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To:
All Community Pharmacists
GPs (Substitute prescribers)

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Dear Colleague

OPIOID SUBSTITUTION TREATMENT (OST) UPDATE

I would like to update you on some issues in relation to Opioid Substitution Treatment.

I. SUPERVISION OF OST

The HSCB recently issued a letter in relation to the standing down of the supervision of consumption of OST in community pharmacy during the pandemic. Following discussions with Addictions services leads, there have been higher risk patients identified by Trust Addiction teams that still require a supervision service in community pharmacies **where the pharmacy is able to safely do so**. There may be issues with the choice of pharmacy in that not all pharmacies can provide the service due to the challenges in respect of social distancing. HSCB will liaise with service providers and Addiction services should there be a necessity to find a suitable pharmacy. For further advice please contact your local Pharmacy Adviser.

II. INCLUSION OF ESPRANOR® ON THE NI LIST FOR SUBSTITUTE PRESCRIBING MEDICATIONS

HSCB has agreed the inclusion of Espranor® for prescribing by the Trust Addiction services and GP substitute prescribers and supply via community pharmacy.

Guidance for healthcare professionals is attached (Appendix 1). I would request that this guidance document is drawn to the attention of anyone who is prescribing or dispensing this medication due to it being a novel formulation.

To avoid confusion, it is recommended that Espranor® is prescribed by brand.

Patient information leaflets will be posted to GP practices who are substitute prescribers and to community pharmacies which usually provide supervised consumption services.

The guidance and leaflets are available on the BSO website: http://www.hscbusiness.hscni.net/services/3010.htm

Community pharmacist supervision fees are currently under discussion and will be reimbursed as soon as possible. Should you have any general queries regarding OST, please contact Susan Patterson, Pharmacy Adviser susan.patterson@hscni.net

Yours sincerely,

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Espranor® A guide for health professionals

Espranor® oral lyophilisate is a freeze-dried buprenorphine wafer which disperses very rapidly **on the tongue.** It is indicated as a substitution treatment for opioid drug dependence within a framework of medical, social and psychological treatment. It is intended for use in adults and adolescents aged 15 years or over who have agreed to be treated for addiction. Prescribers should read the Espranor® Summary of Product Characteristics (SmPC) [1, 2] for full prescribing information. The main clinical differences between Espranor® and sublingual buprenorphine products (both buprenorphine monoproduct and buprenorphine/naloxone) are outlined in the following guidance taken from the Espranor® Health Professional Guide (2018)[3]:

A. "With Espranor®, administration is **oromucosal, not sublingual.** Espranor® should be placed on the tongue, where it dissolves and is absorbed into the bloodstream through the tongue's surface very quickly – usually in less than 15 seconds. This is very different from sublingual buprenorphine tablets which are placed under the tongue. **You should ensure that your patient understands that Espranor® should only be taken by placing it on their tongue, not under it.**

B. Different buprenorphine products have different bioavailability and with Espranor®, **the bioavailability of buprenorphine was found to be 30% higher** than with one of the brands of sublingual buprenorphine tablets.
Therefore;

a. **The initial and maximum doses for Espranor® are different** from sublingual buprenorphine tablets (see below).

b. It is possible that the dose of buprenorphine given to a patient in the sublingual form may be excessive if given to the same patient as Espranor®. Patients' doses should be individually titrated to effect.

c. **Espranor® is not interchangeable with other buprenorphine products. Different buprenorphine products have different bioavailability. Therefore, the dose in milligrams can differ between products. Once the appropriate dose has been identified for a patient with a certain product (brand), the product cannot readily be exchanged with another product."**

Day	Espranor® Dose
Day 1	The recommended starting dose is 2mg An additional one or two Espranor® 2mg oral lyophilisates may be administered on day one depending on the individual patient's requirement.
Dose Adjustment and maintenance	Titrate up or down to clinical effect in steps of 2-6mg. Maximum single daily dose of 18mg

Espranor® dissolves more quickly than sublingual buprenorphine products, thereby reducing:-

- the time taken to supervise Espranor® in a pharmacy setting
- the risk of diversion of Espranor® when daily doses are being consumed under the direct supervision of a pharmacist or nurse.
- the risk of Espranor® being accidentally swallowed as compared to sublingual buprenorphine products. (buprenorphine is essentially inactive when swallowed)

Espranor® may be particularly appropriate for use in a prison or Young Offender Centre where the risk of drug diversion is a significant concern.

Espranor® will not be an acceptable treatment option to some individuals on dietary or religious grounds as it contains gelatin, a protein derived from animal products[1, 2] Gelatin does not appear to be present in the other currently available sublingual buprenorphine products.

Espranor® contains no intrinsic deterrent to prevent take home doses being injected or possibly snorted; the addition of naloxone to sublingual buprenorphine (e.g. Suboxone®) in a 1:4 ratio helps ensure buprenorphine is only used by the sublingual route.

The maximum licensed daily oromucosal dose of Espranor® is 18mg which may not prove to be adequate in all cases. This compares with a maximum daily dose of 24mg for buprenorphine/naloxone products (e.g. Suboxone®) or 32mg for buprenorphine (e.g. Subutex®).

The lowest available dose of Espranor® is 2mg which presents problems for individuals who would benefit from a lower dose during a planned withdrawal from buprenorphine. The Espranor® SmPC suggests that patients may need to be switched to 0.4mg sublingual buprenorphine tablets to enable dose reduction. This should be done accounting for the bioequivalence differences between the buprenorphine products.

Note on overdose:
Opioids, including buprenorphine, can cause respiratory depression and overdose, particularly when taken in conjunction with other central nervous system depressants such as other opioids, alcohol, benzodiazepines or barbiturates. The long duration of action of Espranor® should be considered when determining the length of treatment needed to reverse the effects of overdose.

Guidance on switching to Espranor® from sublingual buprenorphine products and vice versa

Although the bioavailability of Espranor® is reported by the manufacturer to 30% higher than with one of the brands of sublingual buprenorphine tablets the risk of

sedation or overdose caused by buprenorphine appears to be linked not only to its total daily dose but to lower ratios of buprenorphine to its metabolite norbuprenorphine.

Some studies suggest that Espranor® is no more likely than equivalent doses of sublingual buprenorphine to cause respiratory depression. While Espranor® produces higher levels of buprenorphine it also results in higher ratios of buprenorphine to norbuprenorphine as compared to a similar dose of sublingual buprenorphine and this may help to reduce the risk of respiratory depression[4-7].

However prescribers should carefully consider the guidance produced by Ethypharm when switching from Espranor® to sublingual buprenorphine products and vice versa. The NHS Specialist Pharmacy Service published the following advice in 2017 on switching Espranor® with sublingual buprenorphine products:-

"Espranor® is not interchangeable with other buprenorphine sublingual formulations at the same dose ("like for like" switch) as the **bioavailability is 25-30% higher.** If a switch is necessary, (e.g. if a person moves between care settings from the community in to prison or between prisons and doesn't need re-stabilisation) then clinicians should use their professional judgement regarding a new dose"[10].

When people are transferred between care settings or when a person moves from supervised consumption to non-supervised buprenorphine, care plans will need to take account of the continuation of Espranor® versus the change to alternative formulations of buprenorphine given the difference in bioavailability. Collaboration prior to transfer between settings (e.g. community and custodial settings) is advisable so this can be planned as part of the transfer.

Supervision of Espranor® Consumption

Supervised self-administration is a key component of a patient's treatment plan. It:

- Allows the daily monitoring of the patient's condition and well being
- Ensures the patient takes the correct dose
- Prevents deaths resulting from accidental ingestion of the prescribed medication
- Prevents diversion onto the black market and misuse by others

The recommended process of supervised consumption of Espranor® is as follows:

1. The patient should remove any chewing gum from their mouth and dispose of it in a waste bin.
2. Offer the patient a drink of water, before administration to moisten the tongue and speed up dissolution of the oromucosal wafer.
3. The patient should remove the wafer from the packaging in accordance with the manufacturer's directions and place it directly on the tongue.

4. The wafer should not be swallowed. Patients should be advised to swallow as little saliva as possible whilst the wafer dissolves.
5. The patient should be observed for at least 1-2 minutes. During this time the wafer will have dissolved (usual time = 15 seconds) making diversion difficult.

References and resources

1. Electronic Medicines Compendium (eMC) Summary of Product Characteristics (SmPC) Espranor® 8 mg oral lyophilisate. Martindale Pharma, an Ethypharm Group Company https://www.medicines.org.uk/emc/product/2317/smpc (accessed 29.01.20)
2. Electronic Medicines Compendium (eMC) Summary of Product Characteristics (SmPC) Espranor® 2 mg oral lyophilisate. https://www.medicines.org.uk/emc/product/2316/smpc (accessed 29.01.20)
3. Espranor® - Health Professionals' Guide, Ethypharm (2018) https://www.medicines.org.uk/emc/rmm/1584/Document
4. Substance Misuse Management In General Practice (SMMGP) Free Clinical Update Special Edition - Espranor® Published**:** 18th June, 2019 https://www.smmgp-fdap.org.uk/Handlers/Download.ashx?IDMF=79579f0c-e738-4c74-a4cd-11989164eab8
5. Randomised comparison of a novel buprenorphine oral lyophilisate versus existing buprenorphine sublingual tablets in opioid-dependent patients: a first in-patient phase ii randomised open label safety study. *Strang J., Reed K., Bogdanowicz K., Bell J., van der Waal R., Keen J., Beavan P., Baillie S., & Knight A. (2017) European Addiction Research, 23(2): 61-70. doi:10.1159/000456612.*
6. Norbuprenorphine and respiratory depression: exploratory analyses with new lyophilized buprenorphine and sublingual buprenorphine. *Strang J., Knight A., Baillie S., Reed K., Bogdanowicz K. & Bell J. (2018) International Journal of Clinical Pharmacology and Therapeutics, 56(2): 81-85. doi:10.5414/CP203118.*
7. Switching between lyophilized and sublingual buprenorphine formulations in opioid dependent patients: Observations on medication transfer during a safety and pharmacokinetic study**.** *Reed K., Knight A., Baillie S., Bogdanowicz K., Bell J. & Strang J. (2018)* Heroin Addiction and Related Clinical Problems*, 20(5): 19-28.*
8. Espranor® Patients' Guide. Information for health professionals to give to patients prescribed Espranor® Ethypharm (2018) https://www.medicines.org.uk/emc/rmm/1583/Document
9. Patient Information Leaflet (PIL) for Espranor® 2mg and 8mg strength https://www.medicines.org.uk/emc/files/pil.2316.pdf
10. NHS Specialist Pharmacy Service Espranor® (buprenorphine oral lyophilisate) 2mg and 8mg. Considerations for opioid substitution therapy use in community settings and secure environments February 2017 https://www.sps.nhs.uk/wp-content/uploads/2017/02/Espranor®-v6.2-final.pdf

Guidance prepared by Dr William Gregg, NHSCT with input from Dr Helen Toal, BHSCT, Mr Colin Harrison, HSCB, Dr Susan Patterson, HSCB. March 2020