

MEDICAL GUIDANCE

The Use of Elequil Aromatabs® in Oncology

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Overall Conclusion:

It is the opinion of this Medical Director that all four product codes of Beekley®'s Elequil Aromatabs® are safe to use in oncology.

Background:

This guidance will concern itself only with the use of essential oils in oncology patients and only those essential oils found in Elequil Aromatabs®. The use of essential oils in aromatherapy include many different routes of administration such as oral, topical, and inhalation. This guideline will concern itself only with passive inhalation.

Approximately 15 years ago, the virtues of clinical aromatherapy became recognized by the medical community as an effective, supportive, and complimentary therapy for cancer patients. It is in widespread use in the UK^{1,2} and is gaining momentum in the USA³⁻⁵ as well as in Eastern culture countries such as Japan, Korea, China, and India⁶⁻¹⁰.

The use of Aromatherapy in Oncology can be segmented into four distinct phases: pre-diagnostic, diagnostic, treatment, and oncology.

Pre-diagnostic Phase: There are two situations that can occur that place a patient in this phase. First, the patient notices a change in body habitus such as unexplained weight loss, headache, localized pain, vertigo, blurred vision, gastrointestinal issues, and many others. The patient calls their primary care physician to make an appointment. The second situation is an asymptomatic patient that is undergoing an annual physical which yields an abnormal value on their screening bloodwork test results or an abnormal finding on the physical exam such as a breast lump, nodular prostate, pain, and tenderness upon organ palpation, etc. In either situation the doctor will order additional tests and scans (diagnostic workup) to make a diagnosis. During the time between getting an appointment and having the physical exam and again the time between the doctor's visit and the diagnostic workup, the patient may experience anxiousness, changes in mood, pain, and the inability to sleep. All Elequil Aromatabs contain the types of essential oils that have been shown to help eliminate some or all of these symptoms.

Diagnostic Phase: During this phase patients may undergo both non-invasive (scans, additional blood work) and minimally invasive procedures (image guided biopsies, endoscopies, and bronchoscopy). The same symptoms as were present in the pre-diagnostic phase can occur and can be managed with inhalation aromatherapy alongside conventional treatment.

Treatment Phase: The major disciplines involved in the treatment of cancer are surgery, radiation therapy, chemotherapy, and immunotherapy. This phase gives rise to all the symptoms noted above in addition to specific modality adverse effects such as post-surgical pain and infection, radiation induced skin burns, xerostomia (dry mouth) and oral mucositis from head and neck irradiation, and chemotherapy induced queasiness. Many of the symptoms occurring in this phase can be managed with the essential oils found in Beekley Medical® Elequil Aromatabs combined with conventional treatment.

Maintenance/Surveillance Phase: In the ever-changing Oncology arena, patients are living longer after the completion of their initial treatment. This has led to patients being maintained on immunotherapy for months or years. Others, who have had their tumors regress to the point where they are proclaimed “disease free” will be followed every 4-6 months with scans and bloodwork. Again, in this phase all the symptoms mentioned above can occur and inhalation aromatherapy can play an especially important role to help with both the physical and mental challenges of cancer and its treatment.

An in-depth review of three authoritative textbooks on the use and safety of essential oils in aromatherapy¹¹⁻¹³, as well as literature searches in PubMed and Google Scholar and the adverse event databases MAUDE and FAERS (USA), BfArM (Germany), MHRA (UK), ANSM (France) and Swiss Medic, confirm the paucity of toxic events and adverse reactions to essential oils. The few toxic events that have been reported stem from either misadministration (intravenous) or overdose (oral or topical). Non-serious adverse events are mainly queasiness, vomiting, headache following oral ingestion and pruritus and contact dermatitis from topical application.

During the pre- and post-treatment phases the clinical symptoms of mood swings including agitation and irritability, and difficulty sleeping often appear irrespective of the type, location, and extent of disease. During the treatment phase, the additional symptoms of queasiness and emesis appear as well. If the treatment plan includes external beam radiation therapy, skin burns are a potential adverse reaction. This will be mentioned again later. Regardless of the type of treatment (standard single agent, cocktails of multiple agents, or newer immunotherapies), some of these symptoms will occur in nearly all patients. The essential oils chosen for the Elequil Aromatabs were carefully selected to help with these types of symptoms.

Elequil Aromatabs®, General: Beekley introduced Elequil Aromatabs into the healthcare marketplace in 2010 and has sold over two (2) million individual aromatabs® during this 10-year period. Customer feedback has been collected for the past 6 years, including any adverse events with Elequil Aromatabs. It must be noted that during this six-year period where over one million aromatabs have been used there has been only two (2) reports of minor adverse reactions.

Adoption of aromatherapy as an adjunct in combination with standard medical practice is expanding rapidly. The customer base includes short and long-term care facilities, assisted living facilities, small rural hospitals, large metropolitan teaching hospitals, Children’s hospitals and free-standing diagnostic imaging centers. The Elequil Aromatabs come in four different aromas: Lavender and Lavender-Sandalwood Aromatabs help promote relaxation, comfort, and sleep; Orange-Peppermint can uplift, energize, and soothe queasiness and newly introduced Lavender-Peppermint promotes relaxation during pain, calms anxiousness, and soothes queasiness.

The essential oils are on a tab with a medical grade adhesive backing that allows the tab to stick strongly to a patient's clothes or hospital gown. Each tab contains a mixture of 2 to 3 essential oils and the cellophane pouch can be pulled at a maximum level for the full effect or at a minimum level for a lighter effect of the essential oils. The instructions for use clearly indicate that Elequil Aromatabs are to be

placed only on a patient's clothing and not directly on the skin or any other body part. In the pediatric and elderly population, the tabs are most often placed on the back of the patient's clothing on the back of the shoulder so it cannot be reached purposely or accidentally and pulled off.

Elequil Aromatabs®, Specific:

Product Code 370: Elequil Aromatabs Lavender--Sandalwood – To promote relaxation, comfort, and sleep. This product contains a proprietary blend of lavender and sandalwood pure essential oils. Lavender can be a skin irritant and can cause allergic skin reactions when applied topically but aromatabs are only placed on the gown / clothing, so it has no toxic effect. They have been used successfully as therapeutic agents in both adult and pediatric populations. Both essential oils are considered to be non-toxic, have a low allergic potential, and have no known contraindications.

Product Code 371: Elequil Aromatabs Orange–Peppermint – To uplift, energize, and help soothe queasiness. This product contains a proprietary blend of orange and peppermint pure essential oils. It is known to be a skin irritant when applied topically but aromatabs are only placed on the gown / clothing, so it has no toxic effect. Peppermint contains menthol which is a known mucus membrane irritant. Peppermint has neurotoxic activity when given orally in very high dose. The use of peppermint essential oil is not recommended for children under 3 years old. The use of peppermint essential oil is contraindicated for patients with cardiac fibrillation or G6PD Deficiency.

Product Code 372: Elequil Aromatabs Lavender – To promote relaxation, comfort, and sleep. This product contains a proprietary blend of lavender essential oils. The contraindications, precautions, and adverse effects for lavender have been discussed above and will not be repeated here.

Product Code 373: Elequil Aromatabs Lavender – Peppermint – To promote relaxation during pain, calm anxiousness, and soothe queasiness. This product contains a proprietary blend of lavender and peppermint essential oils. The contraindications, precautions, and adverse effects for both lavender and peppermint have been discussed above and will not be repeated here.

Specific situations of concern in the use of aromatherapy in cancer patients:

On page 89 of Buckle¹³, Table 4-5 lists six essentials oils (aniseed, clary sage, sweet fennel, bitter fennel, myrtle, and star anise) that have mild estrogenic activity. It is suggested that these oils should be avoided in estrogen-dependent tumors. There is no clinical evidence to support this suggestion and none of the six listed oils are present in Elequil Aromatabs.

Both lavender and peppermint are known skin irritants and dermatitis has been reported following topical administration of peppermint¹⁴⁻¹⁶. Elequil Aromatabs are not placed on the skin and have never been reported to cause dermatitis.

Many cancer patients have additional underlying health issues which may be adversely affected by essential oils. Memorial Sloan Kettering Cancer Center advises the following with respect to the use of the essential oil, Peppermint¹⁷. Patients with a history of cholelithiasis, cholecystitis, hiatal hernia, or gastroesophageal reflux disease should consult a physician before consuming peppermint¹⁸. Heartburn, nausea, and vomiting were reported by patients with IBS¹⁹, following use of peppermint oil. As noted above, dermatitis was reported following external application of peppermint oil. It must be noted that all of these adverse effects were due to oral ingestion or topical administration of the Peppermint oil. There are no reports and no scientific data to suggest that passive inhalation aromatherapy with Peppermint essential oil is contraindicated in any of the aforementioned health states.

It is well known that many essential oils have the ability to alter the permeability of human skin¹¹⁻¹³. Many cancers are treated with external beam radiotherapy and occasionally give rise to skin burns. These burns are often treated with a cream containing 5-FU, a potent cytotoxin and anti-tumor agent. Essentials oils including peppermint have been shown to increase the absorption of 5FU thru the skin in rats and in excised human skin^{20, 21}. Although relevance of this finding to the human cancer patient is unknown, it may be prudent to avoid the use of topical essential oils when treating skin burns with 5-FU cream. This, in no way, limits the use of peppermint in oncologic patients when delivered by passive inhalation aromatherapy.

There are three additional peppermint-drug interactions that may have relevance in oncology. Peppermint has been shown to increase the bioavailability of felodipine²² and cyclosporin²³. The clinical significance of this finding is unknown. In the case of cytochrome P450 substrates, peppermint oil was shown to inhibit CYP1A2/2C8/2C9/2C19/2D6 and 3A4 enzymes and can affect the intracellular concentration of drugs metabolized by these enzymes^{24,25}. Again, the clinical relevance is not known. All of these reports deal with oral administration of peppermint and have little or no relevance to the use of peppermint in passive inhalation aromatherapy.

Recently, immunotherapy has become a powerful weapon in the oncologic arsenal of cancer treatment modalities. There is no reason to suspect that any of the four (4) essential oils present in Elequil Aromatabs® would be contraindicated in patients undergoing immunotherapy.

The focus of this Medical Guidance was to determine the safety of Beekley®'s Elequil Aromatabs when used in the oncologic population. To make this determination, an in-depth literature search as described above was conducted on the essential oils found in Elequil Aromatabs. Additionally, three leading textbooks on the use and safety of essential oils in Aromatherapy were consulted¹¹⁻¹³ and the complaint history files of the Company were examined. The following facts were compiled from this undertaking:

1. All of the essential oils used in Beekley's Elequil Aromatabs with the exception of sandalwood have achieved FDA GRAS status. Sandalwood is considered non-toxic and non-irritating in the amounts used in aromatherapy.
2. The literature review found very few severe adverse events (SAE) and all related to misadministration or oral overdose. The amounts of essential oils causing any reported toxic event were many orders of magnitude greater than those inhaled from Elequil Aromatabs. There were no adverse events (AE) found in the literature review for passive inhalation for any of these essential oils.

3. The Instructions For Use (IFU) that accompany Beekley's Elequil Aromatabs clearly state that the aromatabs are to be placed on the patients clothing and not directly on the patient's skin. This eliminates the possibility of contact dermatitis or alteration in skin permeability.

A review of the complaint file for Elequil Aromatabs found no SAEs and only two (2) reported AEs for over one million plus units sold over six years.

Given the overwhelming safety profile of all essential oils when used in aromatherapy and, specifically, the lack of a single report of an SAE when used by passive inhalation, **it is the opinion of this Medical Director that all four product codes of Beekley®'s Elequil Aromatabs® are safe to use in oncology.**

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