

CSL Behring LLC

Stimate®  
(desmopressin acetate)

Package Insert  
Revised: December 2010  
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1 **CSL Behring**

PHARMACIST  
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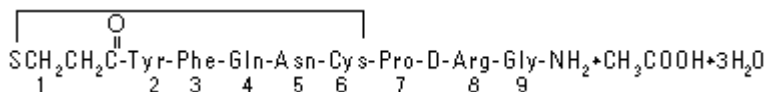
2  
3 **Stimate®**  
4 (desmopressin acetate)  
5 **Nasal Spray, 1.5 mg/mL**  
6

7 **R<sub>x</sub> only**

8  
9 **DESCRIPTION**

10 **Stimate® (desmopressin acetate)** is a synthetic analogue of the natural pituitary hormone 8-  
11 arginine vasopressin (ADH), an antidiuretic hormone affecting renal water conservation.  
12 **Stimate® Nasal Spray** contains 1.5 mg/mL desmopressin acetate in an aqueous solution at a pH  
13 of approximately 5.0. **Stimate® Nasal Spray's** compression pump delivers 0.1 mL (150 mcg) of  
14 solution per spray. It is chemically defined as follows:

15  
16 **Mol. Wt. 1183.34** Empirical formula: C<sub>46</sub>H<sub>64</sub>N<sub>14</sub>O<sub>12</sub>S<sub>2</sub> • C<sub>2</sub>H<sub>4</sub>O<sub>2</sub> • 3H<sub>2</sub>O



19 1-(3-mercaptopropionic acid)-8-D-arginine vasopressin monoacetate (salt) trihydrate.

20 **Stimate® Nasal Spray** is provided as an aqueous solution for intranasal use.

21  
22 Each mL contains:

**Active ingredient:**

Desmopressin acetate 1.5 mg

**Inactive ingredients:**

Sodium chloride 7.5 mg

**Buffer:**

Citric acid monohydrate 1.7 mg

Disodium phosphate dihydrate 3.0 mg

**Preservative:**

Benzalkonium chloride 0.1 mg

Purified water To 1 mL

23  
24 **CLINICAL PHARMACOLOGY**

25 **Stimate® Nasal Spray** contains as active substance, desmopressin acetate, which is a synthetic  
26 analogue of the natural hormone arginine vasopressin. One spray or 0.1 mL (150 mcg) of  
27 **Stimate® Nasal Spray** solution has an antidiuretic activity of about 600 IU.

28  
29 Desmopressin acetate has been shown to be more potent than arginine vasopressin in increasing  
30 plasma levels of Factor VIII activity in patients with hemophilia and von Willebrand's disease  
31 Type I.

33 Dose-response studies were performed in healthy persons using doses of 150 to 450 mcg,  
34 administered as one to three sprays. The response to **Stimate<sup>®</sup> Nasal Spray** is dose-related, with  
35 maximal plasma levels of 150 to 250 percent of initial concentrations achieved for both Factor  
36 VIII and von Willebrand factor.<sup>1</sup> The increase is rapid and evident within 30 minutes, reaching a  
37 maximum at about 1.5 hours.<sup>1</sup>

38

39 The percentage increase of Factor VIII and von Willebrand factor levels in patients with mild  
40 hemophilia A and von Willebrand's disease was not notably different from that observed in  
41 normal healthy individuals when treated with 300 mcg of **Stimate<sup>®</sup> Nasal Spray**.<sup>1-4</sup> In patients  
42 with von Willebrand's disease, levels of Factor VIII coagulant activity and von Willebrand factor  
43 antigen remained greater than 30 U/dL for 8 hours after a 300 mcg dose of **Stimate<sup>®</sup> Nasal  
44 Spray**.<sup>5</sup> After 300 mcg of **Stimate<sup>®</sup> Nasal Spray**, the percentage increase of Factor VIII and von  
45 Willebrand factor levels in patients with mild hemophilia A and von Willebrand's disease was  
46 less than observed after 0.3 mcg/kg of intravenous desmopressin acetate.<sup>2-4</sup>

47

48 Plasminogen activator activity increases rapidly after intravenous desmopressin acetate infusion,  
49 but there has been no clinically significant fibrinolysis in patients treated with desmopressin  
50 acetate.

51

52 The effect of repeated intravenous desmopressin acetate administration when doses were given  
53 every 12 to 24 hours has generally shown a diminution of the Factor VIII activity increase noted  
54 after a single dose. It is possible to reproduce the initial response in some patients after an  
55 interval of one week, but other patients may require as long as 6 weeks.<sup>2,4,6</sup>

56

57 The half-life of **Stimate<sup>®</sup> Nasal Spray** was between 3.3 and 3.5 hours, over the range of  
58 intranasal doses, 150 to 450 mcg.<sup>1</sup> Plasma concentrations of **Stimate<sup>®</sup> Nasal Spray** were  
59 maximal approximately 40 to 45 minutes after dosing.<sup>1</sup>

60

61 The bioavailability of **Stimate<sup>®</sup> Nasal Spray** when administered by the intranasal route as a 1.5  
62 mg/mL solution is between 3.3 and 4.1 percent.<sup>1</sup>

63

64 The change in structure of arginine vasopressin to desmopressin acetate has resulted in a  
65 decreased vasopressor action and decreased actions on visceral smooth muscle relative to the  
66 enhanced antidiuretic activity, so that clinically effective antidiuretic doses are usually below  
67 threshold levels for effects on vascular or visceral smooth muscle.

68

## 69 **INDICATIONS AND USAGE**

70 Before the initial therapeutic administration of **Stimate<sup>®</sup> Nasal Spray**, the physician should  
71 establish that the patient shows an appropriate change in the coagulation profile following a test  
72 dose of intranasal administration of **Stimate<sup>®</sup> Nasal Spray**.<sup>2-4</sup>

73

74 Desmopressin acetate is also available as a solution for injection (**DDAVP<sup>®</sup> Injection**) when the  
75 intranasal route may be compromised. These situations include nasal congestion and blockage,  
76 nasal discharge, atrophy of nasal mucosa, and severe atrophic rhinitis. Intranasal delivery may  
77 also be inappropriate where there is an impaired level of consciousness.

78

79 **Hemophilia A**

80 **Stimate<sup>®</sup> Nasal Spray** is indicated for patients with hemophilia A with Factor VIII coagulant  
81 activity levels greater than 5%.

82

83 Desmopressin acetate will also stop bleeding in patients with hemophilia A with episodes of  
84 spontaneous or trauma-induced injuries such as hemarthroses, intramuscular hematomas or  
85 mucosal bleeding.<sup>2,3</sup>

86

87 In the outpatient setting during two clinical trials where patients recorded bleeding episodes,  
88 **Stimate<sup>®</sup> Nasal Spray** provided effective hemostasis 100% of the time in 2 of the 5 patients. For  
89 those patients not responding in 100% of bleeding occasions, 45% (14 of 31) of bleeding  
90 episodes were effectively controlled with **Stimate<sup>®</sup> Nasal Spray**.

91

92 Desmopressin acetate is not indicated for the treatment of hemophilia A with Factor VIII  
93 coagulant activity levels equal to or less than 5%, or for the treatment of hemophilia B, or in  
94 patients who have Factor VIII antibodies.

95

96 **von Willebrand's Disease (Type I)**

97 **Stimate<sup>®</sup> Nasal Spray** is indicated for patients with mild to moderate classic von Willebrand's  
98 disease (Type I) with Factor VIII levels greater than 5%.

99

100 Desmopressin acetate will also stop bleeding in mild to moderate von Willebrand's disease  
101 patients with episodes of spontaneous or trauma-induced injuries such as hemarthroses,  
102 intramuscular hematomas, mucosal bleeding or menorrhagia.<sup>2,3</sup>

103

104 In the outpatient setting during two clinical trials where patients recorded bleeding episodes,  
105 **Stimate<sup>®</sup> Nasal Spray** provided effective hemostasis 100% of the time in 75% of the patients  
106 (n=16). For those patients not responding in 100% of bleeding occasions, 78% (64 of 82) of  
107 bleeding episodes were effectively controlled with **Stimate<sup>®</sup> Nasal Spray**.

108

109 Patients may respond in a variable fashion depending on the type of molecular defect they have.  
110 Bleeding time and Factor VIII coagulant activity, ristocetin cofactor activity, and von Willebrand  
111 factor antigen should be checked after initial administration of **Stimate<sup>®</sup> Nasal Spray** to ensure  
112 that adequate levels have been achieved.

113

114 **Stimate<sup>®</sup> Nasal Spray** is not indicated for the treatment of severe classic von Willebrand's  
115 disease (Type I) and when there is evidence of an abnormal molecular form of Factor VIII  
116 antigen. See **WARNINGS**.

117

118 **CONTRAINDICATIONS**

119 None.

120

121 **WARNINGS**

122 For intranasal use only.

123

124 Very rare cases of hyponatremia have been reported from world-wide postmarketing experience  
125 in patients treated with Stimate (desmopressin acetate). Stimate is a potent antidiuretic which,  
126 when administered, may lead to water intoxication and/or hyponatremia. Unless properly  
127 diagnosed and treated hyponatremia can be fatal. Therefore, fluid restriction is recommended  
128 and should be discussed with the patient and/or guardian. Careful medical supervision is  
129 required.

130

131 When Stimate Nasal Spray is administered, in particular in pediatric and geriatric patients, fluid  
132 intake should be adjusted downward in order to decrease the potential occurrence of water  
133 intoxication and hyponatremia (See **PRECAUTIONS, Pediatric Use** and **Geriatric Use**.) All  
134 patients receiving Stimate therapy should be observed for the following signs or symptoms  
135 associated with hyponatremia: headache, nausea/vomiting, decreased serum sodium, weight  
136 gain, restlessness, fatigue, lethargy, disorientation, depressed reflexes, loss of appetite,  
137 irritability, muscle weakness, muscle spasms or cramps and abnormal mental status such as  
138 hallucinations, decreased consciousness and confusion. Severe symptoms may include one or a  
139 combination of the following: seizure, coma and/or respiratory arrest. Particular attention should  
140 be paid to the possibility of the rare occurrence of an extreme decrease in plasma osmolality that  
141 may result in seizures that could lead to coma.

142

143 Stimate should be used with caution in patients with habitual or psychogenic polydipsia, who  
144 may be more likely to drink excessive amounts of fluids, putting them at greater risk of  
145 hyponatremia.

146

147 **Stimate® Nasal Spray** should not be used to treat patients with Type IIB von Willebrand's  
148 disease since platelet aggregation may be induced.

149

150 **PRECAUTIONS**

151 **General**

152 Desmopressin acetate has infrequently produced changes in blood pressure causing either a slight  
153 elevation in blood pressure or a transient fall in blood pressure and a compensatory increase in  
154 heart rate. The drug should be used with caution in patients with coronary artery insufficiency  
155 and/or hypertensive cardiovascular disease.

156

157 **Stimate® Nasal Spray** should be used with caution in patients with conditions associated with  
158 fluid and electrolyte imbalance, such as cystic fibrosis, heart failure and renal disorders because  
159 these patients are prone to hyponatremia.

160

161 There have been rare reports of thrombotic events (thrombosis<sup>7</sup>, acute cerebrovascular  
162 thrombosis, acute myocardial infarction) following desmopressin acetate injection in patients  
163 predisposed to thrombus formation. No causality has been determined; however, the drug should  
164 be used with caution in these patients.

165

166 Severe allergic reactions have been reported rarely.<sup>2,8-10</sup> Fatal anaphylaxis has been reported in  
167 one patient who received intravenous DDAVP<sup>®</sup> (desmopressin acetate). It is not known whether  
168 antibodies to desmopressin acetate are produced after repeated administration.

169  
170 Since **Stimate<sup>®</sup> Nasal Spray** is used intranasally, changes in the nasal mucosa such as scarring,  
171 edema, or other disease may cause erratic, unreliable absorption in which case **Stimate<sup>®</sup> Nasal**  
172 **Spray** should be discontinued until the nasal problems resolve. For such situations, DDAVP<sup>®</sup>  
173 Injection should be considered.

#### 174 175 **Information for Patients**

176 Patients should be informed that the bottle accurately delivers 25 doses of 150 mcg each. Any  
177 solution remaining after 25 doses should be discarded since the amount delivered thereafter may  
178 be substantially less than 150 mcg of drug. No attempt should be made to transfer remaining  
179 solution to another bottle. Patients should be instructed to read accompanying directions on use  
180 of the spray pump carefully before use.

181  
182 Patients should also be advised that if bleeding is not controlled, the physician should be  
183 contacted.<sup>2,3</sup>

#### 184 185 **Hemophilia A**

186 Laboratory tests for assessing patient status include levels of Factor VIII coagulant, Factor VIII  
187 antigen and Factor VIII ristocetin cofactor (von Willebrand factor) as well as activated partial  
188 thromboplastin time. Factor VIII coagulant activity should be determined before giving **Stimate<sup>®</sup>**  
189 **Nasal Spray** for hemostasis. If Factor VIII coagulant activity is present at less than 5% of  
190 normal, **Stimate<sup>®</sup> Nasal Spray** should not be relied on.

#### 191 192 **von Willebrand's Disease**

193 Laboratory tests for assessing patient status include levels of Factor VIII coagulant activity,  
194 VWF:RCo and VWF:Ag.

#### 195 196 **Drug Interactions**

197 Although the pressor activity of desmopressin acetate is very low, its use with other pressor  
198 agents should be done only with careful patient monitoring. The concomitant administration of  
199 drugs that may increase the risk of water intoxication with hyponatremia (e.g., tricyclic  
200 antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics,  
201 NSAIDs, lamotrigine and carbamazepine) should be performed with caution.

202  
203 DDAVP<sup>®</sup> Injection has been used with epsilon aminocaproic acid without adverse effects.

#### 204 205 **Carcinogenicity, Mutagenicity, Impairment of Fertility**

206 There have been no long-term studies in animals to assess the carcinogenic, mutagenic or  
207 impairment of fertility potential of **Stimate<sup>®</sup> Nasal Spray**.

208

209 **Pregnancy Category B**

210 Reproduction studies performed in rats and rabbits by the subcutaneous route at doses up to 10  
211 mcg/kg/day have revealed no evidence of harm to the fetus due to desmopressin acetate. This  
212 dose is equivalent to 10 times (for Factor VIII stimulation) or 38 times (for diabetes insipidus)  
213 the systemic human dose based on a mg/M<sup>2</sup> surface area.

214

215 There are no adequate and well-controlled studies in pregnant women. Several publications of  
216 desmopressin acetate's use in the management of diabetes insipidus during pregnancy are  
217 available; these include a few anecdotal reports of congenital anomalies and low birth weight  
218 babies. However, no causal connection between these events and desmopressin acetate has been  
219 established. A 15-year, Swedish epidemiologic study of the use of desmopressin acetate in  
220 pregnant women with diabetes insipidus found the rate of birth defects to be no greater than that  
221 in the general population. As opposed to preparations containing natural hormones,  
222 desmopressin acetate in antidiuretic doses has no uterotonic action and the physician will have to  
223 weigh the therapeutic advantages against the possible risks in each case.

224

225 **Nursing Mothers**

226 There have been no controlled studies in nursing mothers. A single study in postpartum women  
227 demonstrated a marked change in plasma, but little if any change in assayable DDAVP® in breast  
228 milk following an intranasal dose of 10 mcg. It is not known whether this drug is excreted in  
229 human milk. Because many drugs are excreted in human milk, caution should be exercised when  
230 **Stimate® Nasal Spray** is administered to a nursing woman.

231

232 **Pediatric Use**

233 Use in infants and children will require careful fluid intake restriction to prevent possible  
234 hyponatremia and water intoxication. **Stimate® Nasal Spray** should not be used in infants  
235 younger than 11 months in the treatment of hemophilia A or von Willebrand's disease; safety and  
236 effectiveness in children between 11 months and 12 years of age has been demonstrated.<sup>2-4</sup>

237

238 **Geriatric Use**

239 Clinical studies of Stimate® did not include sufficient numbers of subjects aged 65 and over to  
240 determine whether they respond differently than younger subjects. However, other post-  
241 marketing experience has indicated the occurrence of hyponatremia with the use of desmopressin  
242 acetate and fluid overload.

243

244 Therefore, in elderly patients fluid intake should be adjusted downward in an effort to decrease  
245 the potential occurrence of water intoxication and hyponatremia. Particular attention should be  
246 paid to the possibility of the rare occurrence of an extreme decrease in plasma osmolality that  
247 may result in seizures, and that could lead to coma.

248

249 Patients who do not have need of antidiuretic hormone for its antidiuretic effect should be  
250 cautioned to ingest only enough fluid to satisfy thirst, in an effort to decrease the potential  
251 occurrence of water intoxication and hyponatremia.

252

253 As for all patients, dosing for geriatric patients should be appropriate to their clinical condition.

254

255 **ADVERSE REACTIONS**

256 Infrequently, DDAVP® Injection has produced transient headache, nausea, mild abdominal  
257 cramps and vulval pain. These symptoms disappeared with reduction in dosage. Occasional  
258 facial flushing has been reported with the administration of DDAVP® Injection. Infrequently,  
259 high doses of intranasal DDAVP® have produced transient headache and nausea. Nasal  
260 congestion, rhinitis and flushing have also been reported occasionally along with mild abdominal  
261 cramps. These symptoms disappeared with reduction in dosage. Nosebleed, sore throat, cough  
262 and upper respiratory infections have also been reported.

263

264 In addition to those listed above, the following have also been reported in clinical trials with  
265 **Stimate® Nasal Spray**: Somnolence, dizziness, itchy or light-sensitive eyes, insomnia, chills,  
266 warm feeling, pain, chest pain, palpitations, tachycardia, dyspepsia, edema, vomiting, agitation  
267 and balanitis.<sup>1-4</sup>

268

269 DDAVP® Injection (desmopressin acetate) has infrequently produced changes in blood pressure  
270 causing either a slight elevation or a transient fall with a compensatory increase in heart rate.  
271 Severe allergic reactions including anaphylaxis have been reported rarely with DDAVP®  
272 Injection.

273

274 **Post Marketing**

275 There have been rare reports of convulsions from hyponatremia associated with concomitant use  
276 of desmopressin and the following medications: oxybutynin and imipramine.

277

278 See **WARNINGS** for the possibility of water intoxication, hyponatremia and coma.<sup>11</sup>

279

280 **To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring**  
281 **Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or**  
282 [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

283

284 **OVERDOSAGE**

285 Signs of overdose may include confusion, drowsiness, continuing headache, problems with  
286 passing urine and rapid weight gain due to fluid retention. (See **WARNINGS**.) In cases of  
287 overdose, the dosage should be reduced, frequency of administration decreased, or the drug  
288 withdrawn according to the severity of the condition.

289

290 There is no known specific antidote for desmopressin acetate or **Stimate® Nasal Spray**.

291

292 An oral LD<sub>50</sub> has not been established. An intravenous dose of 2 mg/kg in mice demonstrated no  
293 effect.

294

295 **DOSAGE AND ADMINISTRATION**

296 **Hemophilia A and von Willebrand's Disease (Type I)**

297 **Stimate® Nasal Spray** is administered by nasal insufflation, one spray per nostril, to provide a  
298 total dose of 300 mcg. In patients weighing less than 50 kg, 150 mcg administered as a single

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299 spray provided the expected effect on Factor VIII coagulant activity, Factor VIII ristocetin  
300 cofactor activity and skin bleeding time.<sup>3,4</sup> If **Stimate® Nasal Spray** is used preoperatively, it  
301 should be administered 2 hours prior to the scheduled procedure.<sup>12,13</sup>  
302

303 The necessity for repeat administration of **Stimate® Nasal Spray** or use of any blood products  
304 for hemostasis should be determined by laboratory response as well as the clinical condition of  
305 the patient. Fluid restriction should be observed, and fluid intake should be limited to a  
306 minimum, from 1 hour before desmopressin administration, until at least 24 hours after  
307 administration. The tendency toward tachyphylaxis (lessening of response) with repeated  
308 administration given more frequently than once every 48 hours should be considered in treating  
309 each patient.  
310

311 The nasal spray pump can only deliver doses of 0.1 mL (150 mcg) or multiples of 0.1 mL. If  
312 doses other than these are required, DDAVP® Injection may be used.  
313

314 The spray pump must be primed prior to the first use. To prime pump, press down 4 times. The  
315 bottle should be discarded after 25 doses since the amount delivered thereafter per spray may be  
316 substantially less than 150 mcg of drug.  
317

#### 318 **HOW SUPPLIED**

319 A 2.5 mL bottle with spray pump capable of delivering 25 doses of 150 mcg (NDC 0053-6871-  
320 00).  
321

322 Store at room temperature not to exceed 25°C (77°F) for the period indicated by the expiration  
323 date on the label. Discard six months after being opened. Store bottle in upright position.  
324

325 Revised September 2011

IN-8155-07

326  
327 Manufactured for:

328 **CSL Behring LLC**

329 King of Prussia, PA 19406-0901

330 US License No. 1767  
331

332 By:

333 Ferring GmbH

334 Kiel, Germany  
335

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IN-8155-07

**Stimate<sup>®</sup> Nasal Spray  
(Pronounced Stim-ate)  
(desmopressin acetate)**

Read this patient information leaflet before you start taking **Stimate<sup>®</sup> Nasal Spray** and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

**What is the most important information I should know about Stimate<sup>®</sup> Nasal Spray?**

**All patients using Stimate<sup>®</sup> Nasal Spray are at risk for water intoxication, fluid overload and low sodium levels in the blood. You must follow your healthcare provider's instructions on limiting the amount of fluid you can drink when taking Stimate<sup>®</sup> Nasal Spray.**

- Do not drink more than you need to satisfy your thirst.
- You can have serious side effects such as seizures, coma, and death from drinking too much fluid.
- Children and elderly patients are at higher risk for these conditions and must follow their healthcare provider's restrictions on drinking fluids.

Call your healthcare provider right away if you have any of the following symptoms while using Stimate<sup>®</sup> Nasal Spray. They may mean that your blood sodium level is low:

• Headache	• Loss of appetite
• Nausea	• Irritability
• Vomiting	• Muscle weakness
• Weight gain	• Muscle spasms or cramps
• Restlessness	• Hallucinations
• Tiredness	• Confusion

**Using Stimate<sup>®</sup> Nasal Spray the wrong way may cause it not to work to control bleeding.**

- Call your healthcare provider right away if you have any uncontrolled bleeding.

**What is Stimate<sup>®</sup> Nasal Spray?**

Stimate<sup>®</sup> Nasal Spray is a prescription medicine used to stop some types of bleeding in people with mild hemophilia A or mild to moderate von Willebrand's disease Type 1.

Stimate<sup>®</sup> Nasal Spray should not be used in children under 11 months of age.

407 **What should I tell my healthcare provider before I use Stimate<sup>®</sup> Nasal Spray?**

408

409 **Before taking Stimate<sup>®</sup> Nasal Spray, tell your healthcare provider about all of your medical**  
410 **conditions, including if you:**

- 411 • Have any nasal problems such as a stuffy nose, have ever had surgery on your nose, or
- 412 have trouble breathing through your nose. You may need to use another form of this
- 413 medicine.
- 414 • Have or have had any heart, blood circulation, or blood pressure problems.
- 415 • Have a condition that causes fluid or water imbalance problems such as:
  - 416 • Cystic fibrosis
  - 417 • Heart failure
  - 418 • Kidney problems
- 419 • Have or have had a condition that causes you to be very thirsty.
- 420 • Are pregnant or plan to become pregnant. It is not known if Stimate<sup>®</sup> Nasal Spray will
- 421 harm your unborn baby.
- 422 • Are breast-feeding or plan to breast-feed. It is not known if Stimate<sup>®</sup> Nasal Spray passes
- 423 into your breast milk. You and your healthcare provider should decide if you will take
- 424 Stimate<sup>®</sup> Nasal Spray.

425

426 **Tell your healthcare provider and pharmacist about all the medicines you take,** including  
427 prescription and non-prescription medicines, such as over-the-counter medicines, vitamins,  
428 supplements and herbal remedies.

429

430 Using Stimate<sup>®</sup> Nasal Spray with certain other medicines can affect the way Stimate<sup>®</sup> Nasal  
431 Spray works.

432

433 Know the medicines you take. Keep a list of them and show it to your healthcare provider and  
434 pharmacist when you get a new medicine.

435

436 **It is especially important to tell your healthcare provider if you take:**

- 437 • Blood pressure or heart medicines
- 438 • Antidepressants
- 439 • Anti-anxiety medicines
- 440 • Antihistamines
- 441 • Pain relievers such as narcotics or non-steroidal anti-inflammatory medicines (NSAIDs)
- 442 • Seizure medicines
- 443 • Medicines for over-active urinary bladder

444

445 Ask your healthcare provider or pharmacist if you are not sure if your medicine is one of these.

446

447 **How should I use Stimate<sup>®</sup> Nasal Spray?**

- 448       • Use Stimate<sup>®</sup> Nasal Spray exactly as your healthcare provider told you. Do not use more  
449       Stimate<sup>®</sup> Nasal Spray or take it more often than your healthcare provider told you.  
450       • The Stimate<sup>®</sup> Nasal Spray pump provides the correct dose of your medicine. For detailed  
451       instructions on how to use the nasal spray pump, see the *Patient Instructions for Use* at  
452       the end of this leaflet.  
453       • The nasal spray pump delivers 25 doses of Stimate<sup>®</sup> Nasal Spray and each spray contains  
454       a measured amount of medicine. Any medicine left in the spray pump after 25 sprays  
455       should be thrown away because, at that time, the amount of medicine in each spray may  
456       be a lot less than the correct amount. Do not put any leftover medicine into another bottle.  
457       • If your symptoms do not improve, or if they become worse, contact your healthcare  
458       provider. Do not stop taking Stimate<sup>®</sup> Nasal Spray without talking to your healthcare  
459       provider.  
460       • If you use too much Stimate<sup>®</sup> Nasal Spray, call your healthcare provider or go to the  
461       nearest hospital emergency department right away.  
462

463 **What are the possible side effects of Stimate<sup>®</sup> Nasal Spray?**

464 **Stimate<sup>®</sup> Nasal Spray may cause serious side effects**, that come from having too much water  
465 in the body. See “**What is the most important information I should know about Stimate<sup>®</sup>**  
466 **Nasal Spray?**”.

467  
468  
469 Common side effects of Stimate Nasal Spray include:

- 470       • Occasional facial flushing  
471       • Nasal congestion  
472       • Runny nose  
473       • Nosebleed  
474       • Sore throat  
475       • Cough  
476       • Upper respiratory infections.  
477

478 Tell your healthcare provider about any side effect that bothers you or does not go away. These  
479 are not all the possible side effects of Stimate<sup>®</sup> Nasal Spray. If you have questions, talk to your  
480 healthcare provider.

481  
482 Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-  
483 800-FDA-1088.  
484

485 **How should I store Stimate<sup>®</sup> Nasal Spray?**

- 486
- Store at room temperature, but not higher than 77°F (25°C).
  - Throw away Stimate<sup>®</sup> Nasal Spray six months after it is opened, or when the expiration date has passed, if this date is before the six months is up.
  - Store Stimate<sup>®</sup> Nasal Spray standing upright.
- 488
- 489
- 490

491 **Keep Stimate<sup>®</sup> Nasal Spray and all medicines out of the reach of children.**

492

493 **General information about Stimate<sup>®</sup> Nasal Spray**

494 Medicines are sometimes prescribed for conditions that are not mentioned in the patient leaflet.  
495 Do not use Stimate<sup>®</sup> Nasal Spray for a condition for which it was not prescribed. Do not give  
496 Stimate<sup>®</sup> Nasal Spray to other people, even if they have the same symptoms you have. It may  
497 harm them.

498

499 This patient information leaflet summarizes the most important information about Stimate<sup>®</sup>  
500 Nasal Spray. If you would like more information about Stimate<sup>®</sup> Nasal Spray, talk with your  
501 healthcare provider. You can ask your healthcare provider or pharmacist for information about  
502 Stimate<sup>®</sup> Nasal Spray that is written for health professionals. For more information, go to  
503 [www.stimate.com](http://www.stimate.com) or call CSL Behring Medical Affairs at 1-800-504-5434.

504

505 **What are the ingredients in Stimate<sup>®</sup> Nasal Spray?**

506

507 **Active ingredients:** desmopressin acetate

508 **Inactive ingredients:** sodium chloride, citric acid monohydrate, disodium phosphate dihydrate,  
509 benzalkonium chloride, purified water.

510

511 Manufactured for:

512 **CSL Behring LLC**

513 King of Prussia, PA 19406-0901

514 US License No. 1767

515

516 By:

517 Ferring GmbH

518 Kiel, Germany

519

520 **Patient Instructions for Use**

521

522 Read these instructions carefully before you use your Stimate<sup>®</sup> Nasal Spray pump. The  
523 following instructions tell you how to prepare, or prime, your Stimate<sup>®</sup> Nasal Spray pump so that  
524 it is ready to use.

525

526 **Using your Stimate® Nasal Spray Pump**

527

528

1. Remove the protective cap.

529

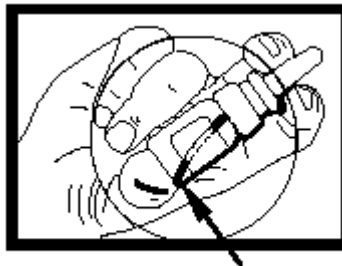
530

2. When using Stimate® Nasal Spray for the first time, the spray pump must be primed by pressing down on the ring at the top of the pump 4 times. Hold the spray tip away from your face and eyes. See Figure A.

531

532

533



CORRECT

534

535 **Figure A**

536

537

538

3. When primed, the Stimate® Nasal Spray pump delivers one dose of medicine each time it is pressed. For the right dose, tilt your Stimate® Nasal Spray pump so that the tube inside the spray pump draws the medicine up from the deepest part of the medicine inside the container. See Figures A and B.

539

540

541

542



INCORRECT

543

544 **Figure B**

545

546

4. Put the spray nozzle tip into your nostril and press the spray pump one time for one dose (150-micrograms). If two doses are prescribed, spray each nostril one time (for a dose of 300-micrograms).

547

548

549

550

5. When you finish using your Stimate® Nasal Spray, put the cap over the tip of the pump.

551

552 **6.** If Stimate<sup>®</sup> Nasal Spray has not been used for one week, you will need to prime the pump  
553 again by pressing one time, or until you see a fine mist.  
554

555 Use this check-off chart to help you keep track of the number of sprays used. This will help  
556 make sure that you receive 25 doses with each bottle of Stimate<sup>®</sup> Nasal Spray. There is extra  
557 medicine in the bottle to allow for priming. When using the chart to check off sprays, do not  
558 count the priming sprays.  
559

560  
561  
562

**Stimate<sup>®</sup> Nasal Spray  
25 Spray Check-off Chart**

①	②	③	④	⑤
⑥	⑦	⑧	⑨	⑩
⑪	⑫	⑬	⑭	⑮
⑯	⑰	⑱	⑲	⑳
㉑	㉒	㉓	㉔	㉕

- 563
- 564 **1.** Keep this chart with your Stimate<sup>®</sup> Nasal Spray or put it someplace where you can easily get  
565 it.  
566
- 567 **2.** Check off number 1 on the chart with your first dose of Stimate<sup>®</sup> Nasal Spray. Check off the  
568 numbers after each use of Stimate<sup>®</sup> Nasal Spray. If your healthcare provider prescribed a 2-  
569 spray dose (300-micrograms), then two numbers should be checked off.  
570
- 571 **3.** Throw away the Stimate<sup>®</sup> Nasal Spray after 25 doses.