

**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:

20-490/S007

20-613/S018

21-262/S006

CHEMISTRY REVIEW(S)

Chemistry Review: # 2	1. Division: HFD-550	2. NDA Number: 20-613
3. Name and Address of Applicant: Allergan 2525 Dupont Drive P.O. Box 19534 Irvine, California 92623-9534	4. Supplement(s): Number: SE5-018 Date(s): August 14, 2001	
5. Name of Drug: ALPHAGAN® (Ophthalmic Solution) 0.2%	6. Nonproprietary name: Brimonidine Tartrate	
7. Supplement Provides for request for pediatric exclusivity determination.	8. Amendment(s): None	
9. Pharmacological Category: Alpha adrenergic receptor agonist.	10. How Dispensed: Rx	11. Related Documents: NDA 20-490/SE5-007 August 14, 2001 NDA 21-262/SE5-006 August 14, 2001
12. Dosage Form: Ophthalmic Solution.	13. Potency: Brimonidine tartrate 0.2%	
14. Chemical Name and Structure: See USAN Bromonidine tartrate, $C_{11}H_{10}BrN_5 \cdot C_4H_6O_6$, Mol. Wt. 442.24. 5-Bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate.		
15. Comments: This pediatric exclusivity supplement includes an environmental assessment statement. In accordance with 21 CFR 25.31(b), the applicant requests categorical exclusion from the requirement to prepare an environmental assessment. Although approval of this supplement will increase the use of the drug substance, the applicant estimates that the concentration of the drug substance at the point of entry into the aquatic environment will be below one part per billion. Given the low concentration of drug substance in this formulation, the applicant's estimated concentration for the amount of substance entering the aquatic environment is reasonable. Therefore, the categorical exclusion is granted.		
16. Conclusions and Recommendations: From the viewpoint of CMC, the environmental assessment section of this supplemental application is recommended for approval.		
17. Name: Libaniel Rodriguez, Chemist	Signature:	Date:
18. Concurrence: Linda Ng, Chemistry Team Leader	Signature:	Date:

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/s/

Libaniel Rodriguez
9/18/01 02:25:48 PM
CHEMIST

Linda Ng
9/18/01 03:35:56 PM
CHEMIST

Chemistry Review: # 1	1. Division: HFD-550	2. NDA Number: 21-262
3. Name and Address of Applicant: Allergan 2525 Dupont Drive P.O. Box 19534 Irvine, California 92623-9534		4. Supplement(s): Number: SE5-006 Date(s): August 14, 2001
5. Name of Drug: ALPHAGAN® P		6. Nonproprietary name: brimonidine tartrate ophthalmic solution
7. Supplement Provides for request for pediatric exclusivity determination.		8. Amendment(s): None
9. Pharmacological Category: Alpha adrenergic receptor agonist.	10. How Dispensed: R _x	11. Related Documents: 20-490/SE5-007 August 14, 2001 20-613/SE5-018 August 14, 2001
12. Dosage Form: Ophthalmic Solution.	13. Potency: brimonidine tartrate 0.15%	
14. Chemical Name and Structure: See USAN Bromonidine tartrate, C ₁₁ H ₁₀ BrN ₅ •C ₄ H ₄ O ₆ , Mol. Wt. 442.24. 5-Bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate.		
15. Comments: This pediatric exclusivity supplement includes an environmental assessment statement. In accordance with 21 CFR 25.31(b), the applicant requests categorical exclusion from the requirement to prepare an environmental assessment. Although approval of this supplement will increase the use of the drug substance, the applicant estimates that the concentration of the drug substance at the point of entry into the aquatic environment will be below one part per billion. Given the low concentration of drug substance in this formulation, the applicant's estimated concentration for the amount of substance entering the aquatic environment is reasonable. Therefore, the categorical exclusion is granted.		
16. Conclusions and Recommendations: From the viewpoint of CMC, the environmental assessment section of this supplemental application is recommended for approval.		
17. Name: Libaniel Rodriguez, Chemist	Signature:	Date:
18. Concurrence: Linda Ng, Chemistry Team Leader	Signature:	Date:

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/s/

Libaniel Rodriguez
9/24/01 01:49:36 PM
CHEMIST
Environmental Assessment

Linda Ng
9/27/01 03:58:49 PM
CHEMIST

Chemistry Review: # 1	1. Division: HFD-550	2. NDA Number: 20-490
3. Name and Address of Applicant: Allergan 2525 Dupont Drive P.O. Box 19534 Irvine, California 92623-9534	4. Supplement(s): Number: SE5-007 Date(s): August 14, 2001	
5. Name of Drug: ALPHAGAN® Ophthalmic Solution	6. Nonproprietary name: Brimonidine Tartrate	
7. Supplement Provides for request for pediatric exclusivity determination.		8. Amendment(s): None
9. Pharmacological Category: Alpha adrenergic receptor agonist.	10. How Dispensed: Rx	11. Related Documents: NDA 20-613/SE5-018 August 14, 2001 NDA 21-262/SE5-006 August 14, 2001
12. Dosage Form: Ophthalmic Solution.	13. Potency(ies): Brimonidine tartrate 0.5%	
14. Chemical Name and Structure: See USAN Bromonidine tartrate, $C_{11}H_{16}BrN_5 \cdot C_4H_6O_6$, Mol. Wt. 442.24. 5-Bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate.		
15. Comments: This pediatric exclusivity supplement includes an environmental assessment statement. In accordance with 21 CFR 25.31(b), the applicant requests categorical exclusion from the requirement to prepare an environmental assessment. Although approval of this supplement will increase the use of the drug substance, the applicant estimates that the concentration of the drug substance at the point of entry into the aquatic environment will be below one part per billion. Given the low concentration of drug substance in this formulation, the applicant's estimated concentration for the amount of substance entering the aquatic environment is reasonable. Therefore, the categorical exclusion is granted.		
16. Conclusions and Recommendations: From the viewpoint of CMC, the environmental assessment section of this supplemental application is recommended for approval.		
17. Name: Libaniel Rodriguez, Chemist	Signature:	Date:
18. Concurrence: Linda Ng, Chemistry Team Leader	Signature:	Date:

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/s/

Libaniel Rodriguez
9/18/01 02:35:45 PM
CHEMIST

Linda Ng
9/18/01 04:02:31 PM
CHEMIST

Chemistry Review: #2	1. Division: HFD-550	2. NDA Number: 20-490
3. Name and Address of Applicant: Allergan 2525 Dupont Drive P.O. Box 19534 Irvine, California 92623-9534		4. Supplement(s): Number: SE5-007 Date(s): August 14, 2001
5. Name of Drug: ALPHAGAN® (Ophthalmic Solution) 0.2%		6. Nonproprietary name: Brimonidine Tartrate
7. Supplement Provides for request for pediatric exclusivity determination.		8. Amendment(s): None
9. Pharmacological Category: Alpha adrenergic receptor agonist.	10. How Dispensed: R _x	11. Related Documents: NDA 20-613/SE5-018 August 14, 2001 NDA 21-262/SE5-006 August 14, 2001
12. Dosage Form: Ophthalmic Solution.	13. Potency: Brimonidine tartrate 0.2%	
14. Chemical Name and Structure: See USAN Bromonidine tartrate, C ₁₁ H ₁₀ BrN ₅ •C ₄ H ₆ O ₆ , Mol. Wt. 442.24. 5-Bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate.		
15. Comments: This pediatric exclusivity supplement includes an environmental assessment statement. In accordance with 21 CFR 25.31(b), the applicant requests categorical exclusion from the requirement to prepare an environmental assessment. Although approval of this supplement will increase the use of the drug substance, the applicant estimates that the concentration of the drug substance at the point of entry into the aquatic environment will be below one part per billion. Given the low concentration of drug substance in this formulation, the applicant's estimated concentration for the amount of substance entering the aquatic environment is reasonable. Therefore, the categorical exclusion is granted.		
16. Conclusions and Recommendations: From the viewpoint of CMC, the environmental assessment section of this supplemental application is recommended for approval. See labeling comments to be conveyed to the applicant.		
17. Name: Libaniel Rodriguez, Chemist	Signature:	Date:
18. Concurrence: Linda Ng, Chemistry Team Leader	Signature:	Date:

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/s/

Libaniel Rodriguez
10/16/01 09:51:31 AM
CHEMIST
label comments

Linda Ng
10/16/01 11:01:02 AM
CHEMIST
Note comments to applicant