

Pfizer Medical Education Group

Appropriate use of Hormone Therapy in Postmenopausal Women

Request for Proposals

December 12, 2012

Background:

The mission of the Pfizer Medical Education Group is to accelerate the adoption of evidence-based innovations that align the mutual interests of healthcare professionals, patients, and Pfizer, through support of independent professional education activities.

The intent of this document is to encourage organizations with a focus in healthcare provider (HCP) education and/or quality improvement to submit letters of intent (LOIs) in response to a Request for Proposal (RFP) that is related to education in a specific disease state, therapeutic area, or broader area of educational need. The new RFP model is a two stage process: Stage 1 is the submission of the LOI. If, after review, your LOI is accepted, then you are invited to submit your full program proposal. Stage 2 is the submission of the Full Grant Proposal.

When a RFP is issued, it is posted on the Pfizer Medical Education Group website (www.pfizer.com/independentsupport) as well as those of other relevant organizations and is sent via e-mail to internal lists of all registered organizations and users in our grants system.

Specific Area of Interest for this RFP:

Design and implement a learning and change-based program that enables the appropriate use of hormone therapy (HT) in postmenopausal women in primary care settings. The program should incorporate current treatment guidelines, utilize electronic health record technologies, and include learning and change components targeting both HCPs and patients. The impact of the program should be assessed by measuring changes in relevant clinical outcomes, such as percent of women screened for menopausal symptoms, and rates of appropriate management of these symptoms. Applicants are encouraged to provide estimates of changes in clinical outcomes that the proposed intervention is expected to drive.

The main focus of the intervention should be enabling the appropriate use of HT (including estrogen therapy and estrogen plus progestogen therapy) for the treatment of moderate to severe vasomotor symptoms (VMS) and symptoms of vulvovaginal atrophy (VVA) due to menopause. Use of HT for the prevention of postmenopausal osteoporosis may also be addressed. Proposed program goals and content should be consistent with approved HT indications, and take into account labeled warnings and precautions.

The successful proposal will provide an individualized, midlife woman-oriented approach enabling the appropriate use of HT in postmenopausal women. The program should aim to:

1. Increase diagnosis and appropriate management of menopausal VMS and VVA. Achievement of this goal may include one or more of the following:
 - Increasing HCP awareness of the negative impact of menopausal VMS and VVA on the quality of life of women;
 - Increasing HCP and women's knowledge of appropriate use of HT in postmenopausal women;
 - Increasing HCP understanding of key randomized clinical trials (RCT's) involving HT, especially WHI and recent age-stratified WHI subanalyses;
 - Increasing HCP and women's comfort level with initiating and continuing discussions about menopause and menopausal VMS and VVA;
 - Improving rates of HCP screening of age-appropriate women for menopause and menopausal VMS and VVA;
 - Increasing women's adherence to lifestyle modifications and approved drug therapies for managing menopausal VMS and VVA.
2. Demonstrate evidence of a positive clinical impact of the program via a rigorous outcomes evaluation (see "Recommendations and Target Metrics" below).

Programs must describe how they directly impact patient care and provide evidence of scalability (e.g., integration with an electronic medical record system), and a plan for extension beyond the proposed institution.

Disease Burden Overview

A recent survey by the Endocrine Society (TES) and its Hormone Health Network found that half of women between the ages of 45 and 60 years were experiencing symptoms of menopause. The survey found that vaginal dryness was experienced by 27%. Hot flashes were experienced by 44%, with 31% stating that their hot flashes were moderate to severe. Less than 25% of women reported receiving some type of treatment for their menopausal symptoms, despite a majority (69%) saying that these symptoms negatively impacted their quality of life.^{1,2}

According to 2011 International Menopause Society (IMS) recommendations on postmenopausal HT and preventive strategies for midlife health, HT should be included in a strategy for managing VMS that focuses on lifestyle approaches like diet, exercise, smoking cessation, and moderate consumption of alcohol.³ The North American Menopause Society's (NAMS) 2012 Position Statement on HT notes that estrogen therapy (ET), with or without a progestogen, is the most effective treatment for menopausal VMS and their potential consequences including poor sleep quality, irritability, trouble concentrating, and decrease in quality of life (QOL).⁴ Furthermore, a recent consensus statement on HT from leading women's health societies including NAMS, TES, and the American Society for Reproductive Medicine (ASRM) states that systemic hormone therapy, at the lowest effective dose for the shortest duration, is an acceptable option for postmenopausal women up to age 59 or within 10 years of menopause who report being bothered by moderate to severe menopausal symptoms.⁵ The statement also notes that the treatment approach should be individualized and that, along with a woman's QOL priorities, risk factors including age, time since menopause, and personal and family history of venous thromboembolism (VTE), cardiovascular disease (CVD), and breast cancer should also be taken into account.⁵ A subanalysis of WHI looking at outcomes after discontinuing conjugated estrogens (CE) in women with prior hysterectomy suggests that there may be safety benefits for women who initiate HT

in their 50's or within 10 years of menopause related to coronary heart disease, myocardial infarction, colorectal cancer, and mortality. This subanalysis also found that there may be potential harm for those treated with CE in later decades with respect to the same disease states. Note that HT is not indicated for CVD prevention, and the above findings on CVD, MI, colorectal cancer and mortality do not relate to approved indications for HT. The recent WHI age-stratified subanalyses are supportive of the "timing hypothesis", which states that there may be benefits for women who initiate HT soon after menopause, compared with those who start taking HT at a later age.⁶ WHI subanalyses also found a lower incidence of breast cancer in women with hysterectomy who were randomized to CE alone. This lower incidence became statistically significant with extended follow-up.⁷ It should be noted that breast cancer prevention is not an approved indication for HT.

HT guidelines note that when prescribing solely for symptoms of VVA, topical vaginal products should be considered.⁴ In addition, when prescribing solely for the prevention of postmenopausal osteoporosis, hormone therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medications should be carefully considered.⁴

Primary care providers (PCPs), in their role of providing routine care to women, have the opportunity to offer appropriate management of menopausal conditions and focus on overall well-being and QOL.⁸ Besides explaining the risks and benefits of HT when prescribed for the management of menopausal VMS and VVA and prevention of osteoporosis, PCPs can inform midlife women that HT may be an acceptable option for treating their menopausal symptoms when prescribed appropriately.⁴

Barriers/Gaps Between Actual and Target, and Possible Reasons for Gaps

Barriers for the appropriate use of hormone therapy in postmenopausal women exist for both HCP's and for women. The program should aim to address the following barriers in menopausal care:

1. Difficulty and/or discomfort with menopause discussions, and inadequate HCP screening and diagnosis of menopausal VMS and VVA

HCP's may not be aware of the burden of menopausal VMS and VVA on a woman's quality of life. Additionally, they may have inadequate knowledge about or lack access to approaches and tools to screen for these conditions. These factors could contribute to sub-optimal screening, diagnosis, and management of these conditions, especially in the primary care setting. Additionally, many women lack the knowledge and tools to have an informed discussion about VMS and VVA and management of these conditions with their HCP, or are uncomfortable with such discussions. In the previously mentioned survey conducted by the Endocrine Society, about half of women 45 to 60 years old (48%) were unfamiliar with hormone therapy, and more than four in ten said information about managing and treating symptoms of menopause was confusing (45%) or that they were not sure who to trust (41%).¹

There is often a lack of ample time for menopause discussions during office visits, particularly for PCPs who often must address a number of chronic conditions in a limited time period. The menopause discussion can be awkward for many HCP's and patients. Some patients may arrive to these discussions with negative preconceptions and fears about hormone therapy. Women may downplay their menopausal symptoms as they are afraid of the solutions the HCP may suggest. Only about half (52%) of patients claim to be very satisfied with their menopause discussion and those dissatisfied with the

dialogue often report feeling dismissed by their HCP, or that they were not given enough information beyond diagnosis.⁹

Screening, diagnosis, and appropriate management of menopausal VMS and VVA should be incorporated into the routine healthcare of the midlife woman.

2. Discomfort with HT and/or inadequate understanding of appropriate use of HT in postmenopausal women

Since the initial results of the Women's Health Initiative (WHI) study were released over 10 years ago, there have been numerous publications and opinions about the benefits and risks of menopausal hormone therapy. Analyses show that in the year immediately following WHI, HT use dramatically decreased 25% to 72%.¹¹ Others (Steinkellner et al) showed that HT utilization decreased approximately 18% within the first 3 months after the release of the WHI trial results. By July 2003, 12 months after the initial WHI publication, HT use had decreased between 32% and 38%, and by 18 months post-WHI, HT use was nearly 45% below mid-2002 levels.¹² Another analysis utilizing the IMS Health National Disease and Therapeutic Index physician survey data obtained from 2000 to 2009 found, for visits in which menopausal hormone therapy use was reported by US office-based physicians, use of oral estrogen therapy dropped by 62%, from 7.4 M in 2001 to 2.8 M in 2009, while estrogen plus progestin therapy declined by 76%, from 6.9 M in 2001 to 1.6 M in 2009.¹³

This dramatically decreased prescription of HT has resulted in many women going untreated for moderate to severe menopausal symptoms. Inadequate management of menopausal symptoms can lead to a substantial decrease in quality of life.⁴ Regarding the observed decrease in appropriate use of HT, Dr. Wulf Utian notes, "Women progressing through and beyond menopause in the next decade need to be spared the unnecessary harm inflicted upon their sisters of the previous decade".¹⁰ Providers and women need to be educated about how HT may be appropriately used to manage menopausal VMS and VVA.

Recommendations and Target Metrics:

Utilization of a control group to help assess program impact should be considered. The program should aim to positively impact the following target metrics:

- Screening rates for menopausal VMS and VVA in age-appropriate women, using validated screening tools (e.g., MenQOL, Menopause Rating Scale (MRS), Women's Health Questionnaire (WHQ), Utian Quality of Life Scale (UQOL), Greene Climacteric Scale). Programs may consider increasing screening for menopausal symptoms through use of EHR and/or other (e.g., tablet or smartphone) technologies.
- Rates of diagnosis and appropriate management of menopausal VMS and VVA. Assessment may include:
 - Patient satisfaction scores related to the management of menopausal symptoms;
 - Chart or EHR documentation of patient counseling related to menopause and menopause symptoms;
 - Rate of appropriate prescription of approved VMS and VVA therapies; and

- Utilization of validated tools to measure program impact on menopausal VMS and VVA
- Women’s understanding of menopause and of menopausal symptoms and related treatment options

The program’s impact on the following may also be assessed:

- HCP understanding of the burden of menopausal symptoms on women’s QOL;
- HCP understanding of relevant HT clinical trial data;
- Women’s adherence to lifestyle modifications and approved drug therapies for managing menopausal VMS and VVA; and
- Health economics.

RFP Requirements

Total Awards	Up to \$2 million will be disbursed across 3-5 projects. Individual projects can be funded for up to a maximum of 24 months duration.
Clinical Area	LOI- Hormone Therapy Postmenopausal Women
Target Settings	The focus of the program should be generating meaningful change in primary care providers and in women. Other HCP audiences may be targeted by the program, such as gynecologists, endocrinologists, and pharmacists.
Geographic Scope	United States only
Specific Area of Interest for this RFP	Hormone Therapy in Postmenopausal Women
Applicant Eligibility Criteria	Medical, dental, nursing, allied health, and/or pharmacy professional schools, healthcare institutions, for-profit health systems, professional associations and other not-for-profit entities may apply. Collaborations between organizations are encouraged.

Selection Criteria	<p>Applicant organizations will be evaluated based upon:</p> <ul style="list-style-type: none"> • Potential impact and expected outcomes of the project • Knowledge of and experience with the area • Capability of carrying out the work • Innovative approaches and applications • Collaboration if appropriate • Dissemination strategies
Key Dates/Deadlines	<p>December 12, 2012 – RFP released</p> <p>December 21, 2012 – All questions due</p> <p>January 25, 2013 – Letter of Intent due</p> <p>March 2013 – Applicants notified via email; Invited to submit full proposal</p> <p>TBD – Full proposals due date to be communicated on acceptance of an LOI</p> <p>May 13-31, 2013 – Notification of decisions</p> <p>June 2013 – Funded projects start</p>

How to Apply

Letter of Intent

The letter of Intent is a brief concept document that describes the proposed project at a high level. The Proposal Review Committee will select letters of intent that are best aligned with the purpose of the RFP. All applicants will be notified with either an acceptance or a declination. Successful applicants will be asked to submit a full grant proposal for funding consideration.

Submission Requirements

1. The letter of intent should be no more than three (3) pages, single spaced using Calibri 12 point font and 1-inch margins. It should contain the following information about the proposed project:
 - a. Project title;
 - b. Organization(s) involved;
 - c. Principal Investigator;
 - d. High level project description including
 - i. Primary goal(s)
 - ii. Description of how the proposal builds upon existing work, projects, or programs
 - iii. Anticipated challenges and solutions

- iv. Expected outcome and how the impact of the project will be evaluated
 - e. Deliverables and dissemination strategies
2. A letter of intent longer than three pages will be **RETURNED UNREVIEWED**.
3. Submit the letter of intent online via the Pfizer Medical Education Group website
 - a. On or after January 2, 2013, please go to the website at www.pfizer.com/independentsupport and click on the button "Go to the Grant System".
 - b. You will be prompted to take the *Eligibility Quiz* to determine the type of support you are seeking. Please ensure you identify yourself as a first-time user.
 - c. Submit your letter of intent in the LOI- Hormone Therapy Postmenopausal Women clinical area.
4. Complete all required sections of the online application and upload the completed letter of intent template.

Full Proposals

A limited number of applicants will be invited to submit for consideration a full proposal of no more than 10 pages, accompanied by a line item budget. The full proposal format will be shared with the invitation to submit.

Questions

If you have questions regarding this RFP, please direct them in writing to the Education Director for this clinical area, Robert Kristofco at (robert.kristofco@pfizer.com), with the subject line "RFP Menopause". Responses to common questions may be posted on the "*Request for Proposals*" section of the Medical Education Group website at www.pfizer.com/independentsupport.

Terms and Conditions

1. Complete TERMS AND CONDITIONS for Certified and/or Independent Professional Healthcare Educational Activities are available upon submission of a grant application on the Medical Education Group website www.pfizer.com/independentsupport.
2. This RFP does not commit Pfizer to award a grant, or to pay any costs incurred in the preparation of a response to this request.
3. Pfizer reserves the right to accept or reject any or all applications received as a result of this request, or to cancel in part or in its entirety this RFP, if it is in the best interest of Pfizer to do so.
4. Pfizer reserves the right to announce the details of successful grant application(s) by whatever means insures transparency, such as on the Pfizer website, in presentations, and/or in other public media.
5. For compliance reasons and in fairness to all applicants, all communications about the RFP must come exclusively from the Medical Education Group. Failure to comply will automatically disqualify applicants.
6. All output (e.g., products, research, data, software, tools, processes, papers and other documents) from funded projects will reside in the public domain.

Transparency

Consistent with our commitment to openness and transparency, Pfizer publicly reports its medical educational grants and support for medical and patient organizations in the United States. A list of all letters of intent selected to move forward may be publicly disclosed, and whatever emanates from this RFP is in the public domain. In addition, all approved full proposals, as well as all resulting materials (e.g., status updates, outcomes reports etc) may be posted on the website. Grantees will be required to submit periodic quarterly reports and/or updates.

Issued RFPs are posted on the Pfizer Medical Education Group website (www.pfizer.com/independentsupport) and are e-mailed to all registered organizations and users in our grants system.

References

1. The Endocrine Society and Hormone Health Network Survey: Majority of Women Suffering Menopausal Symptoms Are Not Receiving Treatment; Many Not Talking to Doctors about Treatment Options, May 1, 2012 (accessed November 21, 2012 at <http://menopausemapprossroom.files.wordpress.com/2012/04/menopause-survey-report.pdf>)
2. Menopause Practice, a clinician's guide. 4th ed. Mayfield Heights, OH: The North American Menopause Society; 2010:4.10.
3. Sturdee DW and Pines A, International Society Writing Group, et al. Updated IMS recommendations on postmenopausal hormone therapy and preventive strategies for midlife health. *Climacteric* 2011;14:302-320.
4. Gass ML, Manson JE, Cosman F, et al. The 2012 Hormone Therapy Position Statement of the North American Menopause Society. *Menopause* 2012;19(3):257-271.
5. Stuenkel CA, Gass ML, Manson JE, et al. A decade after the Women's Health Initiative—the experts do agree. *Menopause* 2012;19(8):846-847.
6. Prentice RL, Manson JE, Langer RD, et al. Benefits and risks of postmenopausal hormone therapy when it is initiated soon after menopause. *Am J Epidemiol* 2009;170(1):12-23.
7. LaCroix AZ, Chlebowski RT, Manson JE, et al. Health Outcomes After Stopping Conjugated Equine Estrogens Among Postmenopausal Women With Prior Hysterectomy, A Randomized Controlled Trial. *JAMA* 2011;305(13):1305-1314.
8. Corbelli JA and Hess R. Hormone therapy prescribing trends in the decade after the Women's Health Initiative: how patients and providers have found a way to sleep better at night. *Menopause* 2012;19(6):600-601.
9. Pfizer data on file, October 2012.
10. Utian, WH. A decade post WHI, menopausal hormone therapy comes full circle – need for independent commission. *Climacteric* 2012;15:320-325.

11. Ettinger B, Wang SM, Leslie RS, et al. Evolution of postmenopausal hormone therapy between 2002 and 2009. *Menopause* 2012;19(6):610-615.
12. Steinkellner AR, Denison SE, Eldridge SL, et al. A decade of postmenopausal hormone therapy prescribing in the United States: long-term effects of the Women's Health Initiative. *Menopause* 2012;19(6):616-621.
13. Tsai SA, Stefanick ML, Stafford RS, et al. Trends in menopausal hormone therapy use of US office-based physicians, 2000-2009. *Menopause*. 2011;18(4):385-392.