

Don't forget

to pick up your
keypads in the
lobby!



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FENTORA™

fentanyl buccal tablet ®

Sales Training on the Risk Minimization Action Plan (RiskMAP)

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What Is a Risk Minimization Action Plan (RiskMAP)

- ▶ A document describing tools and interventions intended to reduce potential risks associated with a product (e.g., diversion)
- ▶ Sponsor may volunteer or FDA proposes
- ▶ Implementation is based upon the risk/benefit ratio of the commercialization of the product
- ▶ Currently there are a number of products with RiskMAPs (e.g., Thalidomide, Accutane, Oxycontin, Actiq)



How Did Cephalon Develop a Risk Minimization Action Plan Program?

- ▶ Historical Perspective from Actiq®
(Oral Transmucosal Fentanyl Citrate)
- ▶ Review of other opioids requiring RiskMAPs
(ie., Palladone)
- ▶ Identified the 3 principal risks associated with
use of product and then developed interventions
aimed at the patient, prescriber and pharmacist
to mitigate such risks

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The NDA was submitted August 2005; initial agreement on RiskMAP reached between FDA and Review Division June 2006; however, change in policy at FDA warranted RiskMAP to then be circulated to chief counsel (lawyers) for their review.

What Are the Risks Associated With *FENTORA*?

Use of *FENTORA* by opioid non-tolerant individuals

Misuse, abuse and diversion of *FENTORA*

Unintended (accidental) exposure to *FENTORA*

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Proper Patient Selection Messages
Definition of opioid tolerant patient
Contraindicated in opioid non-tolerant patients
Contraindicated for use in acute/postop pain
Indicated solely for treatment of BTCP in chronic opioid tolerant cancer patients
Prevention of Diversion/Abuse Messages
Classified as CII medication [Schedule II drugs require distribution tracking, import and export controls, registration of prescribers and dispensers and no refills]
To be used only by patient for whom it is dispensed
May be habit forming
Requires appropriate disposal of unused medication
Child Safety Messages
Keep out of the reach of children
Could be harmful or fatal to a child if accidentally ingested
Must be properly stored and disposed of
Healthcare professionals must counsel patients on child safety messages
Accessible and easily understood directions on what to do in case of accidental ingestion

What Is Impacted by the RiskMAP?

- ▶ Labeling
 - ▼ PI, Med Guide, Carton, Blister, Blister label
- ▶ Education for Pharmacists, Patients, Prescribers
- ▶ Surveillance Activities (e.g., RADARS, DAWN, DAWN Live & TESS)
- ▶ Adverse Event Reporting
- ▶ DEA Communication
- ▶ Continuing Medical Education (CME)
- ▶ Community Outreach

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Labeling includes the blister, carton, package insert and Medication Guide and all have been designed to enhance child safety – covered with warnings and yellow warning triangles (carton only); appearance of tablet impacted – made to look very plain and medicinal – all labeling is described in detail in the RiskMAP

FENTORA Blister (visual)



The blister label and carton both have the product name and dose. The carton also has a yellow warning triangle. .

FENTORA Carton



The FENTORA carton now contains 28 tablets. It also has the yellow warning triangle and all of the safety messages (directions for suspected overdose, plain-language child safety warnings and opioid tolerance warnings).

In addition it has a pharmacy dispensing checklist for the pharmacist to assure that all essential information is relayed to the patient.

FENTORA Package Insert

TRADENAME contains fentanyl, an opioid agonist and a Schedule II controlled substance. **TRADE NAME** is indicated for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine/day, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer. Because life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients, **TRADE NAME** is **contraindicated** in the management of acute or postoperative pain. **This product is not indicated for use in opioid non-tolerant patients.** Patients and their caregivers must be instructed that **TRADE NAME** contains a medicine in an amount which can be fatal to a child. Patients and their caregivers must be instructed to keep all tablets out of the reach of children. (See Information for Patients and Their Caregivers for disposal instructions.) Due to the higher bioavailability of fentanyl in TRADENAME, when converting patients from other oral fentanyl products, including oral transmucosal fentanyl citrate (OTFC and Actiq®), to TRADENAME, do not substitute TRADENAME on a mcg per mcg basis. Adjust doses as appropriate (see DOSAGE AND ADMINISTRATION).

- ▶ Boxed warning
- ▶ Scheduled II product (CII)
- ▶ Prescriber universe
- ▶ Appropriate patient type (opioid tolerant)
- ▶ Potential for abuse and diversion
- ▶ Accidental exposure to children
- ▶ Proper conversion of **FENTORA** from oral fentanyl product such as Actiq

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The PI is attached to the carton via a hitchhiker

- >60 mg morphine/day
- >50 µg transdermal fentanyl/hour
- >1 week

life threatening hypoventilation at any dose in patients not taking chronic opioids
 contraindicated in acute/postoperative pain
 must not be used in opioid non-tolerant patients
 only oncologists/pain specialists... skilled in use of Schedule II opioids
 can be fatal to a child

Feedback on Risk Management Effectiveness

▶ Targets

1. Patients
2. Prescribers
3. Pharmacists

▶ Evaluation

▶ Intervention

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How Does the Cephalon Sales Force Impact the RiskMAP?

- ▶ Stick to your company-approved physician targets
- ▶ Know the three key risks
- ▶ Promote only according to the approved *FENTORA* label
- ▶ Refer to Cephalon Medical Communications Department for any questions outside of the approved indication
- ▶ Make sure practitioners know the proper patient selection
- ▶ Use only the approved promotion pieces to educate
Provision of interventions, as needed, based on surveillance data



As part of the RiskMAP requirements, there is a Promotional Message Audit conducted 2x annually
Preclearance of core promotional pieces was submitted to DDMAC in efforts to get their feedback prior to launch

Quarterly Report to FDA

- ▶ Response to Questionnaires
- ▶ Prescription Monitoring
- ▶ Serious Adverse Event (SAE) Reporting
- ▶ Literature Monitoring
- ▶ Database Monitoring (RADARS, DAWN, TESS)

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The following information listed on the next two slides are provided to FDA on a quarterly basis in a report that is usually between 20 and 25 pgs in length.

Patients who receive an FENTORA prescription at a participating pharmacy will receive a follow-up phone call by a company pharmacist and are asked these questions. They are also reminded about FENTORA's indication; child safety reminders and are given the toll-free number to ask any questions pertaining to the product.

Prescription information are captured in databases and prescribing specialties are monitored segmented by physician specialty to determine prescribing trends.

SAEs are reported for non opioid tolerant population, all unintended pediatric exposures and any SAEs related to diversion.

Literature is monitored for SAEs or pediatric exposure; this is something that is not required for other products

TESS – reviews poison center database for exposure (unusual ingestion, etc.)

Review of Drug Abuse Warning Network (DAWN) – this is voluntary national data collection system that gathers information on substance abuse resulting in an ER visit

How Can the PCS Sales Force Provide Value to the HCP With the *FENTORA* RiskMAP?

- ▶ Make sure physicians know and understand the risks associated with use of *FENTORA*
- ▶ Make sure physicians know how to counsel their patients on product use
- ▶ Become familiar with characteristics of unethical prescribing habits
- ▶ Properly train physicians in the appropriate dose conversion from other oral fentanyl products to *FENTORA*

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The PI recommends that the 1st Rx is for the lowest dose

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