

OraVerse™ (Phentolamine Mesylate) Injection



Novalar Pharmaceuticals, Inc.
San Diego, CA

(888) 888-1441

www.novalar.com



© 2009 Novalar Pharmaceuticals, Inc.
OraVerse and Novalar are trademarks of Novalar Pharmaceuticals, Inc.
0165, Rev. 01/2009

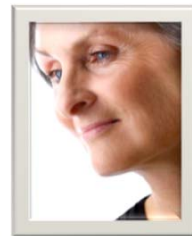
Soft Tissue Anesthesia

Effect of local anesthetic

- Administration of local anesthetics with vasoconstrictors results in prolonged loss of soft tissue sensation and associated functional deficits
- Pulpal anesthesia usually lasts 45-60 min¹
- Lingering soft tissue anesthesia lasts an average of 3-5 hours¹

Functional Deficits Associated with Loss of Sensation

- Difficulty with speaking
- Difficulty in smiling
- Difficulty with drinking
- Uncontrolled drooling
- Patient's perceived sense of altered appearance



¹ Source: Malamed SF. Handbook of Local Anesthesia. 5th ed. C.V. Mosby, St. Louis, MO: 2004;79.
0165, Rev. 01/2009

OraVerse™
(Phentolamine Mesylate) Injection

Local Anesthesia Reversal Agent

- Phentolamine mesylate is a vasodilator (alpha adrenergic antagonist) used in medical indications since 1952
- OraVerse™ is indicated for reversal of soft-tissue anesthesia, i.e., anesthesia of the lip and tongue, and the associated functional deficits resulting from an intraoral submucosal injection of a local anesthetic containing a vasoconstrictor
- OraVerse is not recommended for use in children less than 6 years of age or weighing less than 15 kg (33 lbs)
- There are no contraindications with OraVerse

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

Local Anesthesia Reversal Agent

- Proven safe and effective in adults and children aged 6 and over and weighing 15 kg (33 lbs) or more in nationwide clinical trials
- Accelerates the reversal of lingering soft tissue anesthesia associated with the most widely used local anesthetics containing a vasoconstrictor:

Local Anesthetic	Pulpal Anesthesia Duration (minutes) ¹	Soft Tissue Anesthesia Duration (minutes) ¹
Articaine 4% + epinephrine 1:100,000	45-60	180-240
Lidocaine 2% + epinephrine 1:100,000	60	180-300
Mepivacaine 2% + levonordefrin 1:20,000	60	180-300
Prilocaine 4% + epinephrine 1:200,000	60-90	180-480

¹ Source: Malamed SF. Handbook of Local Anesthesia. 5th ed. C.V. Mosby, St. Louis, MO: 2004;79.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

OraVerse™ (Phentolamine Mesylate) Injection

- Rapidly restores normal sensation and function so patients can speak, smile and drink normally in approximately half the time.
 - Median time to recovery of normal **lip sensation** was reduced by 85 minutes (55%) for lower lip and by 83 minutes (62%) for upper lip compared to control¹
 - Median time to recovery of normal **function** was reduced by 60 minutes (50%) for mandibular procedures and by 45 minutes (43%) for maxillary procedures compared to control¹
- Administered with a standard dental syringe utilizing the same injection site and an identical administration technique as that used for the local anesthetic

¹ Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright ©2008 American Dental Association. All rights reserved. Excerpted by permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

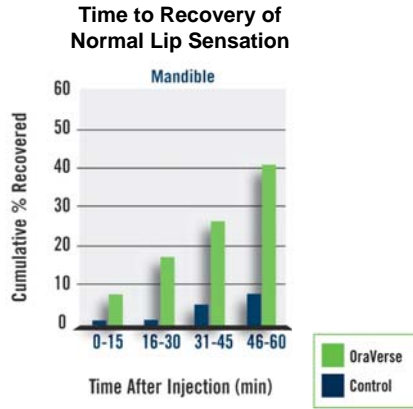
Safety Results

- Toxicity
 - No evident toxicity at tested doses
- Drug Interactions
 - There are no known drug interactions with OraVerse™ (phentolamine mesylate) Injection
- Compared to control, OraVerse had:
 - No effect on adverse events, vital signs or soft-tissue
 - No difference in pain or post-treatment analgesic use
 - Only a 1% difference in reported injection site pain (OraVerse 5% vs. Control 4%)
- The majority of adverse reactions were mild and resolved within 48 hours

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

Adults and Adolescents: 60 Minute Efficacy Data



Mandible

- OraVerse™ (phentolamine mesylate) accelerates the return to normal sensation by **85 min** (54.8%; $p < 0.0001$)
- **41%** OraVerse patients fully recovered in 60 minutes
- **7%** for control patients

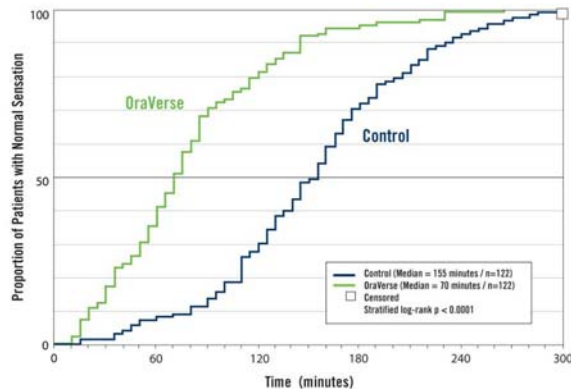
Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright © 2008 American Dental Association. All rights reserved. Excerpted by permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

Adult and Adolescent Trial - Mandible

Time to Recovery of Normal Sensation in the Lower Lip



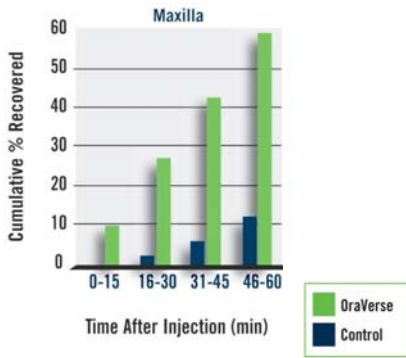
Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright © 2008 American Dental Association. All rights reserved. Adapted 2008 with permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0162, Rev. 01/2009

Adults and Adolescents: 60 Minute Efficacy Data

Time to Recovery of Normal Lip Sensation



Maxilla

- OraVerse™ (phentolamine mesylate) accelerates return to normal sensation by **83 min.** (62.3%; $p < 0.0001$)
- 59%** OraVerse patients fully recovered in 60 minutes
- 12%** for control patients

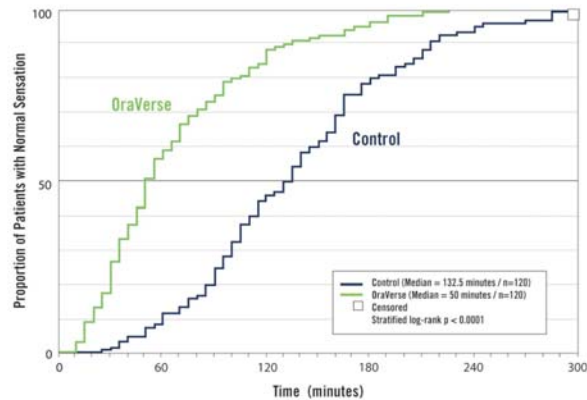
Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright © 2008 American Dental Association. All rights reserved. Excerpted by permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

Adult and Adolescent Trial - Maxilla

Time to Recovery of Normal Sensation in the Upper Lip

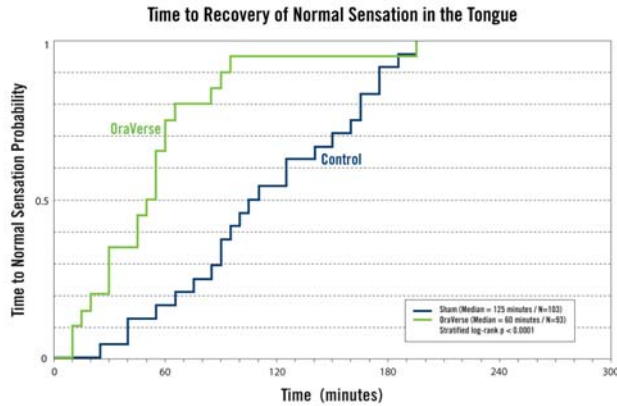


Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright © 2008 American Dental Association. All rights reserved. Adapted 2008 with permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0162, Rev. 01/2009

Adult and Adolescent Trial – Tongue Sensation



Hersh EV, Moore PA, Papas AS and colleagues. Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults. JADA 2008;139(8):1080-1093. Copyright © 2008 American Dental Association. All rights reserved. Adapted 2008 with permission.

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0162, Rev. 01/2009

Clinical Documentation

Adult and Adolescent Trials

- Hersh EV, Moore PA, Papas AS and colleagues.
Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults.
JADA 2008;139(8):1080-1093.

Pediatric Trial

- Tavares M, Goodson JM, Studen-Pavlovich D and colleagues.
Reversal of soft-tissue local anesthesia with phentolamine mesylate in pediatric patients.
JADA 2008;139(8):1095-1104.

Pharmacokinetic Trial, Adults

- Moore PA, Hersh EV, Papas AS, et al.
Pharmacokinetics of lidocaine with epinephrine following local anesthesia reversal with phentolamine mesylate.
Anesthesia Progress 2008;55(2):40-48

Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 01/2009

OraVerse™
(Phentolamine Mesylate) Injection

- OraVerse™ is the first & only local anesthesia reversal agent
- Allows you to bring patients back to normal sensation and function in about half the time
- OraVerse has been proven safe and effective in nationwide clinical trials
- It is easy to incorporate into your practice with no additional training or equipment required
- A new way to increase patient satisfaction



Important Safety Information: Tachycardia, bradycardia, and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic blocking agents. Although such effects are uncommon with OraVerse (phentolamine mesylate), clinicians should be alert to the signs and symptoms of these events, particularly in patients with a history of cardiovascular disease. Following parenteral use of phentolamine at doses between 5 to 15 times higher than the recommended dose of OraVerse, myocardial infarction, and cerebrovascular spasm and occlusion have been reported, usually in association with marked hypotensive episodes producing shock-like states. Please refer to Prescribing Information.

0165, Rev. 09/2008

OraVerse™
(Phentolamine Mesylate) Injection

In addition to brochures and talking to your patients, your Website is a great place to let patients and prospective patients know you utilize advanced techniques and technologies such as OraVerse.

Matthew J. Bernal, DDS
ACCREDITED MEMBER OF THE AMERICAN ACADEMY OF COSMETIC DENTISTRY

Home About Us Cosmetic Technology Smile Gallery FAQ Contact Us For Dental Professionals

Patient Quotes | "Dr. Bernal has provided me with a beautiful smile that has truly enhanced my life."

providing dentistry for patients
who value quality dental care

We are committed to providing the highest quality dental care available. We do this by having state of the art equipment and technology, attending advanced continuing education, and working with a team of professionals that deliver the highest quality dental products in the industry.

OraVerse™
Phentolamine Mesylate Injection
Numbness Reversal Agent

give back a smile™

CEREC
ZOOM!
invisalign

All rights reserved 2006
Matthew J Bernal DDS, 1680 Westwood Drive, San Jose, CA 95125 (408) 269-4484
Quality General and Accredited Cosmetic Dentistry

Home | About Us | Services | Technology | Smile Gallery | FAQ | Contact Us | For Dental Professionals

OraVerse™
(Phentolamine Mesylate) Injection



© 2009 Novalar Pharmaceuticals, Inc.
OraVerse and Novalar are trademarks of Novalar Pharmaceuticals, Inc.
0165, Rev. 01/2009

Matthew J. Bernal, D.D.S.
San Jose, CA



www.bernal-dental.com
matt@bernal-dental.com

Novalar Pharmaceuticals, Inc.
San Diego, CA

(888) 888-1441

www.novalar.com

