 prescribing information for NON-STANDARD/220 ALL RECENCY. VON-STANDARD/220 ALL PROFINCE NETACTS (POLLENS, MOLDS, EPEDERMALS AND INSECTS). NOLDS, FUDERMALS AND INSECTS) Solution for prevanaeous, litradermal, or solutanteness administration litridu. Solution for prevanaeous and painteness of disposis or transmitter, or mapply lastic, (1). Changing to another of the litridus with screeness relations and volumes of non-standardizad litriges solutions and volumes of non-standardizad litriges and painteness of the litridus with screeness administration litridus with screeness relations and volumes of non-standardizad litriges and painteness of the litridus with screeness administration litridus with screeness relations and volumes of non-standardizad litriges and painteness of the litregenession. These produces may not be suitable fo	1 2 3 4	HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use NON-STANDARDIZED ALLERGENIC EXTRACTS (POLLENS, MOLDS. EPIDERMALS AND INSECTS) safely and effectively. See full	 46 Intradermal for diagnostic testing. 47 Subcutaneous for immunotherapy. 48 See full prescribing information for details on dosing and dilution 49 preparation. (2)
 EXTRACTS (POLLXNS, MOLDS, ETIDERMALS AND INSECTS) Non-standardized allegence creater solutions: note concentrate, labeled in 5 (h. 9), and 5 (ml. value, (l. 16) [Ref to be valued label for the graduet concentration of the	5	prescribing information for NON-STANDARDIZED ALLERGENIC	50DOSAGE FORMS AND STRENGTHS
 Solution for percutaneous, intradermal, or subcutaneous administration Triat US: Approval: 123 Solution for complete function of the allogane stated when data intervention of the allogane stated data intervention of the allogane stated when data intervention of the allogane stated data intervention of the allogane state data intervention of allogane intervention data intervention of allogane intervention of allogane intervention data intervention of allogane intervention of allogane intervention data intervention of a	6 7 8 9	EXTRACTS (POLLENS, MOLDS, EPIDERMALS AND INSECTS). NON-STANDARDIZED ALLERGENIC EXTRACTS (POLLENS, MOLDS, EPIDERMALS AND INSECTS)	 51 Non-standardized allergenic extract solutions: stock concentrates, labeled in 52 weight/volume, in a glycerin-preserved extracting fluid, supplied in 5, 10, 30, 53 and 50 mL vials. (3, 16) Refer to the vial label for the product concentration. 54 (11)
 Solution for perchantens, infrademand, or sincilances administration infinitiation processing administration Solution for percent and solution of the end of the second of the end of t	10		55CONTRAINDICATIONS
WARNING: ANAPHYLAXIS See full presentions information for complete kaves of warning. Medical conditions that reduce the ability on survive anaphylaxis. (4) See full presentions information for complete kaves or areas anaphylaxis. Medical conditions that reduce the ability on survive anaphylaxis. (4) Due not atimistice to individuals with severe, unstable or unamonobcapy. Densities of individuals with severe, unstable or unamonobcapy. Common decrease the data of the low of allergon extent exactions that reduce the ability to survive anaphylaxis. (4) Common decrease anaphylaxis. (4) Ob not atimistice to individuals for at least 30 minutes following administration. Energong measures and personnel trained in the core of all full contenting receivers alled and for allergon extracts. (a) Common decrease anaphylaxis. (4) One-contract is down and phylaxis. (4) Charge to another lot allergon: extracts are anaphylaxis. (4) Common decrease the individual stop of every data is the every as light basis. (5) See products may not be similar differences. Common decrease and phylaxis. (4) See relations individual stop of every data is the every as light basis. Common decrease and phylaxis. (4) See relations individual stop of every data is the individual stop of every data is the every as light basis. Common decrease anaphylaxis. (4) See re	11 12 13	Solution for percutaneous, intradermal, or subcutaneous administration Initial U.S. Approval: 1925	 56 • Severe, unstable or uncontrolled asthma. (4) 57 • History of any severe systemic reaction to the allergen extract when
 Note-Indigreestimating information for complete backed warning. WarkINNGS AND PRECAUTIONS. The risk of analophysics in the following individuals with every analophysics. (a) Device Individuals for at least 20 minutes following administrations. that reduce the ability to survive anaphysics. (a) Observe Individuals for at least 20 minutes following administrations. The research and the low individual with extreme sensitivity to these products, on an accelerated immunotherapy build-up, witching to another low. (51) Theres products may and the suitable for individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, witching to another low. (51) Theres products may and the suitable for individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, witching to another low. (51) Theres products may and the suitable for individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, witching to another low. (61) Theres products may and the suitable for individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, witching to another low. (61) Theres products may and build-up, witching to another low. (75) Theres products may and build-up, witching to another low. (76) Theres products may and build-up, witching to another low. (76) Theres products may and build-up, witching to another low. (76) Theres products may and build-up, witching to another low. (76) Theres products may and build-up, witching to another low. (76) There products may and build-up, witching to another low. (76) There products may and build-up, witching to another low. (76) There products may and build-up, witching to another low. (76) Statist stating default of low.	13	WARNING: ANAPHYLAXIS	 administered for diagnosis or treatment. (4) Medical conditions that reduce the ability to survive anaphylaxis. (4)
 Distance analysis and the products of the second probability of the second products of the second pro	15	See full prescribing information for complete boxed warning.	60WARNINGS AND PRECAUTIONS
 Do not administer to individuals with severe, unstable or uncertained to individual exposure to similar allergene current when administered for diagons or treatment, or anaphylaxis. (4) Chemical exposure of administration. Energency measures and personel trained in the additions that redue the ability to survive anaphylaxis. (5) Observe individuals for at least 30 minutes following administration. Energency measures and personel trained in the event of a diagons. (5) Chemical exposure of administration. Energency measures and personel trained in the event of a difference of the photoe exposure of a mapphylaxis. (a) These products may not be suitable for individuals who may be unceposite to e pinephyline or individual stub or cervice subulanceous immunotherapy (e.g., e.g., encertain exposure of a difference of the photoe exposure of a mapphylaxis direct at 1400-495-437 or Adverse. Recentrols, correspondence of a difference of the differ	17	including anaphylactic shock and death. (5.1)	61 The risk of anaphylaxis may be increased in the following situations:
190 uncontrolled ashma, history of severe systemic reaction to the severing of high vents and volumes of sources and vol	18	 Do not administer to individuals with severe, unstable or 	 62 • Extreme sensitivity to non-standardized allergenic extracts. 63 • Concomitant environmental exposure to similar allergens
allergene extract when administered for diagnosis or freatment, or anaphytaxis. (d) allergene extracts. anaphytaxis. (d) (e.g., "nush" immunotenzy). observe individuals for at least 30 minutes following administration. Energency messares and personnel trained in their uses bar available in the event of a life-for-atening reaction. (5.1) (f) (f) (f) (f) (f) <	19	uncontrolled asthma, history of severe systemic reaction to the	64 • Receipt of high concentrations and volumes of non-standardized
 with medical conditions that reduce the abulty to survive amply lass, if the second of a machenized build-up schedule (e.g., "nush" immunotherapy. Observe individuals for at text 30 minutes following administration. Energency messaves and personnel trained in their text of the available in the creat of a life-intractening reaction. Changing to another lot of allergen: .(5) Changing to another lot of allergen: .(5) Changing to another lot, and the creat of a life-intractening reaction. Common adverse reactions neoreting in 26 to 82% of all patients who may be are expensive to epinephrine or inhaled bronchodilators, such as uncreasing any and the vailable for individuals with exemption and the specific or exposed in the injection site, (6) These products may not be vailable for individuals with may be uncreased risk of anaphylaxis. (5.1) Moristandadized allergenic extracts are indicated for: Nor-standadized allergenic extracts are indicated for: Statistic diagnosis of patients with a clinical history of allergy to the specific orresponding allergens. (1) The perfort SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. Certain medications may be fail. (6) To report SUSPECTED ADVERS ERACTIONS. For pertainons, intraction and adverse reactions and Doce Sensitivity	20	allergen extract when administered for diagnosis or treatment, or	65 allergenic extracts.
 and physics. (a) and physics. (b) and physics. (c) (c) (c)<!--</th--><th>21</th><th>with medical conditions that reduce the ability to survive $a_{\rm neuphylaxis}$ (4)</th><th>• Receipt of an accelerated build-up schedule (e.g., "rush"</th>	21	with medical conditions that reduce the ability to survive $a_{\rm neuphylaxis}$ (4)	• Receipt of an accelerated build-up schedule (e.g., "rush"
administration. Emergency measures and personnel trained in their semust be available in the event of a life-threatening reaction. (51) 6 * Changing to another lot of allergen. ADVERSE REACTIONS. 7 Individuals with extreme sensitivity to these products on an accelerated immunotherapy build-pp, witching to another lot, receive subctaneous immunotherapy (e.g., generalized skin erythema, uncesponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (51) Common adverse reactions recursing in 26 to 82% of all patients who receive subctaneous immunotherapy (e.g., generalized skin erythema, uncesponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (51) 7 INDICATIONS AND USAGE	23	 Observe individuals for at least 30 minutes following 	67 immunotherapy).
25 use must be available in the event of a life-threatening reaction. 6.1. 27 • Individuals with extreme sensitivity to these products, on an accelerated immunotherapy build, ps. witching to another to, receiving high does of these products, or exposed to similar accelerate dimmontherapy tells of an anotheraps. 70 28 corrections, fixed analystaxis, (5.1) 71 31 • These products may not be suitable for individuals who may be imresponsive to eniperfure or individuals who may be imresponsive to primperfure individual sub on may be imresponsive to eniperfure or individual sub one subcutaneous immunotherapy (e.g., erythem, swelling, interfuse and prime reactions may be fail. (6) 31 • These products may not be suitable for individuals who may be imresponsive to eniperfure or individuals who may be imresponsive to eniperfure or individual sub on may be imresponsive individuals who may be imresponsive individual and the individual sub on prime individual and in the individual sub on may be imresponsive individual and in the individual sub on may be imresponsive individual and in the individual sub on prime individual sub on prime individual sub on may be individual sub on prime individual sub on prime individual sub on sub on the individual sub on and the individual sub on may be individual sub on prime individual sub on primumotherapy (e.g. erythem, suelling, indindividual sub on prime in	24 24	administration. Emergency measures and personnel trained in their	• Changing to another lot of allergen. (5)
 (5.1) (6.1) (7.2) (7.3) (7.4) (7.4) (7.4) (7.4) (7.4) (7.4) (7.4) (7.4) (7.4) 	25	use must be available in the event of a life-threatening reaction.	69ADVERSE REACTIONS
 Individuals with extreme sensitivity to these products, or an accelerated immunotherapy billing another log, receiving high does of these products, or exposed to similar altergens may be a tincrease risk of anaphysias. (5.1) These products may not be suitable for individuals who may be urresponsive to eipherhier or individuals who may be urresponsive to urresponsive to eipherhier or individuals who may be urresponsive to eipherhier or individuals who may be urresponsive to urresponsive skinet who receive suburbatoresponse the endu	26	(5.1)	70 Common adverse reactions reported for non-standardized allergenic extracts
 accelerate immunoterapy fund-up, switching to anonter in, allergens may be at increased risk of anaphylaxis. (5.1) These products may not be suitable for individuals who may be increased risk of anaphylaxis. (5.1) These products may not be suitable for individuals who may be increased risk of anaphylaxis. (5.1) Mon-standardized allergenic extracts are indicated for: Stin test diagnosis of patients with a clinical history of allergy to the specific corresponding allergenic. (1) Stin test diagnosis of patients with a clinical history of allergy to the specific corresponding allergenic. (1) Immunotherapy for the reduction of allergeni-induced allergis exprisions confirmed by positive skin test or by in vitro testing for allergen-specific [Eff antibodies. (1) Toreport SUSPECTED ADVERSE REACTIONS. contact Jubilant HollisterSite at 1:800-495.7437 or Adverse. Reactions/gibi.jubi.com; or the FDA at 1:800-FDA JUB and Reacting and the holisterSite at 1:800-495.7437 or Adverse. Reactions/gibi.jubi.com; or the FDA at 1:800-FDA JUB and Reacting and antibility and antibility and antibility and antibility and antibility and at the origin and the induction of allergeni-induced allergis exprisions confirmed by positive skin test or by in vitro testing for allergen-specific left antibodies. (1) FULL PRESCRIBING INFORMATION: CONTENTS FULL PRESCRIBING INFORMATION: CONTENTS INDICATIONS AND USAGE Percutaneous for diagnostic testing. FULL PRESCRIBING INFORMATION: CONTENTS Loss Geriatric Use I. INDICATIONS AND USAGE S. Certain medications may decrease shit set wheal and erytherna response, including antihistamines, optical anosthetics Set 17 for PATIENT COUNSELING INFORMATION S. Contra And Ministration S. Contra And Ministration S. Contra And Patiena And Patterna Andiagenia and A	27	Individuals with extreme sensitivity to these products, on an	71 arc. 72 • Local adverse reactions occurring in 26 to 82% of all patients who
 altergam may be at increased risk of anaphysics (51) These products may not be suitable for individuals who may be unresponsive to eignifyerine or indiated brancholitators, such as those taking beta-blockers, (51) These products may not be suitable for individuals who may be unresponsive to eignifyerine or indiated for anaphysics, (51) ————————————————————————————————————	20	accelerated immunotherapy build-up, switching to another lot,	73 receive subcutaneous immunotherapy (e.g., erythema, swelling,
 These products may not be suitable for individuals values may be unresponsive to epinephrine or inhaled bronchodillators, such as those taking beta-blockers. [5,1] INDICATIONS AND USAGE	30	allergens may be at increased risk of anaphylaxis. (5.1)	74 pruritus, tenderness and pain at the injection site). (6)
33 unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1) 76 34 subcentation of the relation of the relatin of the relatin of the relation of the rel	31	• These products may not be suitable for individuals who may be	75 • Systemic adverse reactions, occurring in \leq 7% of patients who receive
33 those taking beta-blockers. (5.1) // 34 // // 35	32	unresponsive to epinephrine or inhaled bronchodilators, such as	76 subcutaneous immunotherapy (e.g., generalized skin erythema,
34	33	those taking beta-blockers. (5.1)	// urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, and
35 INDICATIONS AND USAGE. 79 70	34		76 nypotension). Systemic reactions may be fatal. (6)
36 Non-standardized allergenic extracts are indicated for: 36 Non-standardized allergenic extracts are indicated for: 36 37 Skin test diagnosis of patients with a clinical history of allergen specific corresponding allergens: 16 17 16 17 18	35	INDICATIONS AND USAGE	79 To report SUSPECTED ADVERSE REACTIONS, contact Jubilant
37 Skin test diagnosis of patients with a clinical history of allergy to the specific corresponding allergens. (1) 90 38 Immunotherapy for the reduction of allergen-induced allergie symptoms confirmed by positive skin test or by <i>in vitro</i> testing for allergen-specific lig antibidity in vitro testing in vitro testing in vitro testing or subcutaneous use only. 82 43 For percutaneous for diagnostic testing. 87 90 FULL PRESCRIBING INFORMATION: CONTENTS 20 107 7.3 Tricyclic Antidepressants (7) 91 FULL PRESCRIBING INFORMATION: CONTENTS 31 108 8. USE IN SPECIFIC POPULATIONS (88 92 WARNING: ANAPHYLAXIS 108 109 8.1 Pregnancy (98 8. USE IN SPECIFIC POPULATIONS (96 93 1. INDICATIONS AND USAGE 109 8.1 Pregnancy (98 8. USE IN SPECIFIC POPULATIONS (96 111 8.4 Pediatric Use (109 94 2. DOSAGE AND ADMINISTRATION 110 112 8.5 Geriatric Use (110 112 8.5 Geriatric Use (110 95 2.1 Preparation for Administration 111 8.4 Pediatric Use (110 12.1 Mechanism of Action (12.1 Mechanism of Action (1	36	Non-standardized allergenic extracts are indicated for:	60 HomsterStier at 1-800-495-7437 or Adverse. Keactions@jns.jubl.com; or 81 the EDA at 1 800 EDA 1089 or ywyy file gov/medwatab
38 specific corresponding allergens. (1) ************************************	37	Skin test diagnosis of patients with a clinical history of allergy to the	87DRUC INTERACTIONS
 immunotherapy for the reduction of allergen-induced allergic symptoms confirmed by positive skin test or by in vitro testing for allergen-specific lgE antibodies. (1) international control of allergen-induced allergic symptoms confirmed by bottless skin test with an and tryfucting antihistamines, topical anesthetics, and tricyclic antidepressants. (7) international control of allergen-induced allergic symptoms confirmed by bottless skin test with an and tryfucting antihistamines, topical anesthetics, and tricyclic antidepressants. (7) international control of allergen-induced allergic symptoms confirmed by bottless skin test with an and tryfucting antihistamines, topical anesthetics, and tricyclic antidepressants. (7) international control of allergen-induced allergic symptoms confirmed by bottless skin test with an and tryfucting antihistamines, topical anesthetics, and tricyclic antidepressants. (7) international control of allergen-induced allergic symptoms confirmed by bottless skin test with an and tryfucting antihistamines, topical anesthetics, and tricyclic antidepressants. (7) international control of allergen-induced allergic symptoms control of allergen-induced allergic symptoms control of allergic sy	38	specific corresponding allergens. (1)	82 • Certain medications may decrease skin test wheel and erytheme
41 igfa antibacies. (1) 85 anesthetics, and tricyclic antidepressants. (7) 1.1.1 42 DOSAGE AND ADMINISTRATION	39	Immunotherapy for the reduction of allergen-induced allergic symptoms	84 responses, including antihistamines, topical corticosteroids, topical
42 Be influences 86 43 For percutaneous, intradermal, or subcutaneous use only. 88 44 Administration: 88 45 • Percutaneous for diagnostic testing. 89 • • 90 • • 91 FULL PRESCRIBING INFORMATION: CONTENTS 107 7.3 Tricyclic Antidepressants 92 • • • 93 • INDICATIONS AND USAGE 109 8.1 Pregnancy 94 2. DOSAGE AND ADMINISTRATION 110 8.2 Lactation 95 2.1 Preparation for Administration 111 8.4 Pediatric Use 96 2.2 Diagnostic Testing 112 8.5 Geriatric Use 97 2.3 Immunotherapy 113 11. DESCRIPTION 98 3. DOSAGE FORMS AND STRENGTHS 114 12. CLINICAL PHARMACOLOGY 99 4. CONTRAINDICATIONS 116 14. CLINCAL STUDIES 100 5.1 Anaphylaxis 117 15. REFERENCES 102 5.2 Cross-reactions and Dose Sensitivity 118 16. HOW SUPPLIED/STORAGE AND HANDLING 103 6	40	confirmed by positive skin test or by <i>in vitro</i> testing for allergen-specific	85 anesthetics, and tricyclic antidepressants. (7)
43For percutaneous, intradermal, or subcutaneous use only. Administration:87See 17 for PATIENT COUNSELING INFORMATION. Revised: 2/202245••Percutaneous, intradermal, or subcutaneous use only. Administration:88See 17 for PATIENT COUNSELING INFORMATION. Revised: 2/202245••Percutaneous, intradermal, or subcutaneous use only.8889•••Revised: 2/202290•••••91FULL PRESCRIBING INFORMATION: CONTENTS 921077.3 Tricyclic Antidepressants 94•92WARNING: ANAPHYLAXIS 931088. USE IN SPECIFIC POPULATIONS 961098.1 Pregnancy 94942. DOSAGE AND ADMINISTRATION 961108.2 Lactation 962.2 Diagnostic Testing 971128.5 Geriatric Use 97933. DOSAGE FORMS AND STRENGTHS 9911311. DESCRIPTION 9811412. CLINICAL PHARMACOLOGY 99944. CONTRAINDICATIONS 9911614. CLINCAL STUDIES 11611614. CLINCAL STUDIES 1161015.1 Anaphylaxis 91011715. REFERENCES 11611715. REFERENCES 1161025.2 Cross-reactions and Dose Sensitivity 91011816. HOW SUPPLIED/STORAGE AND HANDLING 11917. PATIENT COUNSELING INFORMATION 1201036. ADVERSE REACTIONS 910120121Sections or subsections omitted from the full prescribing 1221057.1 Antihistamines 9106122Sections or subsections omitted from	42	DOSACE AND ADMINISTRATION	86
44 4 Administration: 4588Revised: 2/202245 90••Percutaneous for diagnostic testing.88Revised: 2/202291FULL PRESCRIBING INFORMATION: CONTENTS 921077.3 Tricyclic Antidepressants92WARNING: ANAPHYLAXIS1088. USE IN SPECIFIC POPULATIONS931. INDICATIONS AND USAGE1098.1 Pregnancy942. DOSAGE AND ADMINISTRATION1108.2 Lactation952.1 Preparation for Administration1118.4 Pediatric Use962.2 Diagnostic Testing1128.5 Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS1201047. DRUG INTERACTIONS1201057.1 Antihistamines1201067.2 Topical Corticosteroids and Topical Anesthetics121123Variation are not listed.122	43	For nercutaneous, intradermal, or subcutaneous use only	87 See 17 for PATIENT COUNSELING INFORMATION.
45 • Percutaneous for diagnostic testing. 90 • 91 FULL PRESCRIBING INFORMATION: CONTENTS 92 WARNING: ANAPHYLAXIS 93 1. INDICATIONS AND USAGE 94 2. DOSAGE AND ADMINISTRATION 95 2.1 Preparation for Administration 96 2.2 Diagnostic Testing 97 2.3 Immunotherapy 98 3. DOSAGE FORMS AND STRENGTHS 99 4. CONTRAINDICATIONS 99 4. CONTRAINDICATIONS 100 5. WARNINGS AND PRECAUTIONS 111 11. DESCRIPTION 99 4. CONTRAINDICATIONS 100 5. WARNINGS AND PRECAUTIONS 101 5.1 Anaphylaxis 102 5.2 Cross-reactions and Dose Sensitivity 103 6. ADVERSE REACTIONS 104 7. DRUG INTERACTIONS 105 7.1 Antihistamines 106 7.2 Topical Corticosteroids and Topical Anesthetics 102 5.2 Topical Corticosteroids and Topical Anesthetics	44	Administration:	88 Revised: 2/2022
899091919191919191919191919191919191919192939494959596979899999091929394949595969798989999999091919293949495959696979898999991919192939394949495959596969797989899999191919192939494959595959696979798989999 <th>45</th> <th>Percutaneous for diagnostic testing.</th> <th></th>	45	Percutaneous for diagnostic testing.	
9091FULL PRESCRIBING INFORMATION: CONTENTS1077.3 Tricyclic Antidepressants92WARNING: ANAPHYLAXIS1088. USE IN SPECIFIC POPULATIONS931. INDICATIONS AND USAGE1098.1 Pregnancy942. DOSAGE AND ADMINISTRATION1108.2 Lactation952.1 Preparation for Administration1118.4 Pediatric Use962.2 Diagnostic Testing1128.5 Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS1201047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics122123123	89		
91FULL PRESCRIBING INFORMATION: CONTENTS1077.3 Tricyclic Antidepressants92WARNING: ANAPHYLAXIS1088. USE IN SPECIFIC POPULATIONS931. INDICATIONS AND USAGE1098.1Pregnancy942. DOSAGE AND ADMINISTRATION1108.2Lactation952.1 Preparation for Administration1118.4Pediatric Use962.2 Diagnostic Testing1128.5Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.11005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1047. DRUG INTERACTIONS1201057.1 Antihistamines1201067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123	90		
92WARNING: ANAPHYLAXIS1088. USE IN SPECIFIC POPULATIONS931. INDICATIONS AND USAGE1098.1Pregnancy942. DOSAGE AND ADMINISTRATION1108.2Lactation952.1Preparation for Administration1118.4Pediatric Use962.2Diagnostic Testing1128.5Geriatric Use972.3Immunotherapy11311.DESCRIPTION983.DOSAGE FORMS AND STRENGTHS11412.CLINICAL PHARMACOLOGY994.CONTRAINDICATIONS11512.1Mechanism of Action1005.WARNINGS AND PRECAUTIONS11614.CLINCAL STUDIES1015.1Anaphylaxis11715.REFERENCES1025.2Cross-reactions and Dose Sensitivity11816.HOW SUPPLIED/STORAGE AND HANDLING1047.DRUG INTERACTIONS1201201201057.1Antihistamines121Sections or subsections omitted from the full prescribing1067.2Topical Corticosteroids and Topical Anesthetics122information are not listed.123	91	FULL PRESCRIBING INFORMATION: CONTENTS	107 7.3 Tricyclic Antidepressants
931.INDICATIONS AND USAGE1098.1Pregnancy942.DOSAGE AND ADMINISTRATION1108.2Lactation952.1Preparation for Administration1118.4Pediatric Use962.2Diagnostic Testing1128.5Geriatric Use972.3Immunotherapy11311.DESCRIPTION983.DOSAGE FORMS AND STRENGTHS11412.CLINICAL PHARMACOLOGY994.CONTRAINDICATIONS11512.1Mechanism of Action1005.WARNINGS AND PRECAUTIONS11614.CLINCAL STUDIES1015.1Anaphylaxis11715.REFERENCES1025.2Cross-reactions and Dose Sensitivity11816.HOW SUPPLIED/STORAGE AND HANDLING1036.ADVERSE REACTIONS11917.PATIENT COUNSELING INFORMATION1047.DRUG INTERACTIONS1201057.1Antihistamines121Sections or subsections omitted from the full prescribing1067.2Topical Corticosteroids and Topical Anesthetics122information are not listed.123	92	WARNING: ANAPHYLAXIS	108 8. USE IN SPECIFIC POPULATIONS
942. DOSAGE AND ADMINISTRATION1108.2Lactation952.1 Preparation for Administration1118.4Pediatric Use962.2 Diagnostic Testing1128.5Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.11005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1Anaphylaxis11715. REFERENCES1025.2Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1Antihistamines1211067.2Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123	93	1. INDICATIONS AND USAGE	109 8.1 Pregnancy
952.1 Preparation for Administration1118.4 Pediatric Use962.2 Diagnostic Testing1128.5 Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123	94	2. DOSAGE AND ADMINISTRATION	110 8.2 Lactation
962.2 Diagnostic Testing1111128.5 Geriatric Use972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123	95	2.1 Preparation for Administration	111 8.4 Pediatric Use
972.3 Immunotherapy11311. DESCRIPTION983. DOSAGE FORMS AND STRENGTHS11412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123124124	96	2.2 Diagnostic Testing	112 8.5 Geriatric Use
983. DOSAGE FORMS AND STRENGTHS11311311412. CLINICAL PHARMACOLOGY994. CONTRAINDICATIONS11412. CLINICAL PHARMACOLOGY1005. WARNINGS AND PRECAUTIONS11512.1 Mechanism of Action1015.1 Anaphylaxis11614. CLINCAL STUDIES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics1221231412. CLINICAL PHARMACOLOGY	97	2.2 Diagnostie resting 2.3 Immunotherany	113 11 DESCRIPTION
994. CONTRAINDICATIONS11412. CLINICAL THARMACOLOGY994. CONTRAINDICATIONS11512.1 Mechanism of Action1005. WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1 Anaphylaxis11715. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123124	08	3 DOSACE FORMS AND STRENCTHS	114 12 CLINICAL PHADMACOLOCY
754. CONTRAINDICATIONS11.512.1Mechanism of Action1005.WARNINGS AND PRECAUTIONS11614. CLINCAL STUDIES1015.1Anaphylaxis11715. REFERENCES1025.2Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036.ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047.DRUG INTERACTIONS1201057.1Antihistamines1211067.2Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing123	70 00	3. Ευδλύε Γυλμό Από σταξιώτησ 4. σομτό είνοις ετίσμο	117 12, CHINCALTHANMACOLOGI 115 121 Machanism of Astion
 100 5. WARKINGS AND FRECAUTIONS 101 5.1 Anaphylaxis 102 5.2 Cross-reactions and Dose Sensitivity 103 6. ADVERSE REACTIONS 104 7. DRUG INTERACTIONS 105 7.1 Antihistamines 106 7.2 Topical Corticosteroids and Topical Anesthetics 110 14. CLINCAL STUDIES 117 15. REFERENCES 118 16. HOW SUPPLIED/STORAGE AND HANDLING 119 17. PATIENT COUNSELING INFORMATION 120 121 Sections or subsections omitted from the full prescribing 122 information are not listed. 	99 100	7. CONTRAINDICATIONS 5. WADNINGS AND DECAUTIONS	115 12.1 WECHANISH OF ACTION
1015.1 Anaphylaxis11/15. REFERENCES1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing	100	5. WAKININGS AND EKEUAU HUINS 5.1. Augustustusia	110 14. ULINUAL STUDIES
1025.2 Cross-reactions and Dose Sensitivity11816. HOW SUPPLIED/STORAGE AND HANDLING1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics122123information are not listed.	101	5.1 Anaphylaxis	11/ IS. KEFEKENCES
1036. ADVERSE REACTIONS11917. PATIENT COUNSELING INFORMATION1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing	102	5.2 Cross-reactions and Dose Sensitivity	118 16. HOW SUPPLIED/STORAGE AND HANDLING
1047. DRUG INTERACTIONS1201057.1 Antihistamines1211067.2 Topical Corticosteroids and Topical Anesthetics121123Sections or subsections omitted from the full prescribing	103	6. ADVERSE REACTIONS	119 17. PATIENT COUNSELING INFORMATION
1057.1 Antihistamines121Sections or subsections omitted from the full prescribing1067.2 Topical Corticosteroids and Topical Anesthetics121information are not listed.123	104	7. DRUG INTERACTIONS	120
1067.2 Topical Corticosteroids and Topical Anesthetics122 information are not listed.123	105	7.1 Antihistamines	121 Sections or subsections omitted from the full prescribing
123	106	7.2 Topical Corticosteroids and Topical Anesthetics	122 information are not listed.
	123		

124 **FULL PRESCRIBING INFORMATION**

WARNING: ANAPHYLAXIS

- Non-standardized allergenic extracts can cause anaphylaxis, including anaphylactic shock and death. (5.1)
- Do not administer to individuals with:
 - severe, unstable or uncontrolled asthma;
 - o history of severe systemic reaction to the allergen extract when administered for diagnosis of treatment;
 - medical conditions that reduce the ability to survive anaphylaxis. (4)
- Observe individuals for at least 30 minutes following administration. Emergency measures and personnel trained in their use must be available in the event of a life-threatening reaction. (5.1)
- Individuals with extreme sensitivity to these products, on an accelerated immunotherapy build-up, switching to another lot, receiving high doses of these products, or exposed to similar allergens may be at increased risk of anaphylaxis. (5.1)
- These products may not be suitable for individuals who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1)

1 INDICATIONS AND USAGE

NON-STANDARDIZED ALLERGENIC EXTRACTS are indicated for:

• Skin test diagnosis of individuals with a clinical history of allergy to the specific corresponding allergens.

NON-STANDARDIZED ALLERGENIC EXTRACTS are indicated for:

• Immunotherapy for the reduction of allergen-induced allergic symptoms confirmed by positive skin test or by *in vitro* testing for allergen specific IgE antibodies for the specific corresponding allergens.

134 2 DOSAGE AND ADMINISTRATION

For percutaneous, intradermal, or subcutaneous administration only. Do not inject intravenously. 136

137 **2.1 Preparation for Administration**

Appearance is clear to slightly opalescent. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard solution if either of these conditions exist.

- Non-standardized allergenic extracts diluted with Albumin Saline with Phenol (0.4%) (stabilized diluent) may be more potent
 than extracts diluted with diluents that do not contain albumin. When switching from non-stabilized to stabilized diluent,
 consider less concentrated initial dilutions for both intradermal testing and immunotherapy.
- Different formulations, preparations, or new lots of non-standardized allergenic extracts are not interchangeable. Dosing
 should be adjusted appropriately when formulations, preparations, or lots of non-standardized allergenic extracts are changed
 [see *Immunotherapy (2.3)* and *Dosage Forms and Strengths (3)*].
- Allergenic extracts may be prepared for intradermal (diagnosis) or subcutaneous (immunotherapy) administration by diluting
 stock concentrates.
- For diluent, use sterile albumin saline with phenol or sterile normal saline with phenol.
- Dilute stock concentrates by a minimum of 100-fold for intradermal testing. Dilutions of 1,000-fold or greater are appropriate starting points for patients with a clinical history of adverse reaction.
- To prepare dilutions for intradermal testing and immunotherapy, start with a stock concentrate, and prepare a ten-fold (1:10)
 dilution by adding 0.5 mL of concentrate to 4.5 mL of sterile aqueous diluent. Prepare subsequent dilutions in a similar
 manner. (see Table 1).

160

125 126

127

128

129 130

131

132

133

141

145

152

161 **Table 1: 10-fold Dilution Series**

Dilution	Extract	Milliliters of Diluent	Dilution Strength (w/v)				
0	Concentrate		1:10	1:20	1:50	1:100	1:650
1	0.5 mL Concentrate	4.5	1:100	1:200	1:500	1:1,000	1:6,500
2	0.5 mL Dilution	4.5	1:1,000	1:2,000	1:5,000	1:10,000	1:65,000
3	0.5 mL Dilution 2	4.5	1:10,000	1:20,000	1:50,000	1:100,000	1:650,000
4	0.5 mL Dilution 3	4.5	1:100,000	1:200,000	1:500,000	1:1,000,000	1:6,500,000
5	0.5 mL Dilution 4	4.5	1:1,000,000	1:2,000,000	1:5,000,000	1:10,000,000	1:65,000,000
6	0.5 mL Dilution 5	4.5	1:10,000,000	1:20,000,000	1:50,000,000	1:100,000,000	1:650,000,000

Note: A lower starting dose and/or less concentrated dilutions may be necessary for highly sensitive patients with a clinical history of sensitivity, or for those who display severe symptoms. [see *Diagnostic Testing (2.2), Percutaneous Skin Testing (2.2.1)* and *Intradermal (Intracutaneous) Skin Test (2.2.2)*].

163 2.2 Diagnostic Testing

164 Testing is performed to identify patients that exhibit an allergic response at the site of administration. False positive reactions 165 may occur. A positive skin test reaction must be interpreted in the context of the individual's clinical history and known 166 exposure to the allergen.

- Administer percutaneous tests prior to administration of intradermal tests to identify highly sensitive patients.
- Do not use allergen mixes for diagnostic testing because a positive reaction would not permit specific identification of the allergen(s) that elicited the reaction. In addition, a negative reaction would fail to indicate whether an individual component allergen would have elicited a positive reaction at full strength.

172 2.2.1 Percutaneous Skin Testing

173 **Dose**

162

171

178

183

Unless an individual is suspected to be at greater risk for anaphylaxis, the initial starting dose is 1 drop (approximately 0.05 mL) of undiluted allergenic extract. For individuals suspected to be at greater risk for anaphylaxis (for example, as indicated by a history of allergen-induced anaphylaxis), initiate percutaneous testing with a sequence of serial 10-fold dilutions of undiluted allergenic extract spaced 15-20 minutes apart [see *Preparation for Administration (2.1)*].

179 Administration

- Percutaneous Test: Place one drop (approximately 0.05 mL) of allergen on the skin and pierce through drop
 superficially into the skin, lifting slightly. Use a skin test device, such as a sterile needle, lancet, or bifurcated needle.
- Percutaneous Test using self-loading devices: Refer to the manufacturer's product instructions.

184 Concurrently, use a positive histamine skin test control to identify patients whose recent use of drugs with antihistamine 185 activity may result in a false negative skin test. Apply a 50% glycerin solution as a negative control, to identify false positive 186 responses to the extracting fluid used in the manufacture of allergenic extracts, or due to dermographism [see *Drug* 187 *Interactions (7)*].

189 Interpreting Results

190 For interpretation of percutaneous skin tests, refer to the information provided in Allergy Diagnostic Testing: An Updated

- 191 Practice Parameter.¹ In addition, follow the directions provided with the percutaneous skin test devices. Measure wheal 192 responses for the histamine positive control test at 15 minutes and for the allergen tests at 15 to 20 minutes.
- The negative control (50% glycerin solution) response should measure < 3 mm wheal and ≤ 10 mm flare.¹
- Response to positive controls should be at least 3 millimeters larger than the response to the negative control.

- If either the response to the histamine positive control or to the negative control do not meet the criteria above for
 acceptable wheal size, the results for the allergenic extracts tested at the same time should be considered invalid and be
 repeated.
- Fire Ant: Percutaneous testing is considered positive when the response occurs at a concentration of 1:100 w/v or less.⁴

200 2.2.2 Intradermal (Intracutaneous) Skin Test

Always perform percutaneous tests prior to intradermal skin tests.^{1, 2}

203 **Dose**

199

206

211

214

218

232 233

235

Perform intradermal tests with at least 100-fold less concentrated solutions than the stock concentrates used in percutaneous tests [see *Preparation and Administration (2.1)*].

Fire Ant: Use 0.02 mL of a 1:100,000 v/v dilution of the concentrate for intradermal tests. Very sensitive individuals such as those who have had nearly fatal anaphylactic reactions may not tolerate even 1:100,000 v/v dilution of concentrate as a starting point. These patients should be tested with a 1:10,000,000 v/v dilution of concentrate [see *Preparation for Administration (2.1)*].

212 Use intradermal tests following a negative or equivocal percutaneous test when the patient continues to report a history of 213 symptoms following exposure to a specific allergen.

215 Administration

Intradermally inject 0.02 mL of the allergen using a 1 mL intradermal testing syringe with a 26 or 27 gauge, 1/2" or 3/8" needle with intradermal bevel, graduated in 0.01 units. Insert needle at a 30° angle, bevel down.

Test concurrently with a positive histamine control at intradermal strength (0.1 mg/mL of histamine base) and an aqueous
 buffer negative control (Sterile Albumin Saline with Phenol, Sterile Buffered Saline with Phenol).

222 Interpreting Results

For interpretation of intradermal skin tests, follow the information provided in Allergy Diagnostic Testing: An Updated Practice Parameter.¹

- Measure wheal responses for the histamine positive control test and allergen tests at 10-15 minutes after injection.
- Response to the positive control should be at least 3 millimeters larger than the response to the negative control.
- The negative control (50% glycerin solution) response should measure < 3-mm wheal and ≤ 10 mm flare (erythema).
- If either the response to the histamine positive control or to the negative control do not meet the criteria above for acceptable wheal size, the results for the allergenic extracts tested at the same time should be considered invalid and be repeated.
- Fire Ant: Intradermal testing is considered positive when the response occurs at a concentration of 1:1,000 w/v or less.⁴

2.3 Immunotherapy

234 For subcutaneous administration only.

236 Administration of Immunotherapy

Administer immunotherapy by subcutaneous injection in the lateral aspect of the arm or thigh. Avoid injection directly into
 any blood vessels. Administer injections with a sterile 1 mL allergy treatment syringe with a 26 or 27 gauge, 1/2", beveled
 needle, graduated in 0.01 units.

The optimal interval between doses of allergenic extract varies among individuals. Injections are usually given one or two times per week until the maintenance dose is reached, at which time the injection interval is increased to 2, 3, and finally 4 weeks.

244

Most adverse reactions occur within 30 minutes after injection. Therefore, observe patients for at least 30 minutes. For high risk patients, 30 minutes of observation may not be sufficient.²

247

248 Dosing of non-standardized allergenic extracts for allergen immunotherapy is highly individualized. Adjust dose according 249 to the degree of sensitivity of the patient, tolerance to the extract administered during the early phases of an injection regimen, and the clinical response. Dosing is individualized by choice of an initial dose, the schedule of dose build-up, the target maintenance dose, the actual maintenance dose, and the duration of treatment.

252

The large volume of solution for immunotherapy may produce increased discomfort in the pediatric population. In order to achieve the total dose required, the volume of the dose may need to be divided into more than one injection per visit.²

256 **2.3.1 Dose Build-up**

Following the first administration of 0.03 mL of the selected initial dilution of allergenic extract, dosing is increased in 0.03 mL to 0.12 mL increments until 0.3 mL is reached, following which 0.03 mL is administered from the next most concentrated allergen extract or allergen mixture vial in the dilution series. The interval between doses is usually 3 to 7 days during dose build-up. Proceed in this manner until a maintenance dose is reached. The final maintenance dose may not be the target maintenance dose selected at the beginning of therapy.

263 The following adjustments may be necessary during dose build-up:

- If allergic symptoms or local reactions develop shortly after dose administration, decrease the dose volume to one-half or one-quarter of the maximum dose previously attained.
- If the patient is experiencing any seasonal allergy symptoms, decrease the dose volume to one-half or one-quarter of the maximum dose previously attained.
- Adjust the dose periodically based on the patient's tolerance and reaction.
- Decrease the dose if the previous injection resulted in a marked local reaction.
- Repeat the previous dose or reduce the dose at the next administration if local reactions persist for longer than 24 hours.
- Decrease the dose if the previous injection resulted in a systemic reaction. Any evidence of a systemic reaction is an indication for a significant (at least 75%) reduction in the subsequent dose or the cessation of immunotherapy.
- Repeated systemic reactions, however mild, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.

276 2.3.2 Maintenance Dose Selection, Adjustments, and Intervals

The maintenance dose is the dose that provides therapeutic efficacy without severe adverse local or systemic reactions. This dose may be limited by adverse reactions and may not be the original targeted maintenance dose. Select a maintenance dose based on the patient's clinical response and tolerance.

- Suggested maintenance dose is 0.3 mL of the undiluted allergen extract. Occasionally, higher doses are necessary to relieve symptoms.
- Maintenance doses larger than 0.3 mL of undiluted allergen extract may cause patient discomfort due to the 50% glycerin content.
- After the maintenance dose is achieved, increase the injection interval to 2 weeks, then 3 weeks, and finally 4 weeks, as tolerated. Administer the maintenance dose at a given interval three or four times before further increasing the interval to assure that no reactions occur. Protection may be lost rapidly if the interval between doses is more than 4 weeks.
- The following adjustments to the maintenance dose may be necessary.

290 Withhold immunotherapy and/or reduce dosage, if any of the following conditions exist:

- Severe symptoms of rhinitis and/or asthma. Decrease dose to one-half or one-quarter of the maximum dose previously attained if the patient has any seasonal symptoms.
- Allergic symptoms or a local reaction following the prior dose.
- Infection accompanied by fever.
- Exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection. 296

297 In situations prompting dose reduction, a cautious increase in dosage can be attempted once the reduced dose is tolerated.

299 Decrease the interval between doses if symptoms develop before the next injection is scheduled.

301 In some patients, the dosage may be increased and/or the dosing interval shortened based on individual responses and

dosing requirements. If the onset of symptoms is soon after the initiation of immunotherapy, decrease the interval between each dose.

304

298

300

305 Changing to a different lot of extract: All extracts can lose allergenic activity over time and extracts vary in allergenic activity. Two different lots of extract could differ substantially in allergenic activity, even if they are the same formula and concentration. The volume of the first dose from the new vial should not exceed 50% of the previous dose. Do not use extracts beyond their expiry date.

Changing to a different formulation of extract or to an extract from a different manufacturer: Decrease the starting dose of the new extract when the extract is the same formula and dilution as the one previously used. In general, a volume dose reduction to 50% of the previous product dose is adequate, but each situation must be evaluated separately considering the patient's history of sensitivity, tolerance of previous injections, and other factors. If the patient tolerates the 50% decrease, then raise the next dose to the previous tolerated dose amount. To re-establish the maintenance dose the starting interval between doses should not be greater than one week.

317 Prolonged period has elapsed since the last injection: Patients may lose tolerance for allergen injections during prolonged 318 intervals (> 4 weeks) between doses. The duration of tolerance is an individual characteristic and varies from patient to 319 patient. In general, the longer the lapse in the injection schedule, the greater dose reduction required.

321 Changes made in the extract concentrate formula: Changes other than those listed above such as a difference in extracting 322 fluid (e.g., change from non-glycerin extracts to 50% glycerin extracts), combining two or more stock concentrates, or any 323 other change can affect a patient's tolerance of the treatment. Extra dilutions are recommended whenever starting a revised 324 formula. The greater the change, the greater the number of dilutions required.

326 **Duration of Treatment**

The duration of treatment for immunotherapy has not been established. A period of two to three years of injection therapy
 constitutes an average minimum course of treatment. Evaluate patients for treatment response at least every 6 to 12 months
 while they receive immunotherapy.

331 **3 DOSAGE FORMS AND STRENGTHS**

Non-standardized allergenic extracts are solutions: stock concentrates, labeled in weight/volume, in a glycerin-preserved
 extracting fluid, supplied in 5, 10, 30, and 50 mL vials. (3, 16) Refer to the vial label for the product concentration. (11)

335 4 CONTRAINDICATIONS

336 Non-standardized allergenic extracts are contraindicated in individuals with the following conditions:

- Severe, unstable or uncontrolled asthma.
- History of any severe systemic reaction to the allergen extract when administered for diagnosis or treatment.
- Medical conditions that reduce the ability to survive anaphylaxis.

341 5 WARNINGS and PRECAUTIONS

342 5.1 Anaphylaxis

Anaphylaxis, which may lead to death, can occur in individuals following the administration of non-standardized allergenic
 extracts, particularly in the following situations:

- Extreme sensitivity to the non-standardized allergenic extract.
- Concomitant environmental exposure to allergens.
- Receipt of high doses of the non-standardized allergenic extract.
- Receipt of an accelerated build-up schedule ("rush" immunotherapy).
- Change from one lot of a particular non-standardized allergenic extract to another lot of the same non-standardized allergenic extract.
- 351

340

316

320

352 Administer non-standardized allergenic extracts in a healthcare setting under the supervision of a physician prepared to

353 manage anaphylaxis; management may include use of inhaled bronchodilators and use of epinephrine. Non-standardized

allergenic extracts may not be suitable for individuals who may be unresponsive to epinephrine or inhaled bronchodilators,

such as those taking beta-blockers. See prescribing information for epinephrine for complete information, particularly on

- 356 medications that blunt or potentiate epinephrine activity. Individuals should remain in the physician's office for a minimum
- of 30 minutes after receiving an injection of non-standardized allergenic extracts, so that any adverse reaction can be

358 observed and properly handled.

360 5.2 Cross-reactions and Dose Sensitivity

361 When determining the final dose of an allergen mixture for immunotherapy, consider cross-reactivity among component 362 extracts.

363

375

377

382

364 Determine the initial dilution of allergenic extract, starting dose, and progression of dosage based on the patient's history and 365 results of skin tests [see *Dosage and Administration (2)*]. Strongly positive skin tests can be indicators for potential adverse 366 reactions.

368 6 ADVERSE REACTIONS

369 Common adverse reactions reported for non-standardized allergenic extracts are:

- Local reactions occurring in 26 to 82% of all patients who receive subcutaneous immunotherapy, at the injection site (e.g., erythema, swelling, pruritus, tenderness and pain).²
- Systemic adverse reactions, occurring in ≤ 7% of patients who receive subcutaneous immunotherapy (e.g., generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, hypotension, and shock).³ Systemic reactions may be fatal.²

376 No clinical trials of non-standardized allergenic extracts have been conducted.

Published studies of non-standardized allergenic extracts report systemic reactions occurring in fewer than 1% in patients receiving conventional immunotherapy and greater than 36% in patients receiving rush immunotherapy. Most systemic reactions occurred within 30 minutes of injection. However, systemic reactions have been reported to occur up to 2 hours after the final injection with rush schedules. Some reactions have occurred up to 6 hours after skin tests or immunotherapy.^{2, 3}

383 7 DRUG INTERACTIONS

384 7.1 Antihistamines

Do not perform skin testing with non-standardized allergenic extracts within 3 to 10 days of first-generation H1-histamine receptor blockers (e.g., clemastine, diphenhydramine) and second-generation antihistamines (e.g., loratadine, fexofenadine) being used. These products suppress histamine skin test reactions and could mask a positive response.^{1,2}

389 7.2 Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids may suppress skin reactivity; therefore, discontinue use at the skin test site for at least 2 to 3 weeks before skin testing. Avoid use of topical local anesthetics at skin test sites because they can suppress flare responses.^{1, 2}

393 7.3 Tricyclic Antidepressants

Tricyclic antidepressants, such as doxepin, can have potent antihistamine effects and may alter skin test results. Allow 7 to 14 days after discontinuation of tricyclic medication prior to skin testing.^{1,2}

397 8 USES IN SPECIFIC POPULATIONS

398 8.1 Pregnancy

399 Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated
 background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%,
 respectively. There are no human or animal data to establish the presence or absence of non-standardized allergenic
 extracts-associated risks during pregnancy.

404

411

396

405 8.2 Lactation

406 Risk Summary

407 It is not known whether non-standardized allergenic extracts are present in human milk. Data are not available to assess the 408 effects of these extracts on the breastfed child or on milk production/excretion. The developmental and health benefits of 409 breastfeeding should be considered along with the mother's clinical need for non-standardized allergenic extracts and any 410 potential adverse effects on the breastfed child from the extracts or from the underlying maternal condition.

412 **8.4 Pediatric Use**

413 For use of these products in children younger than 5 years of age, consideration should be given to the patient's ability to

414 comply and cooperate with receipt of the product and the potential for difficulty in communicating with the child regarding

415 systemic reactions.²

- 416
- The volume of a dose for immunotherapy may need to be divided for pediatric patients [see *Dosage and Administration (2.3)*].

419 8.5 Geriatric Use

Data are not available to determine if subjects 65 years of age and older respond differently to allergen immunotherapy than
 younger subjects.

423 11 DESCRIPTION

424 Non-standardized allergenic extracts are labeled "No U.S. Standard of Potency".

425

Non-standardized allergenic extracts are supplied in a Glycero Cocas extraction solution, which consists of 0.5% sodium
 chloride for isotonicity, 0.275% sodium bicarbonate as a buffer, and 50% glycerin (volume/volume) as preservative.

428

Non-standardized allergenic extracts are supplied as a weight to volume (w/v) solution of allergen in extraction solution.
 Product concentrations vary based on the source. Refer to the vial label for the product concentration.

431

Source material mold mycelia and *Candida albicans* cells are cultivated on liquid medium which may contain one or more of
 the following constituents: casein hydrolysate; malt extract; yeast extract; maltose; dextrose; ammonium nitrate, calcium
 carbonate, calcium chloride, ammonium citrate, potassium phosphate, sodium citrate, citric acid; magnesium sulfate; or trace

435 elements. Acetone and ether may be used as drying and de-fatting agents. *Candida albicans* cells are treated with phenol,
 436 which is removed by dialysis.
 437

438 Dog Hair and Dander extracts are manufactured in 3 product forms:

- Dog Hair and Dander (Regular Process) is derived from extraction of the source material without additional processing,
 and is prepared at 1:10 w/v in Glycero-Cocas.
- Acetone Precipitated (AP) Dog Hair and Dander is derived from the acetone precipitated aqueous extract and is prepared at 1:100 w/v in Glycero-Cocas.
- Ultrafiltered (UF) Dog Hair and Dander is derived from the UF aqueous extract and is prepared at 1:650 w/v in Glycero-Cocas.

446 12 CLINICAL PHARMACOLOGY

447 12.1 Mechanism of Action

The skin test reaction results from interaction of the introduced allergen and allergen-specific IgE antibodies bound to mast cells, leading to mast cell degranulation and release of histamine, tryptase and other mediators, which results in the formation of the wheal and flare.

The precise mechanisms of action of allergen immunotherapy are not known. Immunologic responses to immunotherapy
 include changes in allergen-specific IgE levels, allergen-specific IgG levels, and regulatory T cell responses.²

455 14 CLINICAL STUDIES

Specific immunotherapy with allergenic extracts is helpful in reducing symptoms associated with exposure to the offending
allergens. A summary of effectiveness by the Panel on Review of Allergenic Extracts, an advisory committee to the U.S.
Food and Drug Administration, has been published.⁵

460 **15 REFERENCES**

- Bernstein IL, Li JT, Bernstein Dl, et al. Allergy diagnostic testing: and updated practice parameter. Ann Allergy Asthma Immunol. 2008 Mar;100:S1-148.
- 2. Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, et al. Allergen immunotherapy: A practice parameter third update. J Allergy Clin Immunol. 2011 Jan;127:S1-55.
- 465 3. Greineder DK. Risk management in allergen immunotherapy. J Allergy Clin Immunol. 1996 Dec;98(6 Pt 3):S330-4
- 466
 4. Golden D B K, Demain J, Freeman T, Graft D, et al. Stinging insect hypersensitivity: A practice parameter update 2016.
 467
 468
 469
 469
 469
 469
 469
 460
 460
 460
 461
 461
 462
 463
 464
 465
 465
 466
 466
 467
 467
 468
 469
 469
 469
 469
 460
 460
 460
 460
 460
 461
 462
 462
 463
 464
 465
 465
 466
 467
 467
 468
 468
 469
 469
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
 460
- 468 5. Federal Register Proposed Rule: Biological Products: Implementation of Efficacy Review, Allergenic Extracts, Federal
 469 Register 1985;50:3082-3288.
- 470

471 16 HOW SUPPLIED/STORAGE AND HANDLING

Non-standardized allergenic extracts and mixes are supplied as 50% glycerin stock concentrates labeled in weight/volume
 and provided in 10 milliliter, 30 milliliter and 50 milliliter vials for use in percutaneous skin testing and subcutaneous
 immunotherapy. These extracts may also be supplied in 5 milliliter dropper vials for percutaneous testing only.

475

476 These products are supplied as listed in Table 2.

TABLE 2: AVAILABLE PRODUCTS		
POLLEN – GRASS ALLERGENS		
Bahia Grass, Paspalum notatum		
Brome, Smooth Bromus inermis		
Corn, Cultivated Zea mays		
Grass Mix 8-100,000 BAU/mL each of P. pratensis; A. gigantean; P. pretense; 10,000 BAU/mL of C. dactylon;		
1:20 w/v of S. halepense		
Johnson Grass, Sorghum halepense		
Oats, Common Cultivated, Avena sativa		
POLLEN – TREE ALLERGENS		
Acacia, Golden, Acacia longifolia		
Alder, Red, Alnus rubra		
Ash, White, Fraxinus americana		
Beech, American, Fagus grandifolia		
Birch Mix (PRW)- B. papyrifera, B. pendula, B. nigra		
Bottlebrush, Melaleuca citrina		
Boxelder/Maple Mix (BHR)-A. negundo, A. saccharum, A. rubrum		
Cedar, Mountain, Juniperus ashei		
Cedar, Red, Juniperus virginiana		
Cottonwood, Common, Populus deltoides		
Cyprus, Arizona, Cupressus arizonica		
Cyprus, Bald, Taxodium distichum		
Elm, American, Ulmus americana		
Elm, Chinese, Ulmus parvifolia		
Gum, Sweet, Liquidambar styraciflua		
Hackberry, Celtis occidentalis		
Hickory, Shagbark, Carya ovata		
Maple, Hard/Sugar, Acer saccharum		
Melaleuca, Melaleuca quinquenervia		
Mesquite, Prosopis glandulosa		
Mulberry Mix (RW)- M. rubra, M. alba		
Oak Mix (RVW)- Q. rubra, Q. virginiana, Q. alba		
Oak, Red, Quercus Rubra		
Olive Tree, Olea europaea		
Palm, Queen, Syagrus romanzoffiana		
Pecan Tree, Carya illinoinensis		
Pine Mix (LY)- P. contorta, P. ponderosa		
Privet, Common, Ligustrum vilgare		
Russian Olive, Elaeagnus angustifolia		
Sycamore, American, Platanus occidentalis		
Tree Mix 5-20% each of F. Americana; J. nigra; P. deltoides; U. Americana; 6.7% each of B. papyrifera; B.		
nigra; B. pendula		
Tree Mix 6- Tree Mix 6-20% each of F. Americana; J. nigra; P. deltoides; U. Americana; 6.7% each of B.		
papyrifera; B. nigra; B. pendula		
Tree Mix 11-10% each of F. americana; B. nigra; J. nigra; P. deltoides; U. americana; C. ovata; A. saccharum;		
Q. rubra; P. occidentalis; S. nigra		
Walnut, Black, Juglans nigra		

Willow, Black, Salix nigra		
POLLEN – WEED AND GARDEN PLANT ALLERGENS		
Careless Weed, Amaranthus palmeri		
Careless/Pigweed Mix (CR)- A. palmeri, A. retroflexus		
Cocklebur, Common, Xanthium strumarium		
Dock/Sorrel Mix (DS)- R. crispus, R. acetosella		
Dog Fennel Fastern <i>Functorium canillifolium</i>		
Goldenrod Solidago canadensis		
Kochia Kochia sconaria		
Lamb's Quarters <i>Chenonodium album</i>		
Marshelder/Poverty Mix (BPT)- C xanthifolia L annua L avillaris		
Nettle Urtica dioica		
Piqueed Rough Redroot Amargnthus ratroflamus		
Plantain English Diantago langeolata		
Pagwood Gignt Ambrogig trifidg		
Ragweeu, Glain, Amorosiu irijiuu		
Ragweed Mix (GSw)- A. Irijiaa, A. ariemisiijoila, A. psilosiachya		
Ragweed, western, Ambrosia psilosiacnya		
Kussian Eniste, Salcola Kali Sanah mah, Musawat, Antamining and a min		
Sagebrush, Mugwort, Artemisia vulgaris		
Scale, Wing, Atriplex canescens		
Sorrel, Sheep, Rumex acetosella		
Weed Mix 2630-25% each of X. strumarium; C. album; A. retroflexus; 12.5% each of R. crispus; R. acetosella		
MOLDS		
Alternaria/Hormodendrum Mix- A. tenuis, H. cladosporioides		
Alternaria tenuis (Alternaria alternata)		
Aspergillus fumigatus		
Aspergillus niger var. niger		
Botrytis cinerea		
Candida albicans		
Cephalosporium acremonium (Sarocladium strictum)		
Curvularia spicifera (Cochliobolus spicifer)		
Epicoccum nigrum		
Epidermophyton floccosum		
Fusarium vasinfectum (Fusarium oxysporum vasinfectum)		
Heliminthosporium interseminatum (Dendrvnhiella vinosa)		
Hormodendrum cladosporioides (Cladosporium cladosporioides)		
Mold Mix 4-25% each of A alternata: C cladosportoides: 6 2% each of A fumigatus: A nidulans: A niger var		
niger: A terreus: P digitatum: P expansum: P chrysogenum var chrysogenum: C rosea f rosea		
Mold Mix 10-2.5% each of A fumigatus: A nidulans: A niger var niger: A terreus: P digitatum: P expansum:		
P chrysogenum var chrysogenum. C rosea f rosea: 10% each of A alternata. F oxysporum vasinfectum. D		
vinosa. C cladosporioides: M racemosus: P exigua var exigua: A pullulans var pullutans: R stolonifer		
Mucor racemosus		
Penicillium Mix- P expansion P digitation P chrysogenum C rosea		
Penicillium notatum (Penicillium chrysogenum var. chrysogenum)		
Phoma herbarum (Phoma evigua var evigua)		
Pullularia nullulans (Aerobasidium nullulans var nullulans)		
Phizomy nigricans (Phizomy stolonifor)		
Stamphylium bothyosum (Plaosnorg tarda)		
Trichenbyton Mix T tonguang T without T mentageor bytog		
EDIDEDMALS		
AP Horse Hair and Dander Fauus caballus		
AP norse nair and Dander, Equus caballus		
AP Cattle Hair and Dander, Bos taurus		
AP Dog Hair and Dander, Canis lupus familiaris		

	Dog Hair and Dander, Canis lupus familiaris
	UF Dog Hair and Dander, Canis lupus familiaris
	Feather Mix- G. gallus, A. platyrhynchos, A. anser
	Guinea Pig Hair and Dander, Cavia porcellus
	INSECTS
	Cockroach, American, Periplaneta americana
	Cockroach, German, Blatella germanica
	Cockroach Mix- P. americana, B. germanica
	Fire Ant, Solenopsis invicta
477	
478	16.2 Storage and Handling
479	Store extracts at 2°C to 8°C (36°F to 46°F).
480	
481	17 PATIENT COUNSELING INFORMATION
482	Instruct patients to remain in the office under observation for a minimum of 30 minutes after an injection or longer, if deemed
483	necessary for the individual.

483 484

486

485 Inform patients that reactions may occur more than 30 minutes after skin testing or an injection.

Instruct patient to recognize the following symptoms as systemic adverse reactions and seek emergency medical care right
 away if any of these symptoms occur:

- Unusual swelling and/or tenderness at the injection site.
- Hives or itching of the skin.
- Swelling of face and/or mouth.
- Sneezing, coughing, or wheezing.
- Shortness of breath.
- Nausea.
- 495 Dizziness or faintness.496

497 Manufacturer:

498 Jubilant HollisterStier LLC

- 499 Spokane, WA 99207 U.S.A.
- 500 U.S. Lic. No. 1272
- 501 Version Date: February 24, 2022