2. Recommendation for Following-up Patients Treated with an Opioid for BTcP

General rules

The classical way to follow-up cancer patients treated by opioid for their pain is a deep reassessment which can be summarised by the 4 'A' rules

The 4 'A' rules:

1. Analgesia: What is the patient's average pain intensity?[8]
   Many patients live with a moderate pain; 4-7 on a 10-numerical rating scale.
2. Activities: How has the patient been functioning?[8]
   Patient function can be constructed broadly and includes activities of daily living, social function, sleep etc.
3. Adverse Events: Has the patient had side effects?
   The most common opioid side effects are: constipation, pruritus, nausea and vomiting, sedation, respiratory depression and dizziness.
4. Aberrant behaviour: Has there been any evidence of abuse, misuse, or addiction?[7]

More predictive of addiction	Less predictive of addiction
Selling prescription drugs	Aggressive complaining about need for higher doses
Prescription forgery	Drug hoarding during periods of reduced symptoms
Stealing or borrowing another patient's drugs	Requesting specific drugs
Injecting oral formulation	Acquisitions of similar drugs from other medical sources
Obtaining prescription drugs from non-medical sources	Unsanctioned dose escalations 1-2 times
Concurrent abuse of licit or illicit drugs symptoms	Unapproved use of the drug to treat other conditions
Multiple dose escalations	Reporting psychological effects not intended by the clinician
Recurrent prescription losses	

There is a potential risk of misuse, abuse and diversion with all opioids. Healthcare professionals should therefore pay specific attention to the patient's maintenance opioid therapy and potential accidental exposure

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **IMB Pharmacovigilance**, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; ebsite: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie.

Adverse events should also be reported to **Teva Pharmaceuticals** by mail to Safety. ireland@teva.ie or phone 051 321538

Teva Pharmaceuticals Ireland

Floor 1 – Wing A – Building 1. Finnabair Business & Technology Park
Dundalk Co. Louth. Ireland

3. Additional Recommendations for the Patient Treated with an Opioid for BTcP

In addition to ensuring that BTcP patients understand how and when to take their treatment, they also need to be educated on the appropriate use of opioids. Each patient should be informed of the following recommendations for the treatment of BTcP.

Why is it important to be already receiving opioid therapy?

Patients who are treated for BTcP must already have been taking another opioid medicine around-the-clock for their persistent cancer pain for a week or longer.

What patients need to do:

- **Never stop taking around-the-clock opioid** medicine while taking BTcP treatment without first discussing it with his/her doctor.
- **Never use BTcP therapy for the treatment of short-term pain** from injuries, surgery or headache/ migraines or any type of pain other than BTcP unless advised by his/her doctor.

Protect against misuse, abuse and diversion with BTcP treatment

Patients should be informed that BTcP treatment contains opioids, a strong medicine with the potential to be misused by people who abuse prescription medicines or street drugs.

What patients need to do:

- Keep BTcP treatment in a **safe and secure place,** both in and outside their home to protect it from being stolen, since it could be a target for people who abuse medicines.
- **Never give BTcP treatment to anyone else,** even if they appear to have the same symptoms.
- Ensure that **his/her doctor is aware** of all medical and mental health problems, especially any past or present drug or alcohol abuse, addiction problems or a family history of this problem.

Protect against accidental use of opioids

Patients should be informed that opioids contain a medicine in an amount that **can be fatal** to a child and cause life-threatening breathing problems in anyone who takes it accidentally.

What patients need to do:

- Keep opioid medicines in a **safe and secure** place away from children and anyone to whom it has not been prescribed. If a child accidentally takes an opioid medicine, they should call for emergency medical help immediately.

BTcP patients should be recommended to inform their doctor if they intend to change any medicinal or non-medical treatment

References

1. 1- Portenoy, R.K., Savage, S.R. Journal of pain and symptom Management. Vol. 14N°3 (Supp.) Sept.1997 Fishbain DA, Cole B et al. Pain Medicine 9(4)/ 2008; 444-459.
2. http://www.nci.nih.gov/cancertopics/pdq/supportivecare/substanceabuse/HealthProfessional/page2
3. American Academy of Pain Medicine, American Pain Society, American Academy of Addiction Medicine. Definitions Related to the Use of Opioids fro the Treatment of Pain, Glenview, IL, American Academy of Pain Medicine, 2001.
5. Adapted "Determining the risk of opioid abuse" by lynn R Webster http://www.emergingsolutionsinpain.com/index.php?option=com_content&task=view&id=190&Itemid=42
6. Webster LR, et al. Pain Med. 2005;6:432-442.
7. Savage SR, Kirsk KL, Passik SD. Challenges in using opioids to treat pain in persons with substance use disorders. Addiction a science & clinical practice. 2008 June; 4(2):4-25.
8. Adapted from Webster LR, Webster RM. Predicting Aberrant Drug-Related Behavior in Chronic Pain Patients. New York, NY: International Conference on Pain and Chemical Dependency; 2002.

Date of preparation May 2014. TVIRL/EFF/12/014(1)

TEVA

OPIOID PRESCRIPTION GUIDE FOR PATIENTS SUFFERING FROM BTcP

1. Before Prescribing an Opioid to Patients Suffering from BTcP
   - Diagnosis of patients experiencing BTcP
   - Specific Assessment of the Potential for Abuse
     - Definition
     - Prevalence
     - Review of the patient screening principle for potential medication abuse
     - In practice: check the potential risk for opioid abuse in patients with BTcP
       - Medical history
       - CAGE-AID (Cut down, Annoyed, Guilt, Eye-opener – Adapted to Include Drugs)
       - Recommendations in case of identified risks
   - Verify the contra-indications for Effentora prior to prescribing opioid and/or Effentora
2. Recommendation for Following-up Patients Treated with an Opioid for BTcP
   - General rules
     The 4 'A' rules
       - Analgesia
       - Activities
       - Adverse events
       - Aberrant behaviour
3. Additional Recommendations for the Patient Treated with an Opioid for BTcP

Sponsored by Teva Pharmaceuticals Ireland as a service to medicine

1. Before Prescribing an Opioid to Patients Suffering from BTcP

Prior to initiating an opioid treatment it is extremely important to:

- Verify the correct diagnosis of BTcP
- Assess the patient's potential for drug abuse
- Verify contra-indication for Effentora
- That the prescription of EFFENTORA should only be by physicians experienced in the management of opioid therapy in cancer patients

Effentora should not be used:

- Effentora must not be prescribed in pain other than breakthrough cancer pain
- Effentora must not be prescribed in patients with short term pain only
- Effentora must not be prescribed in patients without around-the-clock opioid pain medication
- Effentora must not be prescribed in patients below 18 years of age

Diagnosis of patients experiencing BTcP

Before initiating opioid treatment for the first time in each new BTcP patient, please ensure that:		
	YES	NO
1. **Patient is suffering from cancer pain**	✔	Not indicated
2. **Patient has been receiving around-the-clock (ATC) medication for persistent pain**	✔	Not indicated
○ For a week or longer ATC therapy must include one of the following: • ≥60 mg/day oral morphine • ≥25 μg/hour transdermal fentanyl • ≥30 mg/day oxycodone • ≥8 mg/day oral hydromorphone daily • An equianalgesic dose of another opioid	✔ ✔	Not indicated
3. **Patient is experiencing transitory exacerbations of pain (i.e. cancer breakthrough pain)**	✔	Not indicated
4. **Patient is experiencing maximum 4 BTcP episodes/day**	✔	Re-assess and adapt the ATC therapy
5. **The patient has no contraindications to opioid treatment**	✔	Re-assess

Opioid treatment can be prescribed to your patients experiencing BTcP when all answers are positive

If opioids are considered for the treatment of pain including BTcP, tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids, such as fentanyl. However, extensive use of opioid therapy for cancer pain has demonstrated that tolerance, physical dependence, and addiction are rarely clinically significant problems.[1]

Specific assessment of the potential for abuse

Definition

The pharmacologic phenomena of tolerance and physical dependence are commonly confused with abuse and addition.[2] The list below gives the commonly accepted definitions for these terms.

Terminology for Substance Abuse

- **Physical dependence:** A state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.[3]
- **Tolerance:** A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.[3]
- **Substance abuse:** Use of a substance in a manner outside sociocultural conventions; according to this definition, all use of illicit drugs and all use of licit drugs in a manner not dictated by convention (e.g. according to physician's orders) is abuse.[2]
- **Addiction:** A primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors, characterised by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.[3]

Prevalence

Substance abuse appears to be very uncommon among cancer patients.[2]

The reported prevalence of substance abuse cases in cancer patients is much lower than the prevalence in society at large.[2]

Review of the patient screening principles for potential medication abuse[5]

1. **Screen new patients** during their initial visits using clinically validated assessments to evaluate, diagnose and possibly predict potential for medication abuse or addiction.
2. Set the level of monitoring appropriate to the **degree of risk demonstrated** by the patient.
3. **Monitor for and document any aberrant, drug-related behaviours** that may be associated with abuse or addiction.
4. **Reassess** the patient regularly for improved or impaired function. Every visit should include some degree of reassessment. The importance of this step cannot be overemphasised.
5. Never make judgements prior to an **appropriate assessment:** do not assume that a high-risk patient will always abuse opioids or that a low-risk patient never will.

The presence of **aberrant behaviours** does not, in itself, indicate addiction or a drug abuse problem. It is important, however, to watch for a pattern of drug-related behaviours and the effect of the therapy on function and quality of life. The goal is an environment where opioids may be safely prescribed and consumed.

In practice: check the potential risk of opioid ABUSE in patients with BTcP[5]

The purpose of assessing patients for the risk of abusing opiates is not to deny treatment to moderate-to highrisk patients. However, the identified at-risk patients require more careful monitoring and clinical vigilance in order to ensure the safe prescription of opioids.

You can use different approaches to evaluate, diagnose, and possibly predict abuse or addition in patients.

– For example, you can ask some 'general questions'[6] based on risk factors for opioid abuse as identified in clinical practice and scientific literature:

Medical History	Yes	No
Personal history of substance abuse	CM	N/A
Family history of substance abuse	CM	N/A
Mental disease (schizophrenia, bipolar disorder, OCD, HDAD)	CM	N/A
History of repeated drug/alcohol rehabilitation	CM	N/A

OCD= Obsessive Compulsive Disorder; HDAD= Hyperactivity Disorder/Attention-Deficit; CM= Close Monitoring

✔ YES to 1 or more questions = probable risk

A positive answer to any of these questions suggests **close monitoring** of the patient is required.

– If an additional questionnaire is needed – e.g. CAGE-AID

In many cases, a more specific and thorough tool can be used

The proposed questionnaire is the **CAGE-AID – Cut down, Annoyed, Guilt, Eye-opener – Adapted to Include Drugs,** a four-item questionnaire developed for the quick screening of patients with possible alcohol or substance abuse problems. Of the drug abuse screening instruments, CAGE-AID (CAGE Adapted to Include Drugs) is the only tool that has been tested with primary care patients.[5] For this study, the CAGE-AID was preceded by the following instruction:

'When thinking about drug use, include illegal drug use and the use of prescription drugs other than as prescribed.'

CAGE-AID (CAGE Adapted to Include Drugs)		
	Yes	No
1. Have you ever felt you ought to cut down on your drinking or drug use?		
2. Have people annoyed you by criticising your drinking or drug use?		
3. Have you ever felt bad or guilty about your drinking or drug use?		
4. Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover?		

✔ YES to 1 or 2 questions = possible risk

✔ YES to 3 or 4 questions = probable risk

– Recommendations in case of potential opioid abuse risk?

If Anamnesis question = YES ≥ 1
and/or CAGE-AID questionnaire = YES ≥ 3

- Split up the delivery[7]
- Inform the pharmacist[7]
- Revaluate the patient more often than your usual follow-up[7]