

Focus on Recent Quality-of-Life, Patient Preference, Tolerability, and Safety Dimensions of **Desiccated Thyroid Extract (DTE)**

Identifying Patients, Monitoring Approaches, and Optimizing DTE-Based
Treatment for Persons with **Hypothyroidism** at The Front Lines of Patient Care

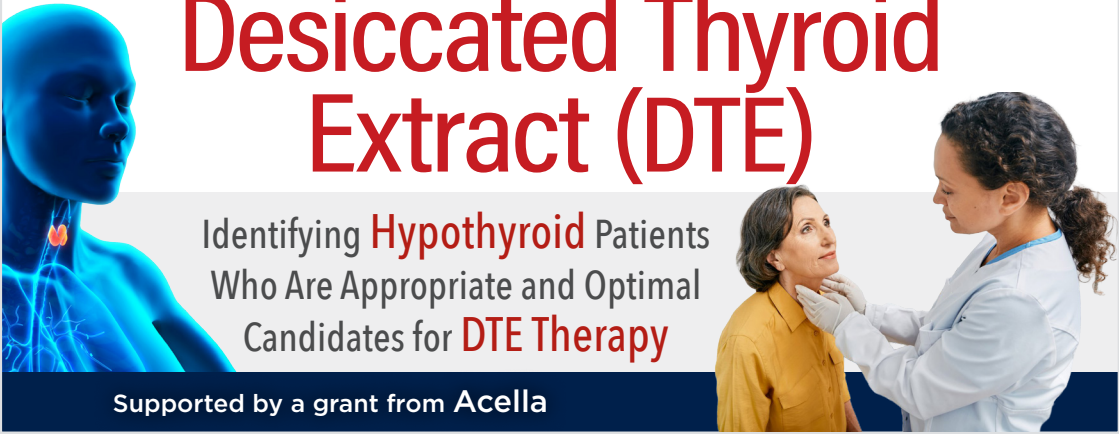
iQ&A *interactive* **Thyroid Hormone Replacement** Medical Intelligence Zone

Quality-of-Life, Patient Preference, and Safety Dimensions of

Desiccated Thyroid Extract (DTE)

Identifying **Hypothyroid** Patients
Who Are Appropriate and Optimal
Candidates for **DTE Therapy**

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QUESTION # 1: Can you please let our primary care and endocrinology specialists know a little bit about yourself, including your previous affiliations and experience treating patients with thyroid disease, especially hypothyroidism?

QUESTION # 2: Given your practice focus and experience, can you discuss the disease burden of hypothyroidism, the spectrum of the disease, treatment options, and how DTE formulations differ in terms of T4 and T3 composition?

QUESTION # 3: Can you discuss your approach to initiating and sequencing thyroid hormone replacement—in particular, how you monitor your patients, guideline-directed therapy, and the importance of metabolic and patient-centric factors in determining when DTE therapy should be considered as a treatment option?

QUESTION # 4: In the real world, what are the actual clinical triggers—among them, lack of symptom control, inability to achieve normalization of thyroid hormone function biomarkers/tests, treatment failure with T4, metabolic co-morbidities affecting T4-to-T3 conversion, and other factors—that prompt you to consider a person with hypothyroidism an ideal candidate for DTE-based hormone replacement? And what properties of DTE make it uniquely advantageous?

QUESTION # 5: What are the clinical trials, patient preference studies, and other evidence that support your systematic, patient-driven approach for deploying DTE in clinically appropriate populations, and in about what percentage of patients with hypothyroidism, overall, does DTE become the treatment modality of choice?

QUESTION # 6: Once you have determined that DTE may be an appropriate treatment approach for a patient with hypothyroidism, how do you transition the patient from T4 to DTE, and what should the thyroid function monitoring strategy be for patients who have been started on DTE?

QUESTION # 7: What persistent hypothyroid-related symptoms do you look for to suggest T4 monotherapy may not be the optimal approach?

QUESTION # 8: Can you summarize for us what current evidence, expert opinion, and clinical experience has taught us, and how it should guide us, in terms of identifying persons with hypothyroidism who should be considered for DTE-based hormone replacement therapy?



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QUESTION # 9: Can you please let our primary care and endocrinology specialists know a little bit about yourself, including your previous affiliations and experience at the Uniformed Services University of the Health Sciences treating patients with thyroid disease, especially hypothyroidism?

QUESTION # 10: Can you highlight some of the most important dimensions of the disease burden associated with hypothyroidism, including decisions related to treatment options and identification of patients who may be refractory to usual therapy?

QUESTION # 11: What are the foundational thyroid function laboratory abnormalities that confirm the diagnosis of hypothyroidism; and, once the diagnosis has been made, what are the guideline-directed treatment strategies that should be implemented initially to manage the condition?

QUESTION # 12: Once you've started a patient on T4 monotherapy, per the guidelines, how do you follow/monitor the patient, with a focus on (a) using laboratory parameters of thyroid function and (b) judging whether or not you've achieved an acceptable or, even, optimal, clinical response to your initial treatment plan?

QUESTION # 13: Can you provide a perspective on what subset of patients treated with guideline-directed T4 monotherapy may continue to have persistent hypothyroid symptoms, how large this subpopulation is based on clinical studies, and how you rule out other causes of these symptoms? What is the timeline and history of how DTE emerged as a treatment for hypothyroidism?

QUESTION # 14: What exactly is the composition of DTE, how does it differ from monotherapeutic agents used to treat hypothyroidism? What is its currently regulatory status?

QUESTION # 15: Once a clinician makes the decision to transition/commit a patient to DTE-based thyroid hormone replacement, what do the recent clinical trials/studies teach us about the comparative treatment, symptomatic response rates, patient preferences, and laboratory outcomes when T4 monotherapy is compared to DTE?

QUESTION # 16: In light of these positive clinical studies, how do you as an endocrinologist navigate the clinical decision tree in which you have to identify persons with hypothyroidism who are not meeting all your clinical objectives on T4 monotherapy and who, therefore, may be ideal candidates for DTE? What tools do you use?

QUESTION # 17: Can you discuss in detail what questions appear on the questionnaire you use to evaluate the success of thyroid hormone replacement therapy and whether, based on these results, a trial of combination therapy with DTE is warranted?

QUESTION # 18: How do you decide in those patients in whom you believe combination T4/T3 therapy may be beneficial, whether you add T3 to T4 monotherapy or whether you commit your patients to DTE as the primary strategy for combination therapy?

QUESTION # 19: Thank you for your insights, practice strategies and reviews of clinical trials demonstrating the potential role and benefits of combination approaches based on DTE in carefully identified patient populations. Can you summarize your recommendations and clinical pathway for this specific subgroup of patients? How do you optimize treatment dosing/titration of DTE to achieve the results you are looking for?



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QUESTION # 20: Despite well-constructed, evidence-based guidelines for thyroid hormone replacement therapy, a significant percentage of patients fail to achieve acceptable/optimal symptom control with T4 monotherapy. Can you characterize features in and the size of this group, and what the role is for alternative combination approaches, such as DTE?

QUESTION # 21: Can you please go into the specifics of the North Star trial, in terms of the trial design, its rationale, and what you were trying to assess as far as DTE-based treatment, including patients' self-reported outcomes as well as FDA regulatory criteria for thyroid replacement in persons with hypothyroidism?

QUESTION # 22: Based on the North Star trial what should the starting dose of DTE be and how should the patient be monitored?

QUESTION # 23: Based on results from the North Star as well as other observational trials, what kind of results should clinicians expect when they transition/convert patients from T4 monotherapy to combination therapy with DTE? What percentage of patients can be expected to respond? What parameters do you follow, and for how long?

QUESTION #24: Can you summarize the current treatment challenges for hypothyroidism as encountered by a broad spectrum of clinicians, including primary care, internal medicine, endocrine, women's health, and geriatric specialists?

QUESTION #25: Can you walk us through the typical presentation of a patient with hypothyroidism and what the guideline-adherent approach is to laboratory evaluation, clinical decision tree and initiation of therapy?

QUESTION #26: Once we decide to treat a patient with laboratory findings and a clinical presentation compatible with hypothyroidism, why and how do we initiate treatment—including dosing specifics—with synthetic LT4? And how do we monitor such a patient with respect to LT4, T3, TSH, and their global symptomatic health?

QUESTION #27: When using LT4 monotherapy, is monitoring of TSH sufficient to guide therapy? Can you elaborate on this?

QUESTION #28: Can you discuss what prompted the consensus report —on which you are a co-author and which was published in *Thyroid* and *The European Journal of Thyroidology*—focused on identifying a subset of patients with hypothyroidism who are failing to achieve optimal symptomatic resolution with LT4 monotherapy; and, therefore, should be considered for combination T4/T3 combination therapy, either with synthetic T3 or as a DTE formulation?

QUESTION #29: The recognition that LT4 monotherapy is inadequate for producing symptomatic improvement across the entire cohort of patients with hypothyroidism has generated the formation of an international working group to tackle issues focused on identifying such patients; in particular, those who might be amenable to DTE combination therapy and how to optimize clinical trials to better understand how this subset can be managed from combination formulations. Can you share your experience, processes, and goals for this endeavor?

QUESTION #30: What laboratory and/or clinical features, especially persistent symptoms, should suggest the possible need for combination therapy—including with a DTE—to optimize clinical management? How is this accomplished? And what have the available trials evaluating patient preferences suggested about the role and rationale for combination therapy?

QUESTION #31: How do you evaluate the success of combination therapy? What laboratory and/or symptom parameters do you assess? And how do you initiate combination therapy with synthetic T4 and T3?

QUESTION #32: Although combination therapy is frequently executed with synthetic T3 and T4, in the primary care/internal medicine setting combination therapy typically consists of DTE as the preferred approach in those patients failing to respond adequately to LT4 monotherapy. Can you provide a therapeutic roadmap for DTE use—including NP Thyroid and other formulations—at the frontlines of care in this setting?

QUESTION #33: Is it preferable to use DTE as a stand-alone combination therapy to substitute for LT4, or can/should it be used to supplement LT4 monotherapy? And what is the safety profile of DTE? And what is the monitoring strategy for combination therapy?

QUESTION #34: What percentage of patients who, for symptomatic reasons, have been switched from LT4 monotherapy to DTE, do you find actually improve on DTE, and what do they report?

QUESTION #35: How would you summarize your experience with hypothyroidism, in particular, your perspective on the current role of combination therapy with DTE?



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QUESTION #36: Can you summarize the current epidemiology, diagnostic evaluation, quality-of-life issues, and treatment challenges for hypothyroidism as encountered by a broad spectrum of clinicians, including primary care, internal medicine, endocrine, women's health, and geriatric specialists?

QUESTION #37: In addition to recognizing subtle clinical signs and symptoms of hypothyroidism—fatigue, decreased energy, and other minor, non-specific findings—what are the guideline-consistent protocols and benchmarks for laboratory evaluation of a person suspected of having hypothyroidism? How do we make the diagnosis of hypothyroidism and what are the thresholds for treatment?

QUESTION #38: What is your management approach to persons who have a TSH level between 4.5 and 10? Do all these patients get treated, or are there other stratification criteria—i.e., the presence of antithyroid antibodies—you use to determine the need for thyroid hormone therapy?

QUESTION #39: What is the role of the thyroid ultrasound in patients being evaluated for hypothyroidism? And why is confirming the diagnosis critical prior to initiating therapy?

QUESTION #40: How do you measure clinical success in persons started on thyroid replacement therapy? What is the balance you are looking to strike in a positive treatment outcome as it relates to the hard metrics of improving laboratory findings—normalizing TSH, T3/T4 levels and so on—and improvements in a patient's well-being, quality-of-life, subjective symptoms, and related patient satisfaction criteria?

QUESTION #41: Although guidelines indicate that normalization of TSH and thyroid hormone levels is an important goal confirming successful treatment with hormone replacement, is this the optimal approach and/or the singular criterion clinicians should focus on in their comprehensive approach to treating the person with hypothyroidism?

QUESTION #42: What is your approach to the patient who has a TSH of 2.5—well within the normal range—but the patient still has symptoms? Is there a rationale for bringing the TSH down to, let's say, 1.0 or 0.7, that is, to a lower level within the normal range?

QUESTION #43: With the understanding that each patient's treatment plan needs to be individualized based on a number of factors, can you review the current ATA-consistent guidelines for what specific thyroid replacement formulations, at what starting dose and titration schedules, are initially recommended in persons newly diagnosed with hypothyroidism? And why is T4 (levothyroxine) alone usually recommended as opposed to a combination of T4 and T3, which is the biologically active hormone? Why not employ both T3 and T4?

QUESTION #44: What is the alternative to using monotherapy with levothyroxine? And what role has desiccated thyroid extract (DTE) played historically in treating hypothyroidism, and what have we learned from this experience? What previous deficiencies in the composition/content of DTE have been addressed and rectified since our initial experience with these formulations 40-50 years ago?

QUESTION #45: Once you begin a patient on thyroid hormone replacement therapy, how is that patient followed clinically to ensure treatment success? What are the recommended starting doses? And how do you titrate the dose over time? What specific instructions do you give patients to optimize success?

QUESTION #46: Despite best efforts using levothyroxine (T4) monotherapy, there is a consistent, considerable subset of patients with hypothyroidism who do not respond to or are dissatisfied with this approach. Approximately what percentage of patients don't respond to conventional therapy? How do you recognize this subset? What symptoms do they complain of? Why is combination therapy with T3/T4 in the form of DTE considered appropriate for this group of patients?

QUESTION #47: Can you give physicians and other clinicians a sense of how many people treated for hypothyroidism with T4 monotherapy fall into a "less than optimal outcome" category and, therefore, should be considered for treatment with combination approaches, including those that might include DTE?

QUESTION #48: What is causing and what do you believe underlies the presence of 10-15% of patients with hypothyroidism who are dissatisfied with levothyroxine monotherapy? Do we understand either the causes or potential solutions for this group of hypothyroid patients who are not optimally satisfied with their T4 monotherapy treatment strategy? What is the role of T3 as a causative factor? And what are the implications for combination therapy and/or DTE?

QUESTION #49: Do you recommend actually measuring T3 levels in the group of patients who are not satisfied with or symptomatically burdened after being launched on a course of T4? What are the pros and cons of measuring T3? And what combination of factors ultimately should support a decision to embark on combination T4/T3 therapy, either by adding T3 as a separate formulation or treating with DTE? And who are the best candidates?

QUESTION #50: Once you commit a person with hypothyroidism to combination therapy with T4/T3, how do you follow the patient and with what frequency? And in your clinical experience as a thyroid specialist, what have you observed as far as improvements in patient status and/or their perceptions about the effects of combination T4/T3 therapy? And what is the time course of reported improvements after combination therapy has been started?

QUESTION #51: From a practical, front lines clinical perspective, exactly what does the treatment roadmap for combination T3/T4 therapy look like? What approach to combination therapy do you recommend for the primary care, internal medicine, and/or women's health specialist? Which formulations—add-on T3 or DTE—are available, and how do you monitor each with laboratory tests? What is the T4/T3 composition/ratio of DTE formulations? And what is the dosing for DTE?

QUESTION #52: What practical prescribing advice would you give to physicians who, because of lack of experience, are not familiar with the specifics of how to initiate and/or monitor therapy with DTE? Are conversion tables available? Is there any data to suggest which approach to combination therapy is better—DTE or T4/T3 (Cytomel)?

QUESTION #53: Among the patients who are started on combination therapy with DTE or add-on T3, what do your patients report? And what is the trial-based evidence that supports use of DTE in a selected group of patients failing to respond optimally to T4? What have we learned about patient preferences for DTE vs. T4 monotherapy?