

December 4, 2013

**Attention:** FDA update on AtroPen® (atropine), DuoDote® (atropine and pralidoxime chloride injection), morphine sulfate, pralidoxime chloride and diazepam Auto-Injectors

Dear Wholesaler, Healthcare Professional and Emergency Personnel:

Please see the attached Alert Notice from the U.S. Food and Drug Administration (FDA) regarding a potential extension of expiration dates for AtroPen® (atropine), DuoDote® (atropine and pralidoxime chloride injection), morphine sulfate, pralidoxime chloride and diazepam auto-injectors.

In the Alert Notice, **the FDA advises users to retain the auto-injector products listed above that are nearing or beyond their labeled expiration dates as it reviews data for the potential use of these products beyond the labeled expiration date.**

If you require further information about the attached FDA Alert Notice, please contact Brad Leissa at [brad.leissa@fda.hhs.gov](mailto:brad.leissa@fda.hhs.gov) or Brooke Courtney at [brooke.courtney@fda.hhs.gov](mailto:brooke.courtney@fda.hhs.gov).

If you require further information about the auto-injectors mentioned in the FDA Alert Notice, please contact Meridian's customer service office at 1-866-478-6277.

Sincerely,



Tom Handel  
SVP-Commercial Pharmaceuticals

#### **Recommendations to wholesalers**

If you further distributed any of the above listed products, please communicate this information to those accounts immediately.

**FDA alerts health care providers and emergency responders of a potential extension of expiration dates for certain auto-injectors manufactured by Meridian Medical Technologies.**

The U.S. Food and Drug Administration is aware of a disruption in supply to health care providers and emergency response personnel of Atropen (atropine), DuoDote (atropine/pralidoxime chloride), morphine sulfate, pralidoxime chloride, and diazepam auto-injectors manufactured by Meridian Medical Technologies, a Pfizer Inc. company. FDA and Meridian are working together to resolve the disruption as quickly as possible, but it is unclear how long this disruption may persist.

As communicated on September 5, 2013, FDA concluded that it was scientifically supported that certain lots of DuoDote can be used for an additional year beyond the manufacturer's original labeled expiration date. FDA is continuing to assess whether these identified lots of DuoDote can receive further expiration date extensions if needed, and whether additional lots of DuoDote that were not listed in FDA's September 5, 2013, memo can have their expiration date extended.

FDA is currently reviewing data for the potential use of Atropen (atropine), DuoDote (atropine/pralidoxime chloride), morphine sulfate, pralidoxime chloride, and diazepam auto-injectors beyond their labeled expiration dates in order to mitigate any potential shortages of these medically necessary drugs. Products nearing or beyond their labeled expiration dates **should be retained** until further guidance is provided by FDA.

**What health care providers and emergency response personnel should know:**

- Health care providers and emergency response personnel who have any of the auto-injectors manufactured by Meridian identified above that are nearing or beyond the labeled expiration date should retain the products until FDA is able to provide additional information regarding the continued use of these products.
- Due to medical necessity and potential drug shortages, FDA is reviewing data for the potential use of these products beyond their labeled expiration dates.
- FDA will provide additional information about use of these products beyond the labeled expiration date in the coming weeks. Until FDA provides additional information, these expired auto-injectors may be used for patient care under emergency situations when no other product is available.
- Health care providers and emergency response personnel should maintain and monitor these products under the storage conditions described in the product labeling information.
- FDA continues to work with Meridian to resolve manufacturing issues.
- It is unclear at this time when Meridian will have additional inventory of these auto-injectors available.

If health care providers and emergency response personnel have additional questions about these auto-injectors, please contact Meridian's customer service office at 1-866-478-6277.

FDA asks health care providers and consumers to report any adverse events that are associated with the use of any of these products to either Pfizer Safety (1-800-438-1985) or to the [FDA's MedWatch Adverse Event Reporting](#) program by:

- completing and submitting the report online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm); or
- downloading and completing the [form](#), then submitting it via fax at 1-800-FDA-0178.

September 11, 2013

**Attention:** DuoDote® (atropine and pralidoxime chloride injection) Auto-Injector

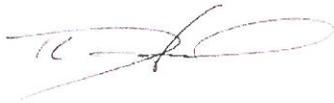
Dear Wholesaler, Healthcare Professional and Emergency Personnel:

Further to Meridian's letter dated August 27, 2013, please see the attached memorandum from the U.S. Food and Drug Administration regarding extending the expiration date of certain lots of DuoDote® (atropine and pralidoxime chloride injection) Auto-Injectors.

If you require further information about the attached memo, please contact Brad Leissa at [brad.leissa@fda.hhs.gov](mailto:brad.leissa@fda.hhs.gov) or Brooke Courtney at [brooke.courtney@fda.hhs.gov](mailto:brooke.courtney@fda.hhs.gov).

If you require further information regarding the August 27 letter, please call Meridian's customer service office at 866-478-6277.

Best Regards,



Tom Handel  
SVP-Commercial Pharmaceuticals



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

**Memorandum**

Date: September 5, 2013

To: Pfizer/Meridian Medical Technologies

From: Janet Woodcock, MD, Director, Center for Drug Evaluation and Research, and  
Luciana Borio, MD, Assistant Commissioner for Counterterrorism Policy and  
Director, Office of Counterterrorism and Emerging Threats

Subject: DuoDote<sup>®</sup> (atropine and pralidoxime chloride injection) Auto-Injector Expiry  
Dating

*Jul 9/5/13*  
*WS 9/5/13*

On August 27, 2013, you issued a Dear Healthcare Provider Letter regarding DuoDote auto-injector potential under-dosing or failure to activate. In the letter, you explained that “based on a review of product lots at its manufacturing site, Meridian personnel determined that a small number of DuoDote<sup>®</sup> Auto-Injectors are out of specification” and that “FDA is actively reviewing data related to DuoDote<sup>®</sup> performance beyond its labeled expiration date, and will provide additional information and guidance regarding expired product or product nearing its expiration date. Product beyond expiry should be held for the time being until further guidance can be provided by FDA.”

In follow up to the letter, FDA requests that this memorandum regarding expired product or product nearing its expiration date be communicated to the wholesalers, healthcare professionals, and emergency personnel who received the August 27 letter. FDA is aware that the following lots of DuoDote are approaching expiration or have already passed their original expiry date (see table below). Based on FDA’s review of scientific data, FDA has concluded that, provided the products have been stored under labeled storage conditions, it is scientifically supportable for lots of DuoDote listed in the following table to be used for an additional year (1 year) beyond the manufacturer’s original labeled expiry date.

DuoDote product is used for organophosphorous nerve agent or insecticide poisoning. FDA authorizes, pursuant to Section 564A of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the following lots of DuoDote to be stored or used for nerve agent poisoning up to one (1) year beyond the manufacturer’s original labeled expiry date, provided that the products have been stored under the labeled storage conditions.<sup>1</sup> While Section 564A does not apply to product held

<sup>1</sup> Section 564A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizes FDA to extend the shelf life of certain stockpiled medical countermeasures intended to support the nation’s ability to protect the public health or military preparedness and effectiveness. Under Section 564A(b) of the FD&C Act, products with extended expiry will not be deemed unapproved, adulterated, or misbranded. An expiration date extension must be supported by an appropriate scientific evaluation that is conducted or accepted by FDA. This authority is limited to eligible products

or used for insecticide poisoning, FDA will not take enforcement action with regard to the storage or use for insecticide poisoning of the following lots of DuoDote up to one (1) year beyond the manufacturer's original labeled expiry date, provided that the products have been stored under the labeled storage conditions.

FDA is not requiring or recommending that the identified lots be relabeled with the new use date.

#### DuoDote Auto-Injector Lots

Lot Number	Manufacturer's Original Expiry Date	New Use Date (up to 1 year beyond manufacturer's original expiry date)
9AE307	March 31, 2013	March 31, 2014
9AE356	March 31, 2013	March 31, 2014
9AE545	March 31, 2013	March 31, 2014
9AE548	May 31, 2013	May 31, 2014
9AE636	May 31, 2013	May 31, 2014
9AE645	June 30, 2013	June 30, 2014
9AE835	September 30, 2013	September 30, 2014

For questions related to this memorandum, please contact Brad Leissa at [brad.leissa@fda.hhs.gov](mailto:brad.leissa@fda.hhs.gov) or Brooke Courtney at [brooke.courtney@fda.hhs.gov](mailto:brooke.courtney@fda.hhs.gov).

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(as defined in FD&C Act Section 564A(a)) that are intended for use to prevent, diagnose, or treat a disease or condition involving a chemical, biological, radiological, or nuclear (CBRN) agent, including a nerve agent. This authority does not extend to non-CBRN uses of products, such as insecticide poisoning uses, but, as noted, FDA will not take enforcement action with respect to such uses.

August 27, 2013

**Attention:** DuoDote® (atropine and pralidoxime chloride injection) Auto-Injector:  
Potential under-dosing or failure to activate

Dear Wholesaler, Healthcare Professional and Emergency Personnel:

Meridian Medical Technologies, a Pfizer Inc. company, would like to inform you that based on a review of product lots at its manufacturing site, Meridian personnel determined that a small number of DuoDote® Auto-Injectors are out of specification. This could potentially prevent some of the units from activating or cause the patient to receive less of the drug than is intended. Delivery of clinically inadequate drug doses is infrequent and occurs in approximately 7 units out of a thousand DuoDote® Auto-Injectors.

DuoDote® Auto-Injector is indicated for the treatment of poisoning by organophosphorous nerve agents as well as organophosphorous insecticides.

Organophosphorus poisoning can result in cardiac arrest, respiratory distress and/or arrest, and seizures. Pralidoxime has its most critical effect in relieving the respiratory muscle paralysis. Inadequate dosing with pralidoxime will delay this effect and if treatment is delayed too long, the reversal of muscle paralysis may no longer occur. Atropine reduces secretions in the mouth and respiratory passages, relieves airway constriction, and may reduce centrally-mediated respiratory paralysis caused by organophosphorus chemicals. Inadequate dosing with atropine will delay resolution of these problems.

In cooperation with the U.S. Food and Drug Administration (FDA) and other government agencies, Meridian currently is investigating the issue, implementing corrective action and developing a product replacement plan.

**Recommendations to Health Care Providers**

We advise customers to retain the product they currently have and to use it per the enclosed product instructions until additional information about replacement product becomes available. Emergency medical professionals and other trained health care providers should carefully follow the product label. As directed in the label, three units of auto-injectors should be available for use with each patient.

Health care providers are directed to verify the visible presence of the needle following administration and to follow these instructions:

1. After the DuoDote® Auto-Injector triggers, hold it firmly against the injection site for approximately 10 seconds. Remove the DuoDote® Auto-Injector from the thigh and look at the green tip.
  - a. If the needle is visible, the drug chamber contents will have been administered but in some instances the DuoDote® may not have contained the full intended dose
  - b. If the needle is not visible, check to be sure the gray safety release has been removed, and then repeat the administration instructions.
  - c. If the needle is still not visible, deploy another unit and repeat the injection.
2. Wait 10 to 15 minutes after the first injection. If the patient does not develop severe symptoms, no further injection is required but definitive medical care should be sought immediately.
3. If at any time after the first injection the patient experiences severe symptoms, two additional injections should be administered in rapid succession and definitive medical care should be sought immediately.

As mentioned above, the company is working with the FDA and other government agencies to resolve the situation. Meridian and government agencies are working together to ensure that customers receive replacement product as quickly as possible, and based on priority of need. FDA is actively reviewing data related to DuoDote® performance beyond its labeled expiration date, and will provide additional information and guidance regarding expired product or product nearing its expiration date. Product beyond expiry should be held for the time being until further guidance can be provided by FDA.

#### **Recommendations to wholesalers**

It is not recommended that you return the product you currently have. However, it is important that this information be provided to all appropriate dispensing staff. If you further distributed this product to any other accounts, please communicate this information to those accounts immediately.

## Reporting

As of the date of this letter there have been no field-related reports of any adverse effects related to this issue.

As with all medical products, healthcare professionals and consumers are strongly encouraged to report any adverse events that are associated with the use of DuoDote® to either Pfizer Safety (1-800-438-1985) or the FDA's MedWatch Adverse Event Reporting Program either online, by regular mail, or fax:

- Online: [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)
- Regular mail: use postage-paid, pre-addressed Form FDA 3500 available at: [www.fda.gov/MedWatch/getforms.htm](http://www.fda.gov/MedWatch/getforms.htm)  
Mail to address on the pre-addressed form
- Fax: 1-800-FDA-0178

## Indication

DuoDote® (atropine and pralidoxime chloride injection) Auto-Injector is indicated for the treatment of poisoning by organophosphorous nerve agents as well as organophosphorous insecticides.

## Important Safety Information

The DuoDote® Auto-Injector should be administered by emergency medical services personnel who have had adequate training in the recognition and treatment of nerve agent or insecticide intoxication. It is intended as an initial treatment of the symptoms of organophosphorous nerve agent or insecticide poisoning; definitive medical care should be sought immediately.

Individuals should not rely solely upon agents such as atropine and pralidoxime to provide complete protection from organophosphorous nerve agents and insecticide poisoning. Primary protection against exposure to organophosphorous nerve agents and insecticides is the wearing of protective garments including masks designed specifically for this use. Evacuation and decontamination procedures should be undertaken as soon as possible. Medical personnel assisting evacuated victims of organophosphorous nerve agent or insecticide poisoning should avoid contaminating themselves by exposure to the victim's clothing.

In the presence of life-threatening poisoning by organophosphorous nerve agents or insecticides there are no absolute contraindications to the use of DuoDote®. When symptoms of poisoning are not severe, DuoDote® should be used with extreme caution in people with heart disease, arrhythmias, recent myocardial infarction, severe narrow angle glaucoma, pyloric stenosis, prostatic hypertrophy, significant renal insufficiency, chronic pulmonary disease, or hypersensitivity to any compound of the product.

No more than three doses should be administered unless definitive medical care (eg, hospitalization, respiratory support) is available. Elderly people and children may be more susceptible to the effects of atropine. DuoDote® is pregnancy Category C and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Safety and effectiveness in children have not been established.

Muscle tightness and sometimes pain may occur at the injection site. The most common adverse effects of atropine can be attributed to its antimuscarinic action and include dryness of mouth, blurred vision, dry eyes, photophobia, confusion, headache, and dizziness among others. Pralidoxime chloride's adverse effects include changes in vision, dizziness, headache, drowsiness, nausea, tachycardia, increased blood pressure, muscular weakness, dry mouth, emesis, rash, dry skin, hyperventilation, decreased renal function, excitement, manic behavior, and transient elevation of liver enzymes and creatine phosphokinase. When atropine and pralidoxime are used together, the signs of atropinization may occur earlier than might be expected when atropine is used alone.

Please see enclosed full Prescribing Information.

If you require further information about this product, please call 1-866-478-6277.

I thank you for your time and consideration in this matter.

Best Regards,



Tom Handel  
SVP-Commercial Pharmaceuticals