylene glycol 400, 2 mg; polyvinyl alcohol 2 mg; purified water to 1 g.

**Clinical Trials**: Denavir was studied in two double-blind, placebo-controlled trials for the treatment of recurrent herpes labialis in otherwise healthy adults. Infection was initiated by the subjects themselves (patients in the placebo group). Denavir was initiated within 48 hours of the first appearance of the lesions. The mean duration of lesion was approximately 4.5 days.

**INDICATIONS AND USAGE**: Denavir is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older.

**Contraindications**: Denavir is contraindicated in patients with known hypersensitivity to the product or any of its components.

**Precautions**: General

**Drug Interactions**: Denavir is a penicillin derivative and may be subject to the same type of interactions as penicillin. Consult the product information for specific details.

**Overdosage**: Denavir is a penicillin derivative and may be subject to the same type of interactions as penicillin. Consult the product information for specific details.

**Adverse Reactions**: Denavir is a penicillin derivative and may be subject to the same type of interactions as penicillin. Consult the product information for specific details.

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Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011

On August 18, 2011, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

This document provides updated guidance for the use of influenza vaccines in the United States for the 2011–12 influenza season. In 2010, the Advisory Committee on Immunization Practices (ACIP) first recommended annual influenza vaccination for all persons aged ≥6 months in the United States (1,2). Vaccination of all persons aged ≥6 months continues to be recommended. Information is presented in this report regarding vaccine strains for the 2011–12 influenza season, the vaccination schedule for children aged 6 months through 8 years, and considerations regarding vaccination of persons with egg allergy. Availability of a new Food and Drug Administration (FDA)-approved intradermally administered influenza vaccine formulation for adults aged 18 through 64 years is reported. For issues related to influenza vaccination that are not addressed in this update, refer to the 2010 ACIP statement on prevention and control of influenza with vaccines and associated updates (1,2).

Methodology for the formulation of the ACIP annual influenza statement has been described previously (1). The ACIP Influenza Work Group meets every 2–4 weeks throughout the year. Work Group membership includes several voting members of the ACIP, as well as representatives from ACIP Liaison Organizations. Meetings are held by teleconference and include discussion of influenza-related issues, such as vaccine effectiveness and safety, coverage in groups recommended for vaccination, feasibility, cost-effectiveness, and anticipated vaccine supply. Presentations are requested from invited experts, and published and unpublished data are discussed. CDC’s Influenza Division provides influenza surveillance and antiviral resistance data, and the Immunization Safety Office and Immunization Services Division provide information on vaccine safety and distribution and coverage, respectively.

Vaccine Strains for the 2011–12 Influenza Season

The 2011–12 U.S. seasonal influenza vaccine virus strains are identical to those contained in the 2010–11 vaccine. These include A/California/7/2009 (H1N1)-like, A/Perth/16/2009 (H3N2)-like, and B/Brisbane/60/2008-like antigens. The influenza A (H1N1) vaccine virus strain is derived from a 2009 pandemic influenza A (H1N1) virus (3).

Recommendations for Vaccination

Routine annual influenza vaccination is recommended for all persons aged ≥6 months (1). To permit time for production of protective antibody levels (4,5), vaccination should optimally occur before onset of influenza activity in the community, and providers should offer vaccination as soon as vaccine is available. Vaccination also should continue to be offered throughout the influenza season.

Although influenza vaccine strains for the 2011–12 season are unchanged from those of 2010–11, annual vaccination is recommended even for those who received the vaccine for the previous season. Although in one study of children vaccinated against A/Hong Kong/68 (H3N2) virus, vaccine efficacy remained high against this strain 3 years later, the estimated efficacy of vaccine decreased over the seasons studied (6). Moreover, several studies have demonstrated that postvaccination antibody titers decline over the course of a year (7–10). Thus, annual vaccination is recommended for optimal protection against influenza.

Vaccine Doses for Children Aged 6 Months Through 8 Years

Children aged 6 months through 8 years require 2 doses of influenza vaccine (administered a minimum of 4 weeks apart) during their first season of vaccination to optimize immune response. In a study of children aged 5 through 8 years who received trivalent inactivated vaccine (TIV) for the first time, the proportion of children with protective antibody responses was significantly higher after 2 doses than after 1 dose (11).

The importance of vaccine priming might depend more on the similarity of the antigenic composition between the priming and second dose than the temporal interval between doses. From the 2003–04 to 2004–05 influenza seasons, the A(H1N1) virus antigen remained unchanged; however, the A(H3N2) virus antigen changed to a drifted strain, and the B virus antigen changed more substantially to a different lineage. In a study conducted over those two seasons, influenza-vaccine naïve children aged 6 through 23 months who received 1 dose of TIV in the spring of their first year of vaccination followed by a second dose in the fall were less likely to have protective antibody responses to the A(H3N2) and B virus antigens when compared with children who received 2 doses of identical vaccine in the fall (12). Response to the unchanged A(H1N1) virus antigen was comparable between the groups. In another study conducted over the same two seasons, unprimed children aged 10 through 24 months who received 1 dose of TIV during the fall of each season had similar responses to the unchanged A(H1N1) virus antigen as well as to the drifted A(H3N2) virus antigen when compared with children aged 6 through 24
months who received 2 doses of the same TIV during the latter season; however, the first group had significantly lower response to the B virus antigen (13). During two seasons in which all influenza vaccine virus antigens were identical, unprimed children aged 6 through 23 months had similar responses when they received 1 dose in the spring followed by a second dose in the fall, as compared with 2 doses received 1 month apart in the fall (14). Studies of inactivated monovalent pandemic 2009 (H1N1) vaccine in children aged <9 years also have demonstrated improved response to this antigen when 2 doses are administered (15–17).

Vaccination providers should note that, in previous seasons, children aged 6 months through 8 years who received only 1 dose of influenza vaccine in their first year of vaccination required 2 doses the following season. However, because the 2011–12 vaccine strains are unchanged from the 2010–11 season, children in this age group who received at least 1 dose of the 2010–11 seasonal vaccine will require only 1 dose of the 2011–12 vaccine. Children in this age group who did not receive at least 1 dose of the 2010–11 seasonal influenza vaccine, or for whom it is not certain whether the 2010–11 seasonal vaccine was received, should receive 2 doses of the 2011–12 seasonal influenza vaccine (Figure 1). Recommendations regarding the number of doses for this age group might change for the 2012–13 season if vaccine antigens change.

Available Vaccine Products and Indications

Multiple influenza vaccines are expected to be available during the 2011–12 season (Table). All contain the same antigenic composition. Package inserts should be consulted for information regarding additional components of various vaccine formulations.

TIV preparations, with the exception of Fluzone Intradermal (Sanofi Pasteur), should be administered intramuscularly. For adults and older children, the deltoid is the preferred site. Infants and younger children should be vaccinated in the anterolateral thigh. Specific guidance regarding site and needle length can be found in the ACIP’s General Recommendations on Immunization (18).

A new intradermally administered TIV preparation, Fluzone Intradermal, was licensed in May 2011. This vaccine is indicated for persons aged 18 through 64 years and contains less antigen than intramuscular TIV preparations (9 μg rather than 15 μg of each strain per dose) in a smaller volume (0.1 mL rather than 0.5 mL). The vaccine is administered intradermally via a single-dose, prefilled microinjection syringe. The preferred site for administration is over the deltoid muscle (19). The most common adverse reactions include injection-site erythema, induration, swelling, pain, and pruritus. With the exception of pain, these reactions occurred more frequently than with intramuscular vaccine, but generally resolved within 3–7 days. This vaccine is an alternative to other TIV preparations for those in the indicated age range, with no preferential recommendation.

As during the 2010–11 season, a vaccine containing 60 μg of hemagglutinin per vaccine strain (rather than 15 μg per strain as in other intramuscular TIV preparations), Fluzone High-Dose (Sanofi Pasteur), is available as an alternative TIV for persons aged ≥65 years. No preference is indicated for this TIV versus other TIV preparations (1).

The intranasally administered live attenuated influenza vaccine (LAIV), FluMist (MedImmune) is indicated for healthy, nonpregnant persons aged 2 through 49 years. Within the indicated groups specified for each vaccine in the package inserts, no preference is indicated for LAIV versus TIV (1).

**Vaccination of Persons Reporting Allergy to Eggs**

Allergy to eggs must be distinguished from allergy to influenza vaccine. Severe allergic and anaphylactic reactions can occur in response to a number of influenza vaccine components, but such reactions are rare. A review of reports to the Vaccine Adverse Events Reporting System (VAERS) of adverse events in adults noted four reports of death caused by anaphylaxis following influenza vaccine during 1990–2005; the vaccine components potentially responsible for these reactions were not reported (20). A prior severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to receipt of influenza vaccine.

All currently available influenza vaccines are prepared by inoculation of virus into chicken eggs. Hypersensitivity to eggs has been listed as a contraindication to receipt of influenza vaccine on most package inserts. However, several recent studies have documented safe receipt of TIV in persons with egg allergy (21–29), and recent revisions of some TIV.
### TABLE. Influenza vaccine information, by age group — United States, 2011–12 influenza season

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>Mercury content (µg Hg/0.5 mL dose)</th>
<th>Ovalbumin content (µg/0.5 mL dose)</th>
<th>Age group</th>
<th>No. of doses</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIV</td>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>0.25 mL prefilled syringe</td>
<td>0.0</td>
<td>—</td>
<td>6-35 mos</td>
<td>1 or 2&lt;sup&gt;6&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>—</td>
<td>≥6 mos</td>
<td>1 or 2&lt;sup&gt;6&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 mL vial</td>
<td>0.0</td>
<td>—</td>
<td>≥6 mos</td>
<td>1 or 2&lt;sup&gt;6&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>25.0</td>
<td>—</td>
<td>≥4 yrs</td>
<td>1 or 2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluvin</td>
<td>Novartis Vaccines</td>
<td>0.5 mL prefilled syringe</td>
<td>≤1</td>
<td>≤1</td>
<td>≥6 yrs</td>
<td>1 or 2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>25.0</td>
<td>≤1</td>
<td>≥6 yrs</td>
<td>1 or 2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluarix</td>
<td>GlaxoSmithKline</td>
<td>0.5 mL prefilled syringe</td>
<td>0</td>
<td>≤0.05</td>
<td>≥3 yrs</td>
<td>1 or 2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Flulaval</td>
<td>ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline)</td>
<td>5.0 mL multidose vial</td>
<td>25.0</td>
<td>≤1</td>
<td>≥18 yrs</td>
<td>1</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Allflur</td>
<td>CSL Biotherapies (distributed by Merck)</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>≤1</td>
<td>≥9 yrs&lt;sup&gt;**&lt;/sup&gt;</td>
<td>1</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>24.5</td>
<td>≤1</td>
<td>≥6 yrs</td>
<td>1</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>—</td>
<td>≥6 yrs</td>
<td>1</td>
<td>IM&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>0.1 mL prefilled microinjection system</td>
<td>0.0</td>
<td>—</td>
<td>18–64 yrs</td>
<td>1</td>
<td>ID</td>
</tr>
<tr>
<td>LAIV</td>
<td>FluMist&lt;sup&gt;65&lt;/sup&gt;</td>
<td>MedImmune</td>
<td>0.2 mL prefilled intranasal sprayer</td>
<td>0.0</td>
<td>—</td>
<td>2–49 yrs&lt;sup&gt;***&lt;/sup&gt;</td>
<td>1 or 2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>IN</td>
</tr>
</tbody>
</table>

**Abbreviations:** TIV = trivalent inactivated vaccine; LAIV = live attenuated influenza vaccine; IM = intramuscular; ID = intradermal; IN = intranasal.

* Vaccination providers should check Food and Drug Administration–approved prescribing information for 2011–12 influenza vaccines for the most updated information.
† Information not included in package insert but is available upon request from the manufacturer, Sanofi Pasteur, by telephone, 1-800-822-2463, or e-mail, MIS.Emails@sanofipasteur.com.
<sup>5</sup> Children aged 6 months through 8 years who did not receive seasonal influenza vaccine during the 2010–11 influenza season should receive 2 doses at least 4 weeks apart for the 2011–12 season. Those children aged 6 months through 8 years who received ≥1 dose of the 2010–11 seasonal vaccine require 1 dose for the 2011–12 season.
<sup>6</sup> For adults and older children, the recommended site of vaccination is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.
<sup>**</sup> Age indication per package insert is ≥5 years; however, the Advisory Committee on Immunization Practices recommends Allflur not be used in children aged 6 months through 8 years because of increased reports of febrile reactions in this age group. If no other age-appropriate, licensed inactivated seasonal influenza vaccine is available for a child aged 5–8 years who has a medical condition that increases the child’s risk for influenza complications, Allflur can be used; however, providers should discuss with the parents or caregivers the benefits and risks of influenza vaccination with Allflur before administering this vaccine. Allflur may be used in persons aged ≥9 years.
<sup>65</sup> TIV high-dose: A 0.5-mL dose contains 60 µg each of A/California/7/2009 (H1N1)-like, A/Perth/16/2009 (H3N2)-like, and B/Brisbane/60/2008-like antigens.
<sup>66</sup> FluMist is shipped refrigerated and stored in the refrigerator at 35°F–46°F (2°C–8°C) after arrival in the vaccination clinic. The dose is 0.2 mL divided equally between each nostril. Health-care providers should consult the medical record, when available, to identify children aged 2–4 years with asthma or recurrent wheezing that might indicate asthma. In addition, to identify children who might be at greater risk for asthma and possibly at increased risk for wheezing after receiving LAIV, parents or caregivers of children aged 2–4 years should be asked: “In the past 12 months, has a health-care provider ever told you that your child had wheezing or asthma?” Children whose parents or caregivers answer “yes” to this question and children who have asthma or who had a wheezing episode noted in the medical record within the past 12 months should not receive FluMist.
<sup>67</sup> Insufficient data available for use of LAIV in egg-allergic persons.
<sup>65</sup> FluMist is indicated for healthy, nonpregnant persons aged 2–49 years.

Package inserts note that only a severe allergic reaction (e.g., anaphylaxis) to egg protein is a contraindication. In general, these studies include relatively fewer persons reporting a history of anaphylactic reaction to egg, compared with less severe reactions. Several documents providing guidance on use of influenza vaccine in persons with egg allergy have been published recently (30–32).

The quantity of egg protein in vaccine is expressed as the concentration of ovalbumin per dose or unit volume. Among studies in which the ovalbumin content of the administered vaccine was reported, up to 1.4 µg/mL (0.7 µg/0.5 mL dose) was tolerated without serious reactions (22,23,25–29); however, a safe maximum threshold of ovalbumin, below which no anaphylactic reactions would be expected, is not known.

Although ovalbumin content is not required to be disclosed on package inserts for vaccines used in the United States, manufacturers either report maximum albumin content in the package inserts or will provide this information on request. Ovalbumin concentration can vary from season to season and from lot to lot for a given vaccine. Independent assessments of
ovalbumin content of commercially available vaccines have noted lower concentrations than those listed on package inserts (33,34).

In several studies evaluating influenza vaccine in persons with egg allergy, additional safety measures have been taken, such as skin prick testing with vaccine (21–24,26,28,29) and administering the vaccine in 2 doses (e.g., 10% of the dose initially, followed by the remaining 90% if no reaction has occurred during a 30-minute observation period) (22,24–29). Skin prick testing with vaccine was poorly predictive of allergic reactions in these studies (22–24,26). In general, administration of both full doses and split doses have been well-tolerated without serious reactions, although systemic reactions (e.g., wheezing, eczema exacerbation, and hives on face/chest) were observed with the initial 10% dose among six (3.5%) of 171 participants in one study (24).

**Recommendations Regarding Persons with Egg Allergy**

Each of the following recommendations applies when considering influenza vaccination of persons who have or report a history of egg allergy:

1. Persons who have experienced only hives following exposure to egg should receive influenza vaccine with the following additional measures (Figure 2):
   a. Because studies published to date involved use of TIV, TIV rather than LAIV should be used.
   b. Vaccine should be administered by a health-care provider who is familiar with the potential manifestations of egg allergy.
   c. Vaccine recipients should be observed for at least 30 minutes for signs of a reaction following administration of each vaccine dose.

Other measures, such as dividing and administering the vaccine by a two-step approach and skin testing with vaccine, are not necessary.

2. Persons who report having had reactions to egg involving angioedema, respiratory distress, lightheadedness, or recurrent emesis, or persons who required epinephrine or other emergency medical intervention, particularly those that occurred immediately or within minutes to hours after egg exposure are more likely to have a serious systemic or anaphylactic reaction upon reexposure to egg proteins. Before receipt of vaccine, such persons should be referred to a physician with expertise in the management of allergic conditions for further risk assessment (Figure 2).

3. All vaccines should be administered in settings in which personnel and equipment for rapid recognition and treatment of anaphylaxis are available. ACIP recommends that all vaccination providers be familiar with the office emergency plan (18).

4. Some persons who report allergy to egg may not be egg allergic. Those who are able to eat lightly cooked egg (e.g., scrambled eggs) without reaction are unlikely to be allergic. Conversely, egg-allergic persons may tolerate egg in baked products (e.g., bread or cake); tolerance to egg-containing foods does not exclude the possibility of egg allergy (35). Egg allergy can be confirmed by a consistent medical history of adverse reactions to eggs and egg-containing foods, plus skin and/or blood testing for immunoglobulin E antibodies to egg proteins.

5. A previous severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to receipt of influenza vaccine.

**FIGURE 2. Recommendations regarding influenza vaccination for persons who report allergy to eggs — Advisory Committee on Immunization Practices (ACIP), 2011–12 influenza season**

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can the person eat lightly cooked egg (e.g., scrambled egg) without reaction?*</td>
<td>Yes: Administer vaccine per usual protocol. No: After eating eggs or egg-containing foods, does the person experience ONLY hives?</td>
</tr>
<tr>
<td>Yes:</td>
<td>Yes: Refer to a physician with expertise in management of allergic conditions for further evaluation. No: Does the person experience other symptoms such as cardiovascular changes (e.g., hypotension), respiratory distress (e.g., wheezing), gastrointestinal (e.g., nausea/vomiting), reaction requiring epinephrine, reaction requiring emergency medical attention.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Persons with egg allergy might tolerate egg in baked products (e.g., bread or cake). Tolerance to egg-containing foods does not exclude the possibility of egg allergy.

**Reported by**

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Concentration Lowered in Tamiflu Medication

When flu season arrives this fall, a liquid form of Tamiflu—the most widely used anti-viral flu medication—will be available in a new, lower concentration to reduce the possibility of medication errors.

The change applies to the oral suspension form of Tamiflu and not the capsule. Oral suspension is a powder form of the prescription medication that a pharmacist mixes with water to make a liquid treatment easier to take by children or adults who are unable to swallow a Tamiflu capsule.

The Tamiflu packaging of its oral suspension product says “new strength” because the concentration of medicine in the liquid has been changed from 12 mg/mL (milligrams per milliliter) to 6 mg/mL. This change in concentration means that the amount of medicine that must be taken has also changed. If taken as directed, the medicine is still as effective as it was before.

The Food and Drug Administration worked with Genentech Inc., manufacturer of Tamiflu, to create the new 6 mg/mL medication to reduce the possibility of errors in getting the correct dose. It will replace the 12 mg/mL concentration, which will no longer be manufactured but will be available until expiration.

Tamiflu is FDA-approved to treat adults and children older than 1 year who have had influenza symptoms for two days or less. Tamiflu stops the virus from spreading in the body and can help shorten the duration of such symptoms as a stuffy or runny nose, sore throat, cough and muscle aches.

Linda Lewis, medical team leader in FDA’s Division of Antiviral Products, explains that there have been no reported cases of serious side effects related to medication errors involving oral suspension Tamiflu. But there were many reports of confusion about administering the right dose during the influenza pandemic in 2009, Lewis says.

That’s because when mixed as directed, the 12 mg/mL concentration gets frothy and bubbly and it can be difficult to get the right amount. “We were concerned that the measurement of the dose was not very reliable,” Lewis says. She adds that the mixture is not frothy when the concentration is lower.

Containers of the low-concentration medication will come with new dosing instructions based on body weight.

In addition, the dosing device has been changed to a 10-milliliter oral syringe, which will make it easier to accurately measure the correct dose. The dosing device originally packaged with the 12 mg/mL suspension was marked in 30 and 45 mg, which caused confusion in measuring the liquid medication.

Preparing for the next flu season
Because there are no quality issues with the 12 mg/mL concentration Tamiflu, it will remain on the market until supplies run out and can be used until its expiration date.

With both dose concentrations being available during the flu season this fall, Kendall Marcus, safety deputy in FDA’s Division of Antiviral Products, cautions that pharmacists and physicians will have to be particularly careful in prescribing and dispensing the medication.

After the next flu season, only the 6 mg/mL concentration will be available.
"We were concerned that the measurement of the dose was not very reliable."

Marcus says consumers need to know the following:
- You could receive either the 6 mg/mL or the 12 mg/mL version at your local pharmacy during the next flu season. If you have any questions about how to use the product safely, speak to your pharmacist or other health care provider.
- If you have taken oral suspension Tamiflu in the past, the container and label will look different.
- The new oral dosing device is different and the volume (mL) of your dose may differ from past prescriptions.
- If you have any problems with the medication, report them to your health care provider and to FDA’s MedWatch program.

Marcus notes that pediatric strength Tamiflu capsules (30 mg and 45 mg) have not changed and are still available for children who can swallow capsules. Another option for parents is to open the capsule and mix its contents with a flavored food, like chocolate syrup. 

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We have reserved this section of our *BioTherapeutics Quarterly* journal for Generic Pharmaceutical topics. In this issue we highlight the industry’s top companies with a special focus on the world’s largest generic manufacturing company, Teva Pharmaceuticals. As previously reported, today generics account for more than 75% of all prescriptions dispensed in the US with the industry poised for yet another period of growth and significant changes. Teva along with the other market leaders are well positioned to continue to lead the way.

According to IMS Health, a leading health care information and consulting company, below are the top 10 US generic companies in 2009 sales.

1. Teva Pharmaceutical  
2. Mylan  
3. Sandoz  
4. Watson Pharmaceuticals  
5. Greenstone  
6. Par Pharma  
7. Hospira  
8. Apotex  
9. Mallinckrodt  
10. Dr. Reddy’s

**Teva by the Numbers**

- No.1 Generic Pharmaceutical Company in the World
- A Top 15 Global Pharmaceutical Company
- $16 Billion in sales 2010
- Direct Presence in 60 Countries
- Product distribution in over 120 Markets
- 42,000 Employees
- 63 Billion tablets manufactured in 2010
- Over 4,000 Quality Assurance employees
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