Onsolis®
fentanyl buccal soluble film (c)

The FOCUS™ Program for ONSOLIS™

Educational Materials for Prescribers and Pharmacists

MEDA PHARMACEUTICALS®

The FOCUS™ Program for ONSOLIS™

The program requires the education of prescribers, pharmacists, patients, and caregivers regarding the safe use of ONSOLIS™. For information on the FOCUS™ Program call 1-877-466-7654 (1-877-4ONSOLIS) or visit www.OnsolisFocus.com.

The FOCUS™ Program for ONSOLIS™ has the following goal:

To mitigate the risk of ONSOLIS™ overdose, abuse, addiction, and serious complications due to medication errors by:

- Helping to assure proper patient selection, including avoidance of the use of ONSOLIS™ in opioid non-tolerant patients;
- Reducing the risk of exposure to ONSOLIS™ in persons for whom it was not prescribed, including accidental exposure in children; and
- Training prescribers, pharmacists, and patients about proper dosing and administration.

The 3-Step FOCUS™ Program Process

1. Complete Prescriber Education, Assessment, and Enrollment

- Review the educational materials on proper use of ONSOLIS™
- Complete the Prescriber Knowledge Assessment; sign and fax the Prescriber Enrollment Form *Satisfactory completion of the Prescriber Knowledge Assessment is required*

2. Complete Patient Counseling and Enrollment

- Determine that the patient meets the necessary requirements and is an appropriate candidate for treatment with ONSOLIS™
- Counsel the patient (or legally authorized representative) about the benefits and risks, and review the Medication Guide for ONSOLIS™
- Provide the patient with the Patient Authorization for Disclosure and Use of Health Information Statement (HIPAA)
- Complete and fax a copy of the Patient Enrollment Form

3. Initiate Delivery Process

- Fax a copy of the initial prescription for ONSOLIS to expedite the dispensing process
- Send the original, hardcopy prescription for ONSOLIS via courier using the supplied, pre-paid shipping label/airbill to initiate secure delivery of ONSOLIS™ directly to the patient or their caregiver

For further information please contact the FOCUS™ Program for ONSOLIS™ directly at **1-877-466-7654 (1-877-4ONSOLIS)**, or visit **www.OnsolisFocus.com**

Prescriber Education, Assessment, and Enrollment

Before you can enroll in The FOCUS™ Program for ONSOLIS™, you must complete the prescriber education and Knowledge Assessment. Satisfactory completion of the Knowledge Assessment is required. Review the information in each of the following sections to complete your education and enrollment.

- Proper Patient Selection: Indications and contraindications
- Dosing & Administration: Maintenance, titration, dosage adjustments
- General Opioid Use: Good medical practice, risk assessment
- Risks of ONSOLIS™: Overdose and addiction
- Program Overview

Proper Patient Selection

ONSOLIS™ (fentanyl buccal soluble film) is an opioid analgesic indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, 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 oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another oral opioid for one week or longer.

ONSOLIS™ is **contraindicated** for use in opioid non-tolerant patients including those using opioids intermittently, on an as needed basis.

ONSOLIS™ is **contraindicated** in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with other fentanyl products.

Patients and their caregivers must be instructed that ONSOLIS™ contains a medicine in an amount which can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid tolerant. All ONSOLIS™ films must be kept out of the reach of children. All unneeded ONSOLIS™ films should be disposed of by removing from the foil package and flushing down a toilet.

ONSOLIS™ is intended to be used only in the care of opioid tolerant patients with cancer and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Dosing & Administration

Appropriate product dosing and administration

As with all opioids, the safety of patients using such products is dependent on healthcare professionals prescribing them in strict conformity with their approved labeling with respect to patient selection, dosing, and proper conditions for use.

Only prescribers enrolled in the FOCUS™ Program may prescribe ONSOLIS™.

Dose titration

The goal of dose titration is to find the individual patient's effective and tolerable dose. The dose of ONSOLIS™ is not predicted from the daily maintenance dose of opioid used to manage the persistent cancer pain and MUST be determined by dose titration.

Starting Dose: Individually titrate ONSOLIS™ to a dose that provides adequate analgesia with tolerable side effects. All patients MUST begin treatment using **one** 200 mcg ONSOLIS™ film.

Due to differences in pharmacokinetic properties and individual variability, **patients switching from another oral transmucosal fentanyl product must be started on no greater than 200 mcg of ONSOLIS. When prescribing, do not switch patients on a microgram per microgram basis from any other oral transmucosal fentanyl product to ONSOLIS™** as ONSOLIS™ is not equivalent on a microgram per microgram basis with any other fentanyl product. ONSOLIS™ is NOT a generic version of any other oral transmucosal fentanyl product.

From the initial dose, closely follow patients and change the dosage level until the patient reaches a dose that provides adequate analgesia.

If adequate pain relief is not achieved after **one** 200 mcg ONSOLIS™ film, titrate using multiples of the 200 mcg ONSOLIS™ film (for doses of 400, 600, or 800 mcg). Increase the dose level by 200 mcg in each subsequent episode until the patient reaches a dose that provides adequate analgesia with tolerable side effects. Do not use more than four of the 200 mcg ONSOLIS™ films simultaneously. When multiple 200 mcg ONSOLIS™ films are used, they **should not be placed on top of each other** and may be placed on both sides of the mouth.

If adequate pain relief is not achieved after 800 mcg ONSOLIS™ (ie, **four** of the 200 mcg ONSOLIS™ films), and the patient has tolerated the 800 mcg dose, treat the next episode by using **one** 1200 mcg ONSOLIS™ film. Doses above 1200 mcg ONSOLIS™ should not be used.

Once adequate pain relief is achieved with a dose between 200 and 800 mcg ONSOLIS™, the patient should use or safely dispose of all remaining 200 mcg ONSOLIS™ films. Patients who require 1200 mcg ONSOLIS™, should dispose of all remaining unused 200 mcg ONSOLIS™ films. The patient should then get a prescription for ONSOLIS™ films of the identified dose strength (ie, 200, 400, 600, 800, or 1200 mcg) to treat subsequent episodes.

Dosing & Administration (cont'd)

Single doses should be separated by at least 2 hours. ONSOLIS™ should only be used once per breakthrough cancer pain episode, ie, ONSOLIS™ should not be redosed within an episode.

During any episode of breakthrough cancer pain, if adequate pain relief is not achieved after ONSOLIS™, the patient may use a rescue medication (after 30 minutes) as directed by their healthcare provider.

Dose Titration

ONSOLIS is available in five dosage strengths:
200, 400, 600, 800, and **1200 mcg**

The initial dose is 200 mcg ONSOLIS

↓ Titrate by incrementally increasing the dose once per episode

Fentanyl dose	**200 mcg**	**400 mcg**	**600 mcg**	**800 mcg**	**1200 mcg**
Using	200 mcg ONSOLIS film(s)				1200 mcg ONSOLIS film
Number of films	1	2	3	4	1

↓

If adequate pain relief *is achieved*, treat subsequent breakthrough cancer pain episodes using the determined dose.

ONSOLIS should only be used once per episode.
ONSOLIS dosing should be separated by at least 2 hours.

During any episode, if adequate pain relief *is not achieved* within 30 minutes, the patient may use a rescue medication as directed.

Dosage adjustment

During maintenance treatment, if the prescribed dose no longer adequately manages the breakthrough cancer pain episode for several consecutive episodes, increase the dose of ONSOLIS™ as described in dose titration (see above). Once a successful dose has been found, each episode is treated with a single film. ONSOLIS™ should be limited to four or fewer doses per day. Consider increasing the dose of the around-the-clock opioid medicine used for persistent cancer pain in patients experiencing more than four breakthrough cancer pain episodes daily.

Administration of ONSOLIS™

- Use the tongue to wet the inside of the cheek or rinse the mouth with water to wet the area for placement of ONSOLIS™.
- Open the ONSOLIS™ package immediately prior to product use.
- Place the entire ONSOLIS™ film near the tip of a dry finger with the pink side facing up.
- Place the pink side of the ONSOLIS™ film against the inside of the cheek.
- Press and hold the ONSOLIS™ film in place for 5 seconds.
- The ONSOLIS™ film should stay in place on its own after this period.

Liquids may be consumed after 5 minutes.

An ONSOLIS™ film, if chewed and/or swallowed, might result in lower peak concentrations and lower bioavailability than when used as directed.

The ONSOLIS™ film should not be cut or torn prior to use.

The ONSOLIS™ film will dissolve within 15 to 30 minutes after application. The film should not be manipulated with the tongue or finger(s) and eating food should be avoided until the film has dissolved.

Drug interactions

Fentanyl is metabolized mainly via the human cytochrome P450 3A4 (CYP3A4) isoenzyme system; therefore potential drug interactions may occur when ONSOLIS™ is given concurrently with agents that affect CYP3A4 activity. Concomitant use of ONSOLIS™ with CYP3A4 inhibitors (e.g., erythromycin, ketoconazole, and certain protease inhibitors) may result in an increase in fentanyl plasma concentrations, and may cause potentially fatal respiratory depression.

General Opioid Use

The following information was abstracted from: The Use of Opioids for the Treatment of Chronic Pain. A consensus statement from American Academy of Pain Medicine and American Pain Society.

- Addiction is a compulsive disorder in which an individual becomes preoccupied with obtaining and using a substance, the continued use of which results in a decreased quality of life.
- Respiratory depression is a major risk of opioid treatment, particularly in patients who are opioid-naïve.
- Tolerance is decreasing pain relief with the same dosage over time.
- Diversion of opioids can occur and should be watched for.

Principles of good medical practice should guide the prescribing of opioids:

- Proper Evaluation of the patient is essential.
- A thorough Treatment Plan includes multiple modalities, documentation of informed consent of risks and benefits, conditions of use and a written patient agreement.
- An opioid trial should not be done in the absence of a complete assessment of the pain complaint.
- Consultation with a specialist in pain medicine or with a psychologist may be warranted.
- Review of treatment should occur periodically, including need for continued opioid therapy and indicators of misuse.
- Documentation is essential for supporting the evaluation, the reason for opioid prescribing, the overall pain management treatment plan, any consultations received, and periodic review of the status of the patient.

The following information was abstracted from: Substance Abuse in Brief Fact Sheet. Pain Management Without Psychological Dependence: A Guide for Healthcare Providers.

Assessment of the Risks of Addiction:

- **Obtain relevant patient background information** regarding history of personal or familial problems with alcohol or drugs, legal problems, or misuse of prescription drugs.
- **Use screening instruments** which may include the Opioid Risk Tool, the Pain Medication Questionnaire, the Screener and Opioid Assessment for Patients with Pain (SOAPP), or the Screening Tool for Addiction Risk.
- **Document appropriately**. Have patients sign an agreement outlining the risks and benefits of the proposed treatment.
- The possibility of psychological dependence should be considered when a pattern of inappropriate behaviors is observed.

Risks of ONSOLIS™

Overdose

There is a high risk of overdose if ONSOLIS™ is given to:

- someone for whom it has not been prescribed; or
- opioid non-tolerant patients.

The manifestations of ONSOLIS™ overdosage are expected to be similar in nature to intravenous fentanyl and other opioids, and are an extension of its pharmacological actions with the most serious significant effect being hypoventilation.

Immediate management of opioid overdose includes removal of the ONSOLIS film, if still in the mouth, ensuring a patent airway, physical and verbal stimulation of the patient, and assessment of level of consciousness, ventilatory and circulatory status.

To treat overdosage (accidental ingestion) in an opioid non-tolerant person, provide ventilatory support, obtain intravenous access, and employ naloxone or other opioid antagonists as clinically indicated. The duration of respiratory depression following overdose may be longer than the effects of the opioid antagonist's action (e.g., the half-life of naloxone ranges from 30 to 81 minutes) and repeated administration may be necessary. Consult the package insert of the individual opioid antagonist for details about such use.

Management of severe ONSOLIS™ overdose includes: securing a patent airway, assisting or controlling ventilation, establishing intravenous access, and GI decontamination by lavage and/or activated charcoal, once the patient's airway is secure. In the presence of hypoventilation or apnea, assist or control ventilation, and administer oxygen as indicated.

Although muscle rigidity interfering with respiration has not been seen following the use of ONSOLIS™, this is possible with fentanyl and other opioids. If it occurs, manage by the use of assisted or controlled ventilation, by the administration of an opioid antagonist, and as a final alternative, by administration of a neuromuscular blocking agent.

Abuse and Addiction

There is a risk of abuse and addiction from exposure to ONSOLIS™. Fentanyl is a Schedule II controlled substance that can produce drug dependence of the morphine type. ONSOLIS™ may be subject to misuse, abuse and addiction.

Manage the handling of ONSOLIS™ to minimize the risk of abuse, including restriction of access and accounting procedures as appropriate to the clinical setting and as required by law.

Concerns about abuse and addiction should not prevent the proper management of pain. However, all patients treated with opioids require careful monitoring for signs of abuse and addiction, because use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Drug addiction is a treatable disease, utilizing a multidisciplinary approach, but relapse is common. "Drug-seeking" behavior is very common in addicts and drug abusers.

Risks of ONSOLIS™ (cont'd)

Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of addiction and is characterized by misuse for nonmedical purposes, often in combination with other psychoactive substances. Since ONSOLIS™ may be abused for nonmedical use; careful record keeping of prescribing information, including quantity, frequency, and renewal requests is strongly advised.

Proper assessment of patients, proper prescribing practices, periodic reevaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Healthcare professionals should contact their State Professional Licensing board or State Controlled Substances Authority for information on how to prevent and detect abuse of this product.

For more information about general opioid use, visit the following websites:

- The Use of Opioids for the Treatment of Chronic Pain. A consensus statement from American Academy of Pain Medicine and American Pain Society (www.ampainsoc.org/advocacy/opioids.htm)
- Substance Abuse in Brief Fact Sheet. Pain Management Without Psychological Dependence: A Guide for Healthcare Providers (www.kap.samhsa.gov/products/brochures/pdfs/saib_0401.pdf)