

**Package insert**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use AFLURIA safely and effectively. See full prescribing information for AFLURIA.

**AFLURIA, Influenza Vaccine**  
**Suspension for Intramuscular Injection**  
**2017-2018 Formula**  
**Initial U.S. Approval: 2007**

**INDICATIONS AND USAGE**

- AFLURIA is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B present in the vaccine. (1)
- AFLURIA is approved for use in persons 5 years of age and older. (1)

**DOSAGE AND ADMINISTRATION**

For intramuscular (IM) injection only, by needle and syringe (5 years of age and older) or by PharmaJet® Stratis® Needle-Free Injection System (18 through 64 years of age). A single dose is 0.5 mL. (2)

Age	Schedule
5 years through 8 years	One dose or two doses at least 1 month apart <sup>a</sup>
9 years and older	One dose

<sup>a</sup>1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines. (2)

**DOSAGE FORMS AND STRENGTHS**

AFLURIA is a suspension for injection supplied in two presentations:

- 0.5 mL pre-filled syringe (single dose) (3, 11)
- 5 mL multi-dose vial (ten 0.5 mL doses) (3, 11)

**CONTRAINDICATIONS**

- Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine including egg protein, or to a previous dose of any influenza vaccine. (4, 11)

**WARNINGS AND PRECAUTIONS**

- Administration of CSL's 2010 Southern Hemisphere influenza vaccine was associated with increased rates of fever and febrile seizures in children predominantly below the age of 5 years as compared to previous years. Febrile events were also observed in children 5 through 8 years of age. (5.1)
- If Guillain-Barré Syndrome (GBS) has occurred within 6 weeks of previous influenza vaccination, the decision to give AFLURIA should be based on careful consideration of the potential benefits and risks. (5.2)
- Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine. (5.3)
- Immunocompromised persons may have a diminished immune response to AFLURIA. (5.4)

**ADVERSE REACTIONS**

- In children 5 through 17 years of age, the most common injection-site adverse reactions when administered by needle and syringe were pain (≥60%), redness (≥20%) and swelling (≥10%). The most common systemic adverse events were headache, myalgia (≥20%), irritability, malaise and fever (≥10%). (6.1)
- In adults 18 through 64 years of age, the most common injection-site adverse reactions when administered by needle and syringe were tenderness (≥60%), pain (≥40%), swelling (≥20%), and redness, itching (≥10%). The most common systemic adverse events were muscle aches (≥30%) and headache, malaise (≥20%). (6.1)
- In adults 18 through 64 years of age, the most common injection-site adverse reactions when administered by the PharmaJet Stratis Needle-Free Injection System up to 7 days post-vaccination were tenderness (≥80%), swelling, pain, redness (≥60%), itching (≥20%) and bruising (≥10%). The most common systemic adverse events within this period were myalgia, malaise (≥30%), and headache (≥20%). (6.1)
- In adults 65 years of age and older, when administered by needle and syringe the most common injection-site adverse reactions were tenderness (≥30%) and pain (≥10%). No systemic adverse events occurred in ≥10% of subjects in this age group (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Seqirus at 1 855 358 8966 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

**USE IN SPECIFIC POPULATIONS**

- AFLURIA is not approved for use in children less than 5 years of age because of increased rates of fever and febrile seizures. One comparator-controlled trial demonstrated higher rates of fever in recipients of AFLURIA as compared to a trivalent inactivated influenza vaccine control. (8.4)
- Antibody responses were lower in geriatric subjects than in younger subjects. (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 03/2017

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1 **FULL PRESCRIBING INFORMATION**

2  
3  
4 **1 INDICATIONS AND USAGE**

5  
6 AFLURIA<sup>®</sup> is an inactivated influenza vaccine indicated for active immunization against  
7 influenza disease caused by influenza virus subtypes A and type B present in the vaccine.  
8 AFLURIA is approved for use in persons 5 years of age and older.  
9

10  
11 **2 DOSAGE AND ADMINISTRATION**

12  
13 For intramuscular (IM) injection only, by needle and syringe (5 years of age and older) or by  
14 PharmaJet<sup>®</sup> Stratis<sup>®</sup> Needle-Free Injection System (18 through 64 years of age). A single dose  
15 is 0.5 mL.  
16

17 The dose and schedule for AFLURIA are presented in Table 1.

18 **Table 1: AFLURIA Schedule**

Age	Schedule
5 years through 8 years	One dose or two doses at least 1 month apart <sup>a</sup>
9 years and older	One dose

19 <sup>a</sup> 1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations  
20 on prevention and control of influenza with vaccines.  
21

22 Shake thoroughly and inspect visually before use. Parenteral drug products should be  
23 inspected visually for particulate matter and discoloration prior to administration, whenever  
24 suspension and container permit. If either of these conditions exists, the vaccine should not be  
25 administered.  
26

27 May be administered by needle and syringe (5 years of age and older) or PharmaJet Stratis  
28 Needle-Free Injection System (18 through 64 years of age only).  
29

30 When using the single-dose pre-filled syringe, shake the syringe thoroughly and administer the  
31 dose immediately.  
32

33 When using the multi-dose vial, shake the vial thoroughly before withdrawing each dose, and  
34 administer the dose immediately.

- 35 • Needle and Syringe: Draw up the exact dose using a separate sterile needle and syringe for  
36 each individual patient. It is recommended that small syringes (0.5 mL or 1 mL) be used to  
37 minimize any product loss.

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- 38 • PharmaJet Stratis Needle-Free Injection System: For instructions on withdrawal of a 0.5  
39 mL dose and use of the PharmaJet Stratis Needle-Free Injection System, refer to the  
40 Instructions For Use for the PharmaJet Stratis Needle-Free Injection System.

41

42 The preferred site for intramuscular injection is the deltoid muscle of the upper arm.

43

44 Between uses, return the multi-dose vial to the recommended storage conditions between  
45 2-8°C (36-46°F). **Do not freeze.** Discard if the vaccine has been frozen.

46

47

### 48 **3 DOSAGE FORMS AND STRENGTHS**

49

50 AFLURIA is a sterile suspension for intramuscular injection (*see Description [11]*).

51

52 AFLURIA is supplied in two presentations:

53

- 54 • 0.5 mL pre-filled syringe (single dose).
- 55 • 5 mL multi-dose vial (ten 0.5 mL doses).

56

57

### 58 **4 CONTRAINDICATIONS**

59

60 AFLURIA is contraindicated in individuals with known severe allergic reactions (e.g.,  
61 anaphylaxis) to any component of the vaccine including egg protein, or to a previous dose of  
62 any influenza vaccine (*see Description [11]*).

63

64

### 65 **5 WARNINGS AND PRECAUTIONS**

66

#### 67 **5.1 Fever and Febrile Seizures**

68 Administration of CSL's 2010 Southern Hemisphere influenza vaccine was associated with  
69 postmarketing reports of increased rates of fever and febrile seizures in children predominantly  
70 below the age of 5 years as compared to previous years; these increased rates were confirmed  
71 by postmarketing studies. Febrile events were also observed in children 5 through 8 years of  
72 age.

73

#### 74 **5.2 Guillain-Barré Syndrome**

75 If Guillain-Barré Syndrome (GBS) has occurred within 6 weeks of previous influenza  
76 vaccination, the decision to give AFLURIA should be based on careful consideration of the  
77 potential benefits and risks.

78

79 The 1976 swine influenza vaccine was associated with an increased frequency of GBS.

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80 Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza  
81 viruses is unclear. If influenza vaccine does pose a risk, it is probably slightly more than one  
82 additional case per 1 million persons vaccinated.

83

84 **5.3 Preventing and Managing Allergic Reactions**

85 Appropriate medical treatment and supervision must be available to manage possible  
86 anaphylactic reactions following administration of the vaccine.

87

88 **5.4 Altered Immunocompetence**

89 If AFLURIA is administered to immunocompromised persons, including those receiving  
90 immunosuppressive therapy, the immune response may be diminished.

91

92 **5.5 Limitations of Vaccine Effectiveness**

93 Vaccination with AFLURIA may not protect all individuals.

94

95

96 **6 ADVERSE REACTIONS**

97

98 In children 5 through 17 years of age, the most common injection-site reactions observed in  
99 clinical studies with AFLURIA administered by needle and syringe were pain ( $\geq 60\%$ ), redness  
100 ( $\geq 20\%$ ) and swelling ( $\geq 10\%$ ). The most common systemic adverse events were headache,  
101 myalgia ( $\geq 20\%$ ), irritability, malaise and fever ( $\geq 10\%$ ).

102

103 In adults 18 through 64 years of age, the most common injection-site adverse reactions  
104 observed in clinical studies with AFLURIA administered by needle and syringe were  
105 tenderness ( $\geq 60\%$ ), pain ( $\geq 40\%$ ), swelling ( $\geq 20\%$ ), redness and itching ( $\geq 10\%$ ). The most  
106 common systemic adverse events observed were muscle aches ( $\geq 30\%$ ), headache and malaise  
107 ( $\geq 20\%$ ).

108

109 In adults 18 through 64 years of age, using the PharmaJet Stratis Needle-Free Injection System,  
110 the most common injection-site adverse reactions observed in a clinical study with AFLURIA  
111 up to 7 days post-vaccination were tenderness ( $\geq 80\%$ ), swelling, pain, redness ( $\geq 60\%$ ), itching  
112 ( $\geq 20\%$ ) and bruising ( $\geq 10\%$ ). The most common systemic adverse events within this period  
113 were myalgia, malaise ( $\geq 30\%$ ) and headache ( $\geq 20\%$ ).

114

115 In adults 65 years of age and older, the most common injection-site adverse reactions observed  
116 in clinical studies with AFLURIA administered by needle and syringe were tenderness ( $\geq 30\%$ )  
117 and pain ( $\geq 10\%$ ). No systemic adverse reactions occurred in  $\geq 10\%$  of subjects in this age  
118 group.

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**6.1 Clinical Trials Experience**

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to rates in the clinical studies of another vaccine and may not reflect the rates observed in clinical practice.

**Children**

In clinical studies, AFLURIA has been administered to, and safety information collected for, 3,009 children ages 6 months through 17 years. The exposure in children includes 1,601 aged 6 months to less than 5 years, 756 children ages 5 years to less than 9 years and 652 children ages 9 years through 17 years. Clinical safety data for AFLURIA in children are presented from three clinical studies (Studies 1, 2 and 3). Data from a comparator-controlled trial (Study 1) are presented, followed by pooled data from two open label studies (Studies 2 and 3). Subjects 6 months through 8 years of age received one or two vaccinations, administered by needle and syringe, as determined by previous vaccination history (for further details on clinical study design, dosing and demographics *see Clinical Studies [14]*).

Study 1 included 1,468 subjects for safety analysis, ages 6 months through 17 years, randomized to receive AFLURIA (735 subjects) or another U.S.-licensed trivalent inactivated influenza vaccine (manufactured by Sanofi Pasteur, Inc.) (733 subjects).

Study 2 included 1,976 subjects for safety analysis, ages 6 months through 17 years. All subjects received AFLURIA.

Study 3 included 298 subjects for safety analysis, ages 6 months through 8 years. All subjects received AFLURIA.

The safety assessment was similar for the three pediatric studies. Local (injection site) adverse reactions and systemic adverse events were solicited for 7 days post-vaccination (Tables 2 and 3). Unsolicited adverse events were collected for 30 days post-vaccination. All adverse events are presented regardless of any treatment causality assigned by study investigators.

Among the pediatric studies, there were no vaccine-related deaths or vaccine-related serious adverse events reported in children 5 years of age and older.

In this section, safety data from the pediatric studies are limited to children 5 years of age and older. AFLURIA is not approved for use in children less than 5 years of age. See Warnings and Precautions [5.1] and Use in Specific Populations [8.4] for risks of AFLURIA in children less than 5 years of age.

In the comparator-controlled trial (Study 1), the rate of fever after the first dose of AFLURIA in subjects aged 5 through 8 years was 16% as compared to 8% in subjects who received the comparator. The rate of fever in subjects aged 9 through 17 years following a single dose of

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162 AFLURIA was 6% as compared to 4% in subjects who received the comparator. In all three  
163 pediatric studies, the rates of fever in subjects aged 5 through 8 years who received AFLURIA  
164 were lower after dose 2 than dose 1.

165

166 Data in Tables 2 and 3 are presented for children 5 years and older.

167

168 **Table 2: Proportion of Subjects 5 through 17 Years of Age with Solicited Local Adverse**  
169 **Reactions or Systemic Adverse Events within 7 Days after Administration of**  
170 **First or Second Dose of AFLURIA, Irrespective of Causality (Study 1)**  
171

	Percentage <sup>a</sup> of Subjects in each Age Group Reporting Event			
	Subjects 5 through 8 years		Subjects 9 through 17 years	
	AFLURIA N=161 <sup>b</sup>	Comparator N=165 <sup>b</sup>	AFLURIA N=254 <sup>b</sup>	Comparator N=250 <sup>b</sup>
<b>After the First Dose</b>				
<b>Local Adverse Reactions</b>				
Pain	63	60	66	60
Redness	23	27	17	17
Induration	17	17	15	16
<b>Systemic Adverse Events</b>				
Myalgia	34	30	40	37
Malaise	24	13	22	20
Headache	21	19	27	26
Any Fever	16	8	6	4
Fever $\geq 102.2^{\circ}\text{F}$	5	1	3	1
Nausea/Vomiting	12	8	9	10
Diarrhea	7	7	8	10
	<b>AFLURIA N=39 <sup>b</sup></b>	<b>Comparator N=53 <sup>b</sup></b>		
<b>After the Second Dose</b>				
<b>Local Adverse Reactions</b>				
Pain	36	38	-	-
Redness	10	19	-	-
Induration	8	17	-	-
<b>Systemic Adverse Events</b>				
Diarrhea	13	6	-	-
Headache	13	13	-	-
Myalgia	13	17	-	-
Malaise	5	8	-	-
Nausea/Vomiting	3	8	-	-
Any Fever	0	2	-	-
Fever $\geq 102.2^{\circ}\text{F}$	0	0	-	-

172 <sup>a</sup> Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on  
173 the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

174 <sup>b</sup> N = number of subjects in the Safety Population for each treatment group.



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**Table 3: Proportion of Subjects 5 through 17 Years of Age with Solicited Local Adverse Reactions or Systemic Adverse Events Within 7 Days after Administration of AFLURIA, Irrespective of Causality (Studies 2 and 3)**

	Percentage <sup>a</sup> of Subjects in each Age Group Reporting Event		
	Studies 2 and 3 Subjects 5 through 8 years		Study 2 Subjects 9 through 17 years
	Dose 1 N=82-595 <sup>b</sup>	Dose 2 N=82-426 <sup>b</sup>	Dose 1 N=397 <sup>b</sup>
<b>Local Adverse Reactions</b>			
Pain	61	56	68
Erythema	24	23	17
Swelling	17	17	13
<b>Systemic Adverse Events</b>			
Irritability <sup>d</sup>	18	16	-
Headache	16	10	27
Malaise or feeling generally unwell <sup>c</sup>	16	8	17
Any Fever	13	6	5
Fever $\geq 102.2^{\circ}\text{F}$	3	2	1
General Muscle Ache (Myalgia)	12	8	20
Nausea/Vomiting <sup>c</sup>	7	3	5
Vomiting/Diarrhea <sup>d</sup>	5	6	-
Loss of appetite <sup>d</sup>	5	4	-
Diarrhea <sup>c</sup>	4	2	5

<sup>a</sup> Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

<sup>b</sup> N = number of subjects in the Safety Population for each treatment group. Denominators for Dose 1 were: N=82 for Vomiting/Diarrhea, Irritability, Loss of appetite, N=513 for Malaise, Diarrhea, Nausea/Vomiting and N=593-595 for all other parameters. Denominators for Dose 2 were: N=82 for Vomiting/Diarrhea, Irritability, Loss of appetite, N=344 for Malaise, Diarrhea and Nausea/Vomiting and N=421-426 for all other parameters.

<sup>c</sup> These preferred terms were used to describe Solicited Adverse Events in Study 2.

<sup>d</sup> These preferred terms were used to describe Solicited Adverse Events in Study 3.

In Study 1, unsolicited adverse events that occurred in  $\geq 5\%$  of subjects who received AFLURIA in ages 5 years through 8 years following the first or second dose included cough (15%) and pyrexia (9%). Unsolicited adverse events that occurred in  $\geq 5\%$  of subjects who received AFLURIA in ages 9 years through 17 years following the first dose included cough (7%), oropharyngeal pain (7%), headache (7%) and nasal congestion (6%).



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195 In Studies 2 and 3, unsolicited adverse events that occurred in  $\geq 5\%$  of subjects ages 5 years  
196 through 8 years after the first or second dose included the following: upper respiratory tract  
197 infection (13%), cough (10%), rhinorrhea (7%), headache (5%), nasopharyngitis (5%) and  
198 pyrexia (5%). Unsolicited adverse events that occurred in  $\geq 5\%$  of subjects who received  
199 AFLURIA in ages 9 years through 17 years following the first dose included upper respiratory  
200 tract infection (9%) and headache (8%).

201

### 202 *Adults*

203 In clinical studies comparing AFLURIA to placebo or a comparator trivalent inactivated  
204 influenza vaccine, a single dose of AFLURIA was administered to, and safety information  
205 collected for, 11,104 subjects ages 18 through 64 years and 836 subjects ages 65 years and  
206 older. Clinical safety data for AFLURIA in adults are presented from three clinical studies  
207 (Studies 4 through 6) conducted in the US and one clinical study (Study 7) conducted in the  
208 UK

209

210 Study 4 included 1,357 subjects for safety analysis, ages 18 through 64 years, randomized to  
211 receive AFLURIA (1,089 subjects) or placebo (268 subjects) (*see Clinical Studies [14]*).

212

213 Study 5 included 15,020 subjects for safety analysis, ages 18 through 64 years, randomized to  
214 receive AFLURIA (10,015 subjects) or placebo (5,005 subjects) (*see Clinical Studies [14]*).

215

216 Study 6 included 1,266 subjects for safety analysis, ages 65 years and older, randomized to  
217 receive AFLURIA (630 subjects) or another U.S.-licensed trivalent inactivated influenza  
218 vaccine (manufactured by Sanofi Pasteur Inc.) as an active comparator (636 subjects) (*see*  
219 *Clinical Studies [14]*). Study 7 included 275 subjects for safety analysis, ages 65 years and  
220 older, randomized to receive AFLURIA (206 subjects) or a UK-licensed trivalent inactivated  
221 influenza vaccine (manufactured by GSK) as an active comparator (69 subjects).

222

223 The safety assessment was identical for the four adult studies. Local (injection-site) adverse  
224 reactions and systemic adverse events were solicited for 5 days post-vaccination (Table 4,  
225 studies 4 through 6). Unsolicited adverse events were collected for 21 days post-vaccination.  
226 All adverse events are presented regardless of any treatment causality assigned by study  
227 investigators.

228

229 Among adult studies, there were no vaccine-related deaths or vaccine-related serious adverse  
230 events reported.

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232 **Table 4: Proportion of Subjects 18 Years of Age and Older with Solicited Local Adverse**  
 233 **Reactions or Systemic Adverse Events within 5 Days after Administration of**  
 234 **AFLURIA or Placebo, Irrespective of Causality (Studies 4, 5 and 6)**  
 235

	Percentage <sup>a</sup> of Subjects in each Age Group Reporting Event					
	Study 4 Subjects 18 through 64 years		Study 5 Subjects 18 through 64 years		Study 6 Subjects ≥ 65 years	
	AFLURIA N=1087-1088 <sup>b</sup>	Placebo N=266 <sup>b</sup>	AFLURIA N=10,015 <sup>b</sup>	Placebo N=5005 <sup>b</sup>	AFLURIA N=630 <sup>b</sup>	Comparator N=636 <sup>b</sup>
<b>Local Adverse Reactions</b>						
Tenderness (Pain on touching)	60	18	69	17	36	31
Pain (without touching)	40	9	48	11	15	14
Redness	16	8	4	<1	3	1
Swelling	9	1	4	<1	7	8
Bruising	5	1	1	1	<1	1
<b>Systemic Adverse Events</b>						
Headache	26	26	25	23	9	11
Malaise	19	19	29	26	7	6
Muscle aches	13	9	21	12	9	8
Nausea	6	9	7	6	2	1
Chills/Shivering	3	2	5	4	2	2
Fever	1	1	3	2	<1	1

236 <sup>a</sup> Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on  
 237 the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

238 <sup>b</sup> N = number of subjects in the Safety Population for each treatment group.

239  
 240 In Study 4, headache was the only unsolicited adverse event that occurred in ≥ 5% of subjects  
 241 who received AFLURIA or placebo (8% versus 6%, respectively).

242  
 243 In Study 5, unsolicited adverse events that occurred in ≥ 5% of subjects who received  
 244 AFLURIA or placebo included headache (AFLURIA 12%, placebo 11%) and oropharyngeal  
 245 pain (AFLURIA 5%, placebo 5%).

246  
 247 In Study 6, headache was the only unsolicited adverse event that occurred in ≥ 5% of subjects  
 248 who received AFLURIA (5%).

249  
 250 Studies 1 to 7 were all conducted when AFLURIA was administered by needle and syringe.

251  
 252 Additionally, safety information has been collected in a clinical study of AFLURIA  
 253 administered using the PharmaJet Stratis Needle-Free Injection System (Study 8). Study 8  
 254 included 1,247 subjects for safety analysis, ages 18 through 64 years, randomized to receive

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255 AFLURIA by either the PharmaJet Stratis Needle-Free Injection System (624 subjects) or  
256 needle and syringe (623 subjects). No deaths or vaccine-related serious adverse events were  
257 reported in Study 8. Local (injection-site) adverse reactions and systemic adverse events were  
258 solicited for 7 days post-vaccination (Table 5).

259  
260 **Table 5: Proportion of Subjects 18 through 64 Years of Age with Solicited Local Adverse**  
261 **Reactions or Systemic Adverse Events within 7 Days after Administration of**  
262 **AFLURIA by PharmaJet Stratis Needle-Free Injection System or Needle and**  
263 **Syringe Irrespective of Causality (Study 8).**

	Percentage <sup>a</sup> of Subjects Reporting Event	
	Study 8	
	Subjects 18 through 64 years	
	AFLURIA	
	PharmaJet Stratis Needle-Free Injection System N=540-616 <sup>b</sup>	Needle and Syringe N=599-606 <sup>b</sup>
<b>Local Adverse Reactions</b>		
Tenderness	89	78
Swelling	65	20
Pain	64	49
Redness	60	19
Itching <sup>c</sup>	28	10
Bruising	18	5
<b>Systemic Adverse Events</b>		
Myalgia	36	36
Malaise	31	28
Headache	25	22
Chills	7	7
Nausea	7	7
Vomiting	1	2
Fever	0	0

265 <sup>a</sup> Proportion of subjects reporting each local adverse reaction or systemic adverse event by treatment group based on the  
266 number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

267 <sup>b</sup> N = number of subjects in the Safety Population for each treatment group. Denominators for the PharmaJet Stratis Needle-  
268 Free Injection System group were: N=540 for itching and N=605-616 for all other parameters. Denominators for the needle  
269 and syringe group were: N=527 for itching and N=599-606 for all other parameters.

270 <sup>c</sup> A total of 155 subjects (approximately randomly distributed between PharmaJet Stratis Needle-Free Injection System and  
271 needle and syringe groups) received Diary Cards without itching listed as a solicited symptom.

272  
273 In Study 8, no unsolicited adverse events occurred in  $\geq 5\%$  of subjects who received  
274 AFLURIA administered via PharmaJet Stratis Needle-Free Injection System up to 28 days  
275 post-vaccination.

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277

**278 6.2 Postmarketing Experience**

279 Because postmarketing reporting of adverse reactions is voluntary and from a population of  
280 uncertain size, it is not always possible to reliably estimate their frequency or establish a causal  
281 relationship to vaccine exposure. The adverse reactions described have been included in this  
282 section because they: 1) represent reactions that are known to occur following immunizations  
283 generally or influenza immunizations specifically; 2) are potentially serious; or 3) have been  
284 reported frequently. These adverse reactions reflect experience in both children and adults and  
285 include those identified during post-approval use of AFLURIA outside the US since 1985.

286

*287 Blood and lymphatic system disorders*

288 Thrombocytopenia

289

*290 Immune system disorders*

291 Allergic or immediate hypersensitivity reactions including anaphylactic shock and serum  
292 sickness

293

*294 Nervous system disorders*

295 Neuralgia, paresthesia, convulsions (including febrile seizures), encephalomyelitis,  
296 encephalopathy, neuritis or neuropathy, transverse myelitis, and GBS

297

*298 Vascular disorders*

299 Vasculitis which may be associated with transient renal involvement

300

*301 Skin and subcutaneous tissue disorders*

302 Pruritus, urticaria, and rash

303

*304 General disorders and administration site conditions*

305 Cellulitis and large injection site swelling

306 Influenza-like illness

307

**308 6.3 Adverse Reactions Associated With Influenza Vaccination**

309 Anaphylaxis has been reported after administration of AFLURIA. Egg protein can induce  
310 immediate hypersensitivity reactions among persons who have severe egg allergy. Allergic  
311 reactions include hives, angioedema, asthma, and systemic anaphylaxis (*see [Contraindications](#)*  
312 *[4]*).

313

314 Neurological disorders temporally associated with influenza vaccination, such as  
315 encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus  
316 neuropathy, have been reported.

317

318 Microscopic polyangiitis (vasculitis) has been reported temporally associated with influenza

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319 vaccination.

320

321

322 **7 DRUG INTERACTIONS**

323

324 **7.1 CONCURRENT USE WITH OTHER VACCINES**

325 There are no data to assess the concomitant administration of AFLURIA with other vaccines.  
326 If AFLURIA is given at the same time as another injectable vaccine(s), the vaccine(s) should  
327 be administered in separate syringes and a separate arm should be used.

328

329 AFLURIA should not be mixed with any other vaccine in the same syringe or vial.

330

331

332 **8 USE IN SPECIFIC POPULATIONS**

333

334 **8.1 Pregnancy**

335

336

337 Pregnancy Category B:

338

339 A reproductive and developmental toxicity study has been performed in female rats at a dose  
340 approximately 265 times the human dose (on a mg/kg basis) and revealed no evidence of  
341 impaired female fertility or harm to the fetus due to AFLURIA. There are, however, no  
342 adequate and well controlled studies in pregnant women. Because animal reproduction studies  
343 are not always predictive of human response, AFLURIA should be given to a pregnant woman  
344 only if clearly needed.

345 In the reproductive and developmental toxicity study, the effect of AFLURIA on embryo-fetal  
346 and pre-weaning development was evaluated in pregnant rats. Animals were administered  
347 AFLURIA by intramuscular injection twice prior to gestation, once during the period of  
348 organogenesis (gestation day 6), and once later in pregnancy (gestation day 20), 0.5  
349 mL/rat/occasion (approximately a 265-fold excess relative to the projected human dose on a  
350 body weight basis). No adverse effects on mating, female fertility, pregnancy, parturition,  
351 lactation parameters, and embryo-fetal or pre-weaning development were observed. There  
352 were no vaccine-related fetal malformations or other evidence of teratogenesis.

353

354

355 **8.3 Nursing Mothers**

356 AFLURIA has not been evaluated in nursing mothers. It is not known whether AFLURIA is  
357 excreted in human milk. Because many drugs are excreted in human milk, caution should be  
358 exercised when AFLURIA is administered to a nursing woman.

359

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360

**361 8.4 Pediatric Use**

362 AFLURIA is not approved for use in children less than 5 years of age. In a clinical study in  
363 which children received AFLURIA or a US-licensed comparator vaccine (Study 1, *see Clinical*  
364 *Trials Experience, [6.1]*), the incidence of fever in children 6 months through 35 months of age  
365 following the first and second doses of AFLURIA were 37% and 15%, respectively, as  
366 compared to 14% following each dose in the comparator group. Among children 3 years  
367 through 4 years of age, the incidence of fever following the first and second doses of  
368 AFLURIA were 32% and 14%, respectively, as compared to 11% and 16% in the comparator.  
369 In an open-label study (Study 2), fever, irritability, loss of appetite, and vomiting/diarrhea  
370 occurred more frequently in children 6 months through 35 months of age as compared to older  
371 children. Across three pediatric studies of AFLURIA (Studies 1, 2, and 3), 1.2% of eligible  
372 children (n=1,764) were discontinued from the second vaccination because of severe fever  
373 ( $\geq 104^{\circ}\text{F}$ ) within 48 hours of the first vaccination. Across the three pediatric studies, two  
374 children, a 7-month old and a 3-year old, experienced vaccine-related febrile seizures (rate of  
375 0.07% across studies), one of which was serious.

376

377 Administration of CSL's 2010 Southern Hemisphere influenza vaccine was associated with  
378 increased rates of fever and febrile seizures, predominantly in children below the age of 5 years  
379 as compared to previous years, in postmarketing reports confirmed by postmarketing studies  
380 (*see Warnings and Precautions [5.1]*).

381

382 The PharmaJet Stratis Needle-Free Injection System is not approved as a method of  
383 administering AFLURIA to children and adolescents less than 18 years of age due to lack of  
384 adequate data supporting safety and effectiveness in this population.

385

**386 8.5 Geriatric Use**

387 In clinical studies, AFLURIA has been administered to, and safety information collected for,  
388 836 subjects ages 65 years and older (*see Clinical Trials Experience [6.1]*). After  
389 administration of AFLURIA, hemagglutination-inhibiting antibody responses in persons 65  
390 years of age and older were lower as compared to younger adult subjects (*see Clinical Studies*  
391 *[14]*).

392

393 The PharmaJet Stratis Needle-Free Injection System is not approved as a method of  
394 administering AFLURIA to adults 65 years of age and older due to lack of adequate data  
395 supporting safety and effectiveness in this population.

396

397

**398 11 DESCRIPTION**

399

400 AFLURIA, Influenza Vaccine for intramuscular injection, is a sterile, clear, colorless to  
401 slightly opalescent suspension with some sediment that resuspends upon shaking to form a



## Package insert

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402 homogeneous suspension. AFLURIA is prepared from influenza virus propagated in the  
403 allantoic fluid of embryonated chicken eggs. Following harvest, the virus is purified in a  
404 sucrose density gradient using continuous flow zonal centrifugation. The purified virus is  
405 inactivated with beta-propiolactone, and the virus particles are disrupted using sodium  
406 taurodeoxycholate to produce a “split virion”. The disrupted virus is further purified and  
407 suspended in a phosphate buffered isotonic solution.

408  
409 AFLURIA is standardized according to USPHS requirements for the 2017-2018 influenza  
410 season and is formulated to contain 45 mcg hemagglutinin (HA) per 0.5 mL dose in the  
411 recommended ratio of 15 mcg HA for each of the three influenza strains recommended for the  
412 2017-2018 Northern Hemisphere influenza season: A/Singapore/GP1908/2015 (H1N1), IVR-  
413 180A, A/Hong Kong/4801/2014 (H3N2), NYMC X-263B, and B/Brisbane/46/2015.

414  
415 Thimerosal, a mercury derivative, is not used in the manufacturing process for the single dose  
416 presentations; therefore these products contain no preservative. The multi-dose presentation  
417 contains thimerosal, added as a preservative; each 0.5 mL dose contains 24.5 mcg of mercury.

418  
419 A single 0.5 mL dose of AFLURIA contains sodium chloride (4.1 mg), monobasic sodium  
420 phosphate (80 mcg), dibasic sodium phosphate (300 mcg), monobasic potassium phosphate  
421 (20 mcg), potassium chloride (20 mcg), and calcium chloride (0.5 mcg). From the  
422 manufacturing process, each 0.5 mL dose may also contain residual amounts of sodium  
423 taurodeoxycholate ( $\leq 10$  ppm), ovalbumin ( $< 1$  mcg), sucrose ( $< 10$  mcg), neomycin sulfate  
424 ( $\leq 61.5$  nanograms [ng]), polymyxin B ( $\leq 10.5$  ng), and beta-propiolactone ( $\leq 2$  ng).

425  
426 The rubber tip cap and plunger used for the preservative-free, single-dose syringes and the  
427 rubber stoppers used for the multi-dose vial were not made with natural rubber latex.

## 430 12 CLINICAL PHARMACOLOGY

### 432 12.1 Mechanism of Action

433 Influenza illness and its complications follow infection with influenza viruses. Global  
434 surveillance of influenza identifies yearly antigenic variants. For example, since 1977  
435 antigenic variants of influenza A (H1N1 and H3N2) and influenza B viruses have been in  
436 global circulation. Specific levels of hemagglutination inhibition (HI) antibody titers post-  
437 vaccination with inactivated influenza vaccine have not been correlated with protection from  
438 influenza virus. In some human studies, antibody titers of 1:40 or greater have been associated  
439 with protection from influenza illness in up to 50% of subjects.<sup>2,3</sup>

440  
441 Antibody against one influenza virus type or subtype confers limited or no protection against  
442 another. Furthermore, antibody to one antigenic variant of influenza virus might not protect  
443 against a new antigenic variant of the same type or subtype. Frequent development of



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444 antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the  
445 reason for the usual change to one or more new strains in each year's influenza vaccine.  
446 Therefore, inactivated influenza vaccines are standardized to contain the HA of three strains  
447 (i.e., typically two type A and one type B) representing the influenza viruses likely to be  
448 circulating in the US during the upcoming winter.

449  
450 Annual revaccination with the current vaccine is recommended because immunity declines  
451 during the year after vaccination and circulating strains of influenza virus change from year to  
452 year.<sup>1</sup>

453

454

455 **13 NONCLINICAL TOXICOLOGY**

456

457 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

458 AFLURIA has not been evaluated for carcinogenic or mutagenic potential, or male infertility  
459 in animals. A reproductive study of female rats vaccinated with AFLURIA revealed no  
460 impairment of fertility (see Pregnancy, 8.1).

461

462

463 **14 CLINICAL STUDIES**

464

465 **14.1 Efficacy Against Laboratory-Confirmed Influenza**

466 In Study 5, the efficacy of AFLURIA was demonstrated in a randomized, observer-blind,  
467 placebo-controlled study conducted in 15,044 subjects. Healthy subjects 18 through 64 years of  
468 age were randomized in a 2:1 ratio to receive a single dose of AFLURIA (enrolled subjects:  
469 10,033; evaluable subjects: 9,889) or placebo (enrolled subjects: 5,011; evaluable subjects:  
470 4,960). The mean age of all randomized subjects was 35.5 years. 54.4% were female and  
471 90.2% were White. Laboratory-confirmed influenza was assessed by active and passive  
472 surveillance of influenza-like illness (ILI) beginning 2 weeks post-vaccination until the end of  
473 the influenza season, approximately 6 months post-vaccination. ILI was defined as at least one  
474 respiratory symptom (e.g., cough, sore throat, nasal congestion) and at least one systemic  
475 symptom (e.g., oral temperature of 100.0°F or higher, feverishness, chills, body aches). Nasal  
476 and throat swabs were collected from subjects who presented with an ILI for laboratory  
477 confirmation by viral culture and real-time reverse transcription polymerase chain reaction.  
478 Influenza virus strain was further characterized using gene sequencing and pyrosequencing.

479

480 Attack rates and vaccine efficacy, defined as the relative reduction in the influenza infection  
481 rate for AFLURIA compared to placebo, were calculated using the per protocol population.  
482 Vaccine efficacy against laboratory-confirmed influenza infection due to influenza A or B  
483 virus strains contained in the vaccine was 60% with a lower limit of the 95% CI of 41% (Table  
484 6).

485

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486 **Table 6: Laboratory-Confirmed Influenza Infection Rate and Vaccine Efficacy in Adults**  
 487 **18 through 64 Years of Age (Study 5)**  
 488

	Subjects <sup>a</sup>	Laboratory-Confirmed Influenza Cases	Influenza Infection Rate	Vaccine Efficacy <sup>b</sup>	
	N			n/N %	%
<b>Vaccine-matched Strains</b>					
AFLURIA	9889	58	0.59	60	41
Placebo	4960	73	1.47		
<b>Any Influenza Virus Strain</b>					
AFLURIA	9889	222	2.24	42	28
Placebo	4960	192	3.87		

489 Abbreviations: CI, confidence interval  
 490 <sup>a</sup> The Per Protocol Population was identical to the Evaluable Population in this study.  
 491 <sup>b</sup> Vaccine efficacy = 1 minus the ratio of AFLURIA/placebo infection rates. The objective of the study was to demonstrate that  
 492 the lower limit of the CI for vaccine efficacy was greater than 40%.  
 493

494 **14.2 Immunogenicity in Children – Administration via Needle and Syringe**

495 Study 1 was a randomized, observer-blind, comparator-controlled study to evaluate the  
 496 immunological non-inferiority of AFLURIA to a U.S.-licensed trivalent inactivated influenza  
 497 vaccine (manufactured by Sanofi Pasteur, Inc.) in subjects 6 months through 17 years of age.  
 498 Study vaccines were administered by needle and syringe. Results are presented for children 5  
 499 through 17 years of age (Table 7). A total of 832 subjects (aged 5 through 17 years) were  
 500 enrolled. Subjects were randomized in a 1:1 ratio to receive AFLURIA (enrolled subjects:  
 501 417; evaluable subjects: 383) or the comparator vaccine (enrolled subjects: 415; evaluable  
 502 subjects: 383).  
 503

504 Children 6 months through 8 years of age with no history of influenza vaccination received 2  
 505 doses approximately 28 days apart. Children 6 months through 8 years of age with a history of  
 506 influenza vaccination and children 9 years of age and older received 1 dose. Children 6  
 507 months through 35 months of age received 0.25 mL of AFLURIA or comparator influenza  
 508 vaccine, and children 3 years of age and older received 0.5 mL of AFLURIA or comparator  
 509 influenza vaccine. Nearly equal proportions of subjects were male (49.9%) and female  
 510 (50.1%), and the majority were White (85.0%) or Black (10.3%).  
 511

512 Immunogenicity assessments were performed prior to vaccination and at 21 days after  
 513 vaccination. The co-primary endpoints were HI Geometric Mean Titer (GMT) ratios (adjusted  
 514 for baseline HI titers) and the difference in seroconversion rates for each vaccine strain 21 days  
 515 after the final vaccination. Pre-specified non-inferiority criteria required that the upper bound  
 516 of the 2-sided 95% CI of the GMT ratio (Comparator/AFLURIA) did not exceed 1.5 and the  
 517 upper bound of the 2-sided 95% CI of the seroconversion rate difference (Comparator minus

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518 AFLURIA) did not exceed 10.0% for each strain. As shown in Table 7, non-inferiority of  
 519 AFLURIA to the comparator vaccine was demonstrated in the per protocol population for  
 520 influenza A subtypes A(H1N1) and A(H3N2), but not for influenza type B. For influenza type  
 521 B, non-inferiority was demonstrated for HI GMTs, but not for seroconversion rates. Note that  
 522 the study was powered to assess the pre-specified non-inferiority criteria based on 1400  
 523 evaluable subjects. Analysis of the 761 subjects aged 5 through 17 years reduced the power of  
 524 the study and widened the confidence intervals. In the pre-specified analysis, AFLURIA was  
 525 not inferior to the comparator vaccine for all three virus strains. Post-hoc analyses of  
 526 immunogenicity by gender did not demonstrate significant differences between males and  
 527 females. The study was not sufficiently diverse to assess differences between races or  
 528 ethnicities.

530 **Table 7: Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and Analyses of**  
 531 **Non-Inferiority of AFLURIA to a U.S.-Licensed Comparator, Subjects 5**  
 532 **through 17 Years of Age (Study 1)**  
 533

Strain	Post-vaccination GMT		GMT Ratio <sup>a</sup>	Seroconversion % <sup>b</sup>		Difference	Met both non-inferiority criteria? <sup>c</sup>
	Comparator N=381	AFLURIA N=380	Comparator over AFLURIA (95% CI)	Comparator N=381	AFLURIA N=380	Comparator minus AFLURIA (95% CI)	
A(H1N1)	526.2	507.4	1.03 (0.88, 1.21)	62.7	62.6	0.1 (-6.8, 7.0)	Yes
A(H3N2)	1060.0	961.3	1.07 (0.94, 1.23)	72.2	69.7	2.4 (-4.0, 8.9)	Yes
B	123.3	110.1	1.10 (0.94, 1.29)	75.1	70.0	5.1 (-1.3, 11.4)	No

534 Abbreviations: CI, confidence interval; GMT, geometric mean titer.

535 <sup>a</sup> GMT ratios are adjusted for baseline HI titers

536 <sup>b</sup> Seroconversion rate is defined as a 4-fold increase in post-vaccination HI antibody titer from pre-vaccination titer  $\geq$  1:10 or  
 537 an increase in titer from  $<$  1:10 to  $\geq$  1:40.

538 <sup>c</sup> Note that the study was powered to assess the pre-specified non-inferiority criteria based on 1400 evaluable subjects.

539  
 540 **14.3 Immunogenicity in Adults and Older Adults – Administration via Needle**  
 541 **and Syringe**

542 Two randomized, controlled clinical studies of AFLURIA evaluated the immune responses by  
 543 measuring HI antibody titers to each virus strain in the vaccine in adults as compared to  
 544 placebo (adults 18 through 64 years) or another U.S.-licensed trivalent influenza vaccine  
 545 (adults  $\geq$  65 years). In these studies, post-vaccination immunogenicity was evaluated on sera  
 546 obtained 21 days after administration of a single dose of AFLURIA.

547  
 548 Study 4 was a randomized, double-blinded, placebo-controlled, multi-center study in healthy  
 549 subjects ages 18 through 64 years. A total of 1,357 subjects were vaccinated (1,089 subjects  
 550 with AFLURIA and 268 with a placebo). Subjects who received AFLURIA were vaccinated

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551 using either the preservative-free or thimerosal-containing presentation. The evaluable  
552 population consisted of 1,341 subjects (1,077 in the AFLURIA group and 264 in the placebo  
553 group). The mean age of the entire evaluable population receiving AFLURIA was 38 years.  
554 62.5% of subjects were female, 81.3% were White, 12.1% were Black, and 6.2% were Asian.

555  
556 Serum HI antibody responses to AFLURIA met the pre-specified co-primary endpoint criteria  
557 for all three virus strains (Table 8). Similar responses were observed between genders. The  
558 study was not sufficiently diverse to assess immunogenicity by race or ethnicity.

559  
560 **Table 8: Serum Antibody Responses in Subjects 18 through 64 Years of Age Receiving**  
561 **AFLURIA (Study 4)**  
562

Strain Variable	AFLURIA N=1077 value (95% CI)	Placebo N=264 value (95% CI)
<b>A(H1N1)</b>		
HI Titer $\geq$ 1:40 <sup>a</sup>	97.8% (96.7, 98.6)	74.6% (68.9, 79.8)
Seroconversion Rate (%) <sup>b</sup>	48.7% (45.6, 51.7)	2.3% (0.8, 4.9)
<b>A(H3N2)</b>		
HI Titer $\geq$ 1:40 <sup>a</sup>	99.9% (99.5, 100.0)	72.0% (66.1, 77.3)
Seroconversion Rate (%) <sup>b</sup>	71.5% (68.7, 74.2)	0.0% (N/A)
<b>B</b>		
HI Titer $\geq$ 1:40 <sup>a</sup>	94.2% (92.7, 95.6)	47.0% (40.8, 53.2)
Seroconversion Rate (%) <sup>b</sup>	69.7% (66.9, 72.5)	0.4% (< 0.1, 2.1)

563 <sup>a</sup> HI titer  $\geq$  1:40 is defined as the proportion of subjects with a minimum post-vaccination HI antibody titer of 1:40. Lower  
564 bound of 95% CI for HI antibody titer  $\geq$  1:40 should be > 70% for the study population.

565 <sup>b</sup> Seroconversion rate is defined as a 4-fold increase in post-vaccination HI antibody titer from pre-vaccination titer  $\geq$  1:10 or  
566 an increase in titer from < 1:10 to  $\geq$  1:40. Lower bound of 95% CI for seroconversion should be > 40% for the study  
567 population.

568  
569 Study 6 was a randomized, observer-blind, comparator-controlled study that enrolled 1,268  
570 subjects 65 years of age and older (Table 9). This study compared the immune response  
571 following administration of AFLURIA to that following a US-licensed trivalent inactivated  
572 influenza vaccine (manufactured by Sanofi Pasteur Inc.). Subjects were randomized in a 1:1  
573 ratio to receive a single vaccination of AFLURIA (enrolled subjects: 631; evaluable subjects:  
574 605) or the comparator vaccine (enrolled subjects: 637; evaluable subjects: 610).  
575 Immunogenicity assessments were performed prior to vaccination and at 21 days after  
576 vaccination. Most of the subjects in the per-protocol immunogenicity population were female  
577 (56.7%) and White (97.4%). 2.0% were Black and less than 1.0% were of other races or  
578 ethnicities.

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579  
580 The co-primary endpoints were HI GMT ratios (adjusted for baseline HI titers) and the  
581 difference in seroconversion rates for each vaccine strain 21 days after vaccination. Pre-  
582 specified non-inferiority criteria required that the upper bound of the 2-sided 95% CI of the  
583 GMT ratio (Comparator/AFLURIA) did not exceed 1.5 and the upper bound of the 2-sided  
584 95% CI of the seroconversion rate difference (Comparator minus AFLURIA) did not exceed  
585 10.0% for each strain. As shown in Table 9, non-inferiority of AFLURIA to the comparator  
586 vaccine was demonstrated in the per protocol population for influenza A subtypes A(H1N1)  
587 and A(H3N2), but not for influenza type B. For the B strain, non-inferiority was demonstrated  
588 for HI GMTs, but not for seroconversion rates. Post-hoc analyses of immunogenicity by  
589 gender did not demonstrate significant differences between males and females. The study was  
590 not sufficiently diverse to assess differences between races or ethnicities.

591  
592 **Table 9: Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and Analyses of**  
593 **Non-Inferiority of AFLURIA to a U.S. Licensed Comparator, Adults 65 Years of**  
594 **Age and Older (Study 6)**  
595

Strain	Post-vaccination GMT		GMT Ratio <sup>a</sup>	Seroconversion % <sup>b</sup>		Difference	Met both pre-defined non-inferiority criteria?
	Comparator N=610	AFLURIA N=605	Comparator over AFLURIA (95% CI)	Comparator N=610	AFLURIA N=605	Comparator minus AFLURIA (95% CI)	
A(H1N1)	59.2	59.4	1.04 (0.92, 1.18)	43.0	38.8	4.1 (-1.4, 9.6)	Yes
A(H3N2)	337.7	376.8	0.95 (0.83, 1.08)	68.7	69.4	-0.7 (-5.9, 4.5)	Yes
B	33.4	30.4	1.12 (1.01, 1.25)	34.4	29.3	5.2 (-0.1, 10.4)	No

596 Abbreviations: CI, confidence interval; GMT, geometric mean titer.  
597 <sup>a</sup> Post-vaccination GMTs were adjusted for baseline HI titers.  
598 <sup>b</sup> Seroconversion rate is defined as a 4-fold increase in post-vaccination HI antibody titer from pre-vaccination titer  $\geq 1:10$  or  
599 an increase in titer from  $< 1:10$  to  $\geq 1:40$ .

600  
601 **14.4 Immunogenicity in Adults – Administration via PharmaJet Stratis Needle-**  
602 **Free Injection System**

603 Study 8 was a randomized, comparator-controlled non-inferiority study that enrolled 1,250  
604 subjects 18 through 64 years of age. This study compared the immune response following  
605 administration of AFLURIA when delivered IM using either the PharmaJet Stratis Needle-Free  
606 Injection System or needle and syringe. Immunogenicity assessments were performed prior to  
607 vaccination and at 28 days after vaccination in the immunogenicity population (1,130 subjects,  
608 562 PharmaJet Stratis Needle-Free Injection System group, 568 needle and syringe group).  
609 The co-primary endpoints were HI GMT ratios for each vaccine strain and the absolute  
610 difference in seroconversion rates for each vaccine strain 28 days after vaccination. As shown

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611 in Table 10, non-inferiority of administration of AFLURIA by the PharmaJet Stratis Needle-  
612 Free Injection System compared to administration of AFLURIA by needle and syringe was  
613 demonstrated in the immunogenicity population for all strains. Post-hoc analyses of  
614 immunogenicity by age showed that younger subjects (18 through 49 years) elicited higher  
615 immunological responses than older subjects (50 through 64 years). Post-hoc analyses of  
616 immunogenicity according to gender and body mass index did not reveal significant influences  
617 of these variables on immune responses. The study population was not sufficiently diverse to  
618 assess immunogenicity by race or ethnicity.  
619

620 **Table 10: Baseline and Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and**  
621 **Analyses of Non-Inferiority of AFLURIA Administered by PharmaJet Stratis**  
622 **Needle-Free Injection System or Needle and Syringe, Adults 18 through 64**  
623 **Years of Age (Study 8)**  
624

Strain	Baseline GMT		Post-vaccination GMT		GMT Ratio <sup>a</sup>	Seroconversion % <sup>b</sup>		Difference	Met both pre-defined non-inferiority criteria? <sup>c</sup>
	Needle and Syringe N=568	PharmaJet Stratis Needle-Free Injection System N=562	Needle and Syringe N=568	PharmaJet Stratis Needle-Free Injection System N=562	Needle and Syringe over PharmaJet Stratis Needle-Free Injection System (95% CI)	Needle and Syringe N=568	PharmaJet Stratis Needle-Free Injection System N=562	Needle and Syringe minus PharmaJet Stratis Needle-Free Injection System (95% CI)	
A(H1N1)	79.5	83.7	280.6	282.9	0.99 (0.88, 1.12)	38.4	37.5	0.8 (-4.8, 6.5)	Yes
A(H3N2)	75.4	68.1	265.9	247.3	1.08 (0.96, 1.21)	45.1	43.8	1.3 (-4.5, 7.1)	Yes
B	12.6	13.5	39.7	42.5	0.94 (0.83, 1.06)	35.2	34.9	0.3 (-5.2, 5.9)	Yes

625 Abbreviations: CI, confidence interval; GMT, geometric mean titer  
626 <sup>a</sup> GMT ratio is defined as post-vaccination GMT for Needle and Syringe/PharmaJet Stratis Needle-Free Injection System  
627 <sup>b</sup> Seroconversion rate is defined as a 4-fold increase in post-vaccination HI antibody titer from pre-vaccination titer  $\geq 1:10$  or  
628 an increase in titer from  $< 1:10$  to  $\geq 1:40$ .  
629 <sup>c</sup> Non-inferiority (NI) criteria for the GMT ratio: upper bound of 2-sided 95% CI on the ratio of Needle and Syringe/PharmaJet  
630 Stratis Needle-Free Injection System. GMT should not exceed 1.5. NI criteria for the seroconversion rate (SCR) difference:  
631 upper bound of 2-sided 95% CI on the difference between SCR Needle and Syringe – SCR PharmaJet Stratis Needle-Free  
632 Injection System should not exceed 10%.  
633  
634

635 **15 REFERENCES**

636  
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642 3. Hobson D, Curry RL, Beare AS, et al. The Role of Serum Hemagglutination-  
643 Inhibiting Antibody in Protection against Challenge Infection with Influenza A2 and B  
644 Viruses. *J Hyg Camb* 1972;70:767-777.  
645

646  
647 **16 HOW SUPPLIED/STORAGE AND HANDLING**

648  
649 **16.1 How Supplied**

650 Each product presentation includes a package insert and the following components:

Presentation	Carton NDC Number	Components
Pre-Filled Syringe	33332-017-01	<ul style="list-style-type: none"> <li>Ten 0.5 mL single-dose syringes fitted with a Luer-Lok™ attachment without needles [NDC 33332-017-02]</li> </ul>
Multi-Dose Vial	33332-117-10	<ul style="list-style-type: none"> <li>One 5 mL vial, which contains ten 0.5 mL doses [NDC 33332-117-11]</li> </ul>

651  
652 **16.2 Storage and Handling**

- 653
- 654 • Store refrigerated at 2–8°C (36–46°F).
  - 655 • Do not freeze. Discard if product has been frozen.
  - 656 • Protect from light.
  - 657 • Do not use AFLURIA beyond the expiration date printed on the label.
  - 658 • Once the stopper of the multi-dose vial has been pierced the vial must be discarded within 28 days.
- 659  
660

661 **17 PATIENT COUNSELING INFORMATION**

- 662
- 663 • Inform the vaccine recipient or guardian of the potential benefits and risks of immunization with AFLURIA.
  - 664 • Inform the vaccine recipient or guardian that AFLURIA is an inactivated vaccine that cannot cause influenza but stimulates the immune system to produce antibodies that protect against influenza, and that the full effect of the vaccine is generally achieved approximately 3 weeks after vaccination.
  - 665 • Instruct the vaccine recipient or guardian to report any severe or unusual adverse reactions to their healthcare provider.
  - 666 • Provide the vaccine recipient or guardian with Vaccine Information Statements which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website ([www.cdc.gov/vaccines](http://www.cdc.gov/vaccines)).
  - 667 • Instruct the vaccine recipient or guardian that annual revaccination is recommended.
- 668  
669  
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