



National Influenza Vaccine Summit

Jeff Levine, MD
GlaxoSmithKline
Director, Medical Affairs
North American Vaccine Development

©2013 The GlaxoSmithKline Group of Companies.
All Rights Reserved.

Table of Contents

- GSK Influenza Brands and Approved Indication for use
- Important Safety Information
- 2012/2013 Market Performance
- 2013/2014 Projected Supply
- Research and Burden of B-Disease
- GSK Investments and Commitment to Influenza Vaccination
 - Pediatric Indications
 - Quadrivalent Vaccines
 - Cell Culture Vaccine Development, Manufacturing and Pandemic Preparedness
 - Increased U.S. Supply for Quadrivalent Vaccines for 2014 and beyond
 - Global Research and Development and Vaccine Donation Efforts

GSK Influenza Brands

Fluarix **Quadrivalent®** Influenza Virus Vaccine

- Approved for use in persons 3 years of age and older
- Available in a 0.5 mL single-dose pre-filled syringe (tip caps of the prefilled syringes may contain latex)
- Thimerosal- free
- Manufactured in Dresden, Germany

GSK Influenza Brands

Fluarix® Influenza Virus Vaccine

- Approved for use in persons 3 years of age and older
- Available in a 0.5 mL single-dose pre-filled syringe (tip caps of the prefilled syringes may contain latex)
- Thimerosal- free
- Manufactured in Dresden, Germany

FluLaval® Influenza Virus Vaccine

- Approved for adults 18 years of age and older
- Available in a 5 mL multi-dose vial containing 10 doses (0.5 mL each)
- Contains thimerosal as a preservative. Each 0.5 mL dose contains 25 micrograms of mercury
- Manufactured in Quebec, Canada

FLUARIX QUADRIVALENT is a vaccine indicated for active immunization for the prevention of disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. FLUARIX QUADRIVALENT is approved for use in persons 3 years of age and older.

▪ **Important Safety Information**

- Do not administer FLUARIX QUADRIVALENT to anyone with known severe allergic reactions (anaphylaxis) to any component of the vaccine, including egg protein, or a life-threatening reaction to previous administration of any influenza vaccine.
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUARIX QUADRIVALENT should be based on careful consideration of the potential benefits and risks.
- The tip caps of the prefilled syringes may contain natural rubber latex which may cause allergic reactions in latex-sensitive individuals.
- If FLUARIX QUADRIVALENT is administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the immune response may be lower than in immunocompetent persons.
- Syncope (fainting) can occur in association with administration of injectable vaccines. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.
- In clinical trials with FLUARIX QUADRIVALENT, the most common adverse reactions in adults were pain at the injection site, muscle aches, headaches, and fatigue. In children 3 through 17 years of age, injection site adverse reactions were pain, redness, and swelling. In children 3 through 5 years of age, the most common systemic adverse events were drowsiness, irritability, and loss of appetite. In children 6 through 17 years of age, the most common systemic adverse events were fatigue, muscle aches, headache, arthralgia, and gastrointestinal symptoms. (See Adverse Reactions section of the Prescribing Information for FLUARIX QUADRIVALENT for other potential adverse reactions and events).
- Vaccination with FLUARIX QUADRIVALENT may not result in protection in all vaccine recipients.

FLUARIX is a vaccine indicated for active immunization for the prevention of disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUARIX is approved for use in persons 3 years of age and older.

▪ **Important Safety Information**

- Do not administer FLUARIX to anyone with known severe allergic reactions to egg proteins (a vaccine component) or a life-threatening reaction to previous administration of any influenza vaccine
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUARIX should be based on careful consideration of the potential benefits and risks
- The tip caps of the prefilled syringes may contain natural rubber latex which may cause allergic reactions in latex-sensitive individuals
- If FLUARIX is administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the immune response may be lower than in immunocompetent persons
- Syncope (fainting) can occur in association with administration of injectable vaccines. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope
- In clinical trials with FLUARIX, the most common adverse reactions in adults included injection site pain and redness, muscle aches, fatigue, and headache. In children 5 years to <18 years of age, the most common adverse reactions were similar to those in adults but also included injection site swelling. In children 3 years to <5 years of age, the most common adverse reactions included pain, redness, and swelling at the injection site, irritability, drowsiness, and loss of appetite. (See Adverse Reactions section of the Prescribing Information for FLUARIX for other potential adverse reactions and events.)
- Vaccination with FLUARIX may not result in protection in all vaccine recipients

FLULAVAL is a vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLULAVAL is approved for use in persons 18 years of age and older. This indication is based on immune response elicited by FLULAVAL, and there have been no controlled trials adequately demonstrating a decrease in influenza disease after vaccination with FLULAVAL.

▪ **Important Safety Information**

- Do not administer FLULAVAL to anyone with known severe allergic reactions (eg, anaphylaxis) to any component of the vaccine including egg protein or to a previous dose of any influenza vaccination
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLULAVAL should be based on careful consideration of the potential benefits and risks
- If FLULAVAL is administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the immune response may be lower than in immunocompetent persons
- Syncope (fainting) can occur in association with administration of injectable vaccines. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope
- In comparator-controlled clinical trials with FLULAVAL, adverse reactions included pain, redness, and swelling at the injection site; headache; fatigue; and myalgia/arthralgia. (See Adverse Reactions section of the Prescribing Information for FLULAVAL for other potential adverse reactions and events)
- Vaccination with FLULAVAL may not result in protection in all vaccine recipients

2012/2013 Market Performance

- GSK supplied ~21 million doses to the pre-booking market demand and projected in-season demand.
- GSK notified 100% of our customers that their orders were ready to be scheduled for shipment by September 15th, 2012
- GSK made more than 3M doses of flu vaccine available for immediate shipping starting on August 16th to help with the U.S. epidemic. GSK sold out of vaccine in January of 2013

2013-2014 Vaccine Delivery Projections and Timing

- GSK estimates 22 to 24 million doses will be supplied to the US with up to 10M doses in Quadrivalent vaccines.
- Shipments are expected to begin mid-July; however, all estimates are dependent on regulatory approval and internal QA review/approval and adjusted based on final customer demand received by GSK
- GSK is planning on making limited volumes of FluLaval Quadrivalent available for the 2013 season should it receive FDA approval prior to the start of the vaccination season. These doses would be potentially available in-season since discussion of product orders with providers can only be discussed upon FDA product approval
- *These are early estimates provided for planning purposes and are not a commitment to dates and amounts of vaccine*

In 6 of the 11 past flu seasons the B lineage in the influenza vaccine did not match the predominantly circulating B lineage

Predominant circulating influenza B lineage compared with the influenza B lineage selected: 2001-2012^{5,6}

Season	Influenza B: Circulating B Lineage (%)		B Lineage in Vaccine	Circulating B Lineage Match With Vaccine (%)	Predominant Circulating B Lineage vs B Lineage in Vaccine
	Victoria	Yamagata			
2001-02	77	23	Yamagata	23	Mismatch
2002-03	100	0	Victoria	100 ^a	Match
2003-04	7	93	Victoria	7	Mismatch
2004-05	26	74	Yamagata	74	Match
2005-06	81	19	Yamagata	19	Mismatch
2006-07	77	23	Victoria	77	Match
2007-08	2	98	Victoria	2	Mismatch
2008-09	83	17	Yamagata	17	Mismatch
2009-10	88	12	Victoria	88	Match
2010-11	94	6	Victoria	94	Match
2011-12 ⁵	49	51	Victoria	49	Mismatch

^a Actual percentage = 99.6%⁶

Research and Burden of B Disease

- Research program looking at B disease
 - Influenza Burden in the US (IBUS Study)
 - Presented to ACIP WG in March 2013
 - Presently being submitted for publication
 - B disease causes significant morbidity and mortality across all age groups
- FluLaval-Quadrivalent (IIV4) Data
 - Data presentation a draft agenda item for the June 2013 ACIP
 - Previously presented at ID Week October 2012 and to the ACIP WG August 2012
 - 73% efficacy in preventing moderate to severe disease in pediatric ages 3-8 years old

GSK Investment in Influenza Vaccines: Pediatric Influenza Vaccines

- In addition to pending approval for FluLaval Quadrivalent (IIV4) in children 3 years and older, GSK is currently seeking approval for FluLaval (IIV3) for expanded use to include children age 3 years and above
 - sBLA submitted with an action date in Q3, 2013
 - Proposed Indication: age 3 years and above
 - Available in a 5mL multi-dose vial
- GSK has on-going clinical studies to evaluate and support the potential approval and use of both Fluarix Quadrivalent and FluLaval Quadrivalent in persons 6 months and above

GSK Investment in Influenza Vaccines: Quadrivalent Influenza Vaccines

- Fluarix Quadrivalent: GSK received FDA approval for the first Intramuscular Quadrivalent Inactivated Influenza Vaccine (IIV4) on December 14, 2012
 - Approved for use in persons 3 years of age and older
 - Available in a 0.5 mL single-dose pre-filled syringe (tip caps of the pre-filled syringes may contain latex)
 - Thimerosal- free
 - Manufactured in Dresden, Germany
- FluLaval Quadrivalent : GSK is currently seeking approval of a second Intramuscular Quadrivalent Inactivated Influenza Vaccine (IIV4) in Q3, 2013
 - sBLA submitted with an action date in Q3, 2013
 - Proposed Indication: age 3 years and above
 - Proposed availability in both a 0.5mL single-dose pre-filled syringe (Thimerosal- free, tip caps of the pre-filled syringes may contain latex) and a 5mL multi-dose vial
 - Manufactured in Quebec, Canada
- Ongoing clinical development program to seek approval for 6 -35 month indication for Fluarix Quadrivalent and FluLaval Quadrivalent

GSK Investment in Influenza Vaccines: Increased Production Capabilities

- GSK continues to invest in manufacturing capabilities at our sites in Ste Foy, Canada and Dresden, Germany.
- With the anticipated approval of FluLaval Quadrivalent for use in persons 3 years and above; GSK anticipates the capacity to supply ~ 35 million doses of Quadrivalent vaccine (Fluarix Quadrivalent and FluLaval Quadrivalent) to the U.S. market for the 2014-15 influenza season
- GSK's final production volumes are determined based on customer and patient demand and are only limited by our production capacity.

GSK Investment in Influenza Vaccines: Pandemic Preparedness and U.S. Based Manufacture of Flu Vaccines

- GSK is under contract to HHS/BARDA to develop adjuvanted pandemic influenza vaccines against avian influenza A subtypes H5, H7 and H9. This work supports the pandemic preparedness of the US
- GSK and the Texas A&M University System recently announced the U.S. Department of Health and Human Services (DHHS) has approved the establishment of a \$91 million influenza-vaccines manufacturing facility as the anchor of the Center for Innovation in Advanced Development and Manufacturing (CIADM) in Bryan-College Station, Texas.
- This is one of three U.S. facilities that will lead a rapid national vaccine response to a pandemic. When the facility is completed, the CIADM will be capable of producing 50 million doses of pandemic flu vaccine within four months of an outbreak.
- This center sets a new standard for public-private influenza vaccines manufacturing collaboration: It is the only CIADM led by an academic-research university with significant partnership from BARDA, the State of Texas and GSK.
- This will be the first time GSK has manufactured influenza vaccines on U.S. soil. In addition to pandemic- vaccines, the Texas center also will manufacture future GSK seasonal flu vaccines developed from the proprietary Vivalis cell-culture line, EB66®.
 - **More information available at: <http://ciadm.tamus.edu/medi-kit/>**

Commitment to Patients: WHO Pandemic Pledge

- GSK commercial activity in the developed world fuels our commitment to ensuring access to vaccines in the developing world.
- In December 2012, GSK announced it will donate to WHO 7.5 percent of our real-time pandemic-influenza vaccines and reserve another 2.5 percent for WHO allocation.
 - Our hope is that other companies quickly jump on board in making similar commitments for real-time supply to WHO so the world's least-developed countries get access to pandemic vaccines at the same time as more developed countries.
- GSK will also donate two million doses of the anti-viral Relenza and reserve another 8 million doses for WHO as needed.
- For the portion of the commitment involving WHO purchase of vaccines and anti-virals, we will make product available at prices that reflect the wealth and development status of the recipient countries as determined by organizations such as the World Bank, the Global Alliance for Vaccines and Immunization (GAVI) and the United Nations.

Thank You

