Canadian Drug Expert Committee
Final Recommendation – Plain Language Version

FENTANYL CITRATE BUCCAL SOLUBLE FILM RESUBMISSION
(Onsolis – Meda Valeant Pharma Canada Inc.)
Indication: Pain (Breakthrough), Cancer (Adults)

Recommendation:
The Canadian Drug Expert Committee (CDEC) recommends that Onsolis, which is also called fentanyl citrate buccal soluble film, not be listed by Canada's publicly funded drug plans at the submitted price for the management of breakthrough cancer pain.

Reasons for the Recommendation:
1. At the submitted price, the cost of Onsolis greatly exceeds that of other available oral (taken by mouth) opioids.
2. There are no well-designed medical studies comparing Onsolis with other less costly opioids for the management of breakthrough cancer pain.

Of Note:
Based on a review of the evidence, the Committee felt that a lower price would increase the chance of a recommendation to "list" or "list with criteria".

Background:
Onsolis belongs to a class of drugs called opioids. Opioids are the strongest pain medicines available. Onsolis is approved by Health Canada for adults aged 18 years and older, for treatment of the sudden flares of pain that can occur unexpectedly while the patient is taking regular doses of opioid painkillers for constant cancer pain. The sudden flares of pain are described as "breakthrough pain" because they happen or break through the regularly taken opioid pain killers used for constant cancer pain, and usually last for a short while. Onsolis is only for use by patients who have already been taking 60 mg of morphine per day (or the equivalent) for a week or longer.

Onsolis comes in a small film, which attaches to the inside of the cheek to deliver fentanyl quickly into the patient's bloodstream.

Onsolis is available in the following strengths: 200 mcg, 400 mcg, 600 mcg, 800 mcg, and 1,200 mcg. The Health Canada-approved dose includes a first dose of 200 mcg. If pain control is not reached with the first dose, the dose may be increased by 200 mcg at a time with each new attack of pain until the pain is controlled (as long as the side effects are not too great). Doses greater than 1,200 mcg should not be used. Doses should not be given less than four hours apart and should be used only once per breakthrough cancer pain episode; i.e., Onsolis should not be given more than once during any one episode of breakthrough pain.

Submission History:
Onsolis was originally submitted to the Common Drug Review (CDR) in May 2011. The submission was withdrawn by the manufacturer and resubmitted in September 2011.

Summary of CDEC Considerations:
To make its decision, the Committee considered the following information prepared by the CDR: a review of the medical studies of Onsolis and a review of economic information prepared by the manufacturer of Onsolis. No patient groups responded to the CDR Call for Patient Input.

No medical studies met the CDR review requirements because there were no well-designed medical studies that compared Onsolis with other fast-acting opioids or other pain-relieving products that contain fentanyl. The Committee reviewed a summary of information relevant to Onsolis, prepared by the CDR, which included: (i) studies of oral transmucosal (absorbed through the mouth lining) fentanyl products that did not meet the CDR review requirements; (ii) pharmacokinetics (how the drug is absorbed, where it works, and how it is broken down and gotten rid of by the body); (iii) the potential for abuse; and (iv) additional harms.

Summary of Findings
CDR identified five medical studies that provided information on the effectiveness and harms of either Onsolis or other oral transmucosal fentanyl products. One study compared Onsolis with placebo (a film containing no active medication). This study showed that the amount of breakthrough pain in cancer patients decreased during the study compared with the start of the study, and that Onsolis provided a greater decrease in pain than placebo. The most commonly reported side effects were common ones found with opioid treatment, including nausea, vomiting, and dizziness. No new side effects for the buccal (cheek) formulation compared with other formulations of fentanyl were found in this study.

The remaining four studies compared other oral transmucosal fentanyl products (also called Actiq and Fentora) with other opioids. All four studies looked at cancer patients, except for one study, which looked at patients with chronic pain from other causes, as well as cancer. The results of these studies suggest that other oral transmucosal preparations of fentanyl are better than oral morphine and oxycodone, but not intravenous (given into the vein) morphine, for the relief of breakthrough cancer pain.

The pharmacokinetic profile of Onsolis is very similar to that of other oral transmucosal fentanyl products in humans, although there can be noticeable differences from person to person. It takes longer for fentanyl to reach its highest blood concentration when it is given as an oral transmucosal product compared with when it is given intravenously.

Although no information about the abuse potential of Onsolis compared with other fentanyl products was found, Onsolis is expected to have a high abuse potential, similar to other fast-acting opioid formulations.
There is not a lot of information about the harms of Onsolis. However, serious side effects that include difficulty breathing, blood clots in the legs, blood clots in the brain, and shortness of breath were reported in the Periodic Safety Update Reports and are listed in the product monograph.

Cost and Cost-Effectiveness
The manufacturer submitted economic information comparing Onsolis with other medications for the management of breakthrough cancer pain currently available in Canada. It was assumed that Onsolis had similar benefits and side effects to these other medications, even though no studies were done to compare Onsolis with any of the comparison treatments. Also, it is not clear whether the doses of the different medications compared are equivalent.

Based on recommended doses (up to four 200 mcg, 400 mcg, 600 mcg, 800 mcg, or 1,200 mcg films per day) of Onsolis, the daily cost ($12.00 to $65.40) is higher than the daily cost of immediate-release formulations of morphine ($1.15 to $2.58), oxycodone ($0.71 to $1.74), and hydromorphone ($0.57 to $1.34).

Other Discussion Points:
- The Committee recognized the need for an effective, easily administered, and fast-acting opioid formulation to treat breakthrough cancer pain in the outpatient setting.
- The Committee felt the abuse potential of Onsolis is considerable.
- There are no studies comparing Onsolis with other pain-relieving products; thus, there is no evidence to support paying more for Onsolis than for other oral opioid formulations.

CDEC Members:
Dr. Robert Peterson (Chair), Dr. Lindsay Nicolle (Vice-Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Julia Lowe, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. James Silvius, and Dr. Adil Virani.

January 18, 2012 Meeting

Regrets:
None.

Conflicts of Interest:
None.

About this Document:
The information contained within this plain language version of the Canadian Drug Expert Committee (CDEC) Recommendation about this drug is based on the information found within the corresponding technical version of the CDEC Recommendation.

In making its recommendation, CDEC considered the best clinical and pharmacoeconomic evidence available, up to that time. Health care professionals and those requiring more detailed information are advised to refer to the technical version available in the CDR Drug Database on the CADTH website (www.cadth.ca).

Background on CDEC:
CDEC is a committee of the Canadian Agency for Drugs and Technologies in Health (CADTH). The committee is made up of drug evaluation experts and public members. CDEC provides recommendations about whether or not drugs should be listed for coverage through the participating publicly funded drug plans; however, the individual drug plans make their own decision about whether or not to cover a drug.

In making its recommendations, CDEC decides if the drug under review ought to be covered by the participating public drug plans based on an evidence-informed review of the medication's effectiveness and safety, and based on an assessment of its cost-effectiveness in comparison with other available treatments. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

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The statements, conclusions, and views expressed herein do not necessarily represent the views of Health Canada, the federal government, any provincial or territorial government, or any pharmaceutical manufacturer.

The manufacturer has reviewed this document and has not requested the deletion of any confidential information.