

Considered Judgement Form

This form is a checklist of issues that may be considered by the Purchasing Guidance Advisory Group when making purchasing recommendations.

Meeting date: 12 August 2005

Topic: Coumarin for lymphoedema following cancer treatment--- effectiveness and safety

Background and Purpose: Lymphoedema may be defined as the abnormal accumulation of protein rich fluid in soft tissues as a result of the interruption of lymphatic flow or dysfunction of the lymphatic system. It can be classified into primary or secondary lymphoedema. Secondary lymphoedema is more common and has many different causes, e.g. cancer and its treatment, and parasitic infection. Secondary lymphoedema in upper limbs among patients who received radiosurgical treatment for breast cancer is a very common complication in clinical practice. Secondary lymphoedema in lower limbs can be a complication following treatment for melanoma, lower abdominal or pelvic cancers.

Coumarin (1,2-benzopyrone or 5,6-benzo-[alpha]-pyrone) belongs to a class of compounds known as benzopyrones and has been used to treat lymphoedema and other clinical conditions. For lymphoedema, it is considered that benzopyrones stimulate macrophage activities by increasing both their numbers and their proteolysis. As a result, excess stagnant protein in the tissue spaces could be removed. Theoretically, this would reduce colloidal osmotic pressure in the tissues affected and may lead to the improvement of oedema and chronic inflammation caused by the excess stagnant protein.

1. Effectiveness, Volume of Evidence, Applicability /Generalisability and Consistency

Comment here on the extent to which the service/product/ procedure achieves the desired outcomes. Specific reference needs to be made to safety. Report number needed to treat and harm where possible, any issues concerning the quantity of evidence and its methodological quality and the extent to which the evidence is directly applicable or generalisable to the New Zealand Population, and the degree of consistency demonstrated by the available evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence

Five randomised studies were included in the review. All included studies have considerable weakness in methodology including using crossover study design, short treatment period and the heterogeneity of study population.

There appears to be no consistent results from these studies that compared coumarin with placebo for lymphoedema following cancer treatment. Clinical effectiveness of coumarin for lymphoedema following cancer treatment cannot be determined from available randomised studies.

The risk of coumarin attributable hepatotoxicity is a major concern for its clinical application. From a relatively valid study, incident rate of coumarin attributable hepatotoxicity was reported to be 0.37%. This figure appears to be significantly higher than a risk range of 1/10,000 to 1/100,000 for most drugs.

<p>2. Cost</p> <p>Comment on any economic costs associated with this service, product or procedure</p> <p>No cost effectiveness studies of using coumarin for lymphoedema were found.</p>
<p>3. Clinical impact</p> <p>Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.</p> <p>It is generally agreed that drug therapy only has a small or very little role the lymphoedema management</p>
<p>4. Equity, Maori Health, Pacific Health, Acceptability</p> <p>Comment on the extent to which the service, product or procedure reduces disparities in health status (equity of access, resources, health outcome), is consistent with the treaty of Waitangi and encourages Maori/ Pacific participation in providing and using service, product and procedures, and is consistent with values and expectations of New Zealanders.</p>
<p>5. Possible Purchasing Options</p> <p>List the possible purchasing options.</p> <p>A. Don't purchase B. Don't purchase at this stage, but the decision will be reviewed when new evidence available C. Purchase subject to special controls: case-based approval D. Purchase</p>
<p>6. Evidence Statement</p> <p>Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.</p> <p>The available randomised controlled studies do not provide good quality evidence to analyse the effectiveness of coumarin for lymphoedema following cancer treatment. There appears to be no consistent results from randomised controlled studies that compared coumarin with placebo for lymphoedema following cancer treatment. Clinical effectiveness of coumarin cannot be determined from these studies. Coumarin attributable hepatotoxicity appears to be a big concern for its clinical application.</p>
<p>7. Purchasing Recommendations</p> <p>What recommendation(s) does the advisory group draw from this evidence?</p> <p>Do not purchase</p>

PGAG Discussion

The drug has been suspended or restricted in some countries due to the concern of hepatotoxicity attributable to coumarin and the lack of solid evidence of effectiveness.

This drug can be obtained from at least one pharmacy in New Zealand with prescription.