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Clinical Expert Summary
Pegvisomant (Somavert®) 10 mg, 15 mg, 20 mg, 25 mg and 30 mg powder and solvent for solution for injection

Pegvisomant (Somavert®) for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalize IGF-1 concentrations or was not tolerated

1. Existing guidelines

There are no UK-specific guidelines for the management of acromegaly. It was noted that the most recently published consensus guidelines that influence clinical management is published by the American Endocrine Society (2014): *"Acromegaly: An Endocrine Society clinical practice guideline"*.

2. Disease prevalence/incidence

Overall, it was estimated that fewer than five patients in Wales would be candidates for pegvisomant. This estimate is based on prevalence of acromegaly at 60 per million, with an incidence of 3–4 per million annually; this equates to approximately 185 people with acromegaly in Wales at any one time. The majority of these people will have had treatment and be biochemically 'cured', but approximately 19 people with acromegaly would have inadequately controlled disease and would be eligible for pegvisomant. Radiotherapy or occasionally pasireotide would currently be considered for this population. Approximately 60% will normalise following radiotherapy, but acromegaly would remain uncontrolled in eight people. In practice, it would be this group where pegvisomant (or pasireotide) would be considered. However, clinicians would usually distinguish between 'mild' growth hormone excess (slightly raise IGF-1 with few symptoms) and more severe acromegaly that would definitely need treatment. This results in the estimated five eligible patients.

3. Current treatment options

95% of people with acromegaly will receive pituitary surgery, 70% of whom would be expected to achieve biochemical control. For people where surgery is not appropriate or does not achieve biochemical control, medical therapy is used: either a somostatin analogue (SSA), or a dopamine agonist, or both. Long-acting SSAs (octreotide and lanreotide) are the predominant treatment options in patients uncontrolled after surgery or where surgery is not undertaken. Dopamine agonists (cabergoline) are used occasionally in patients with mild growth hormone excess and/or coexisting hyperprolactinaemia. Approximately 70% would be expected to achieve biochemical control. For the people who do not achieve biochemical control, radiotherapy or pasireotide would be considered, as described above.

4. Unmet needs

There is a definite unmet need for the minority of patients who are not controlled by the current treatment options. These patients normally have disabling symptoms (sweating, arthralgia, changes in appearance) and comorbidities (hypertension, glucose intolerance/diabetes, cardiomyopathy), leading to impaired quality of life and premature mortality.

One clinical expert noted that they were conscious of the inequality of access to pegvisomant in Wales compared to other parts of the UK (as it has recently been approved by NHS England).

Whilst pasireotide has been approved by AWMSG, it can be associated with worsening glucose tolerance, diabetes and gastrointestinal side effects, whereas pegvisomant

may improve glucose tolerance. However, pasireotide does have the potential to inhibit tumour growth directly, unlike pegvisomant. It would therefore be useful to have access to both pasireotide and pegvisomant in difficult-to-control cases.

5. Knowledge of product in given indication

It is expected to use pegvisomant in patients with uncontrolled disease (IGF-1 above normal range and growth hormone > 1 microgram/l), despite treatment with surgery, SSAs, dopamine agonists and radiotherapy. As radiotherapy results in hypopituitarism, pegvisomant may be considered before radiotherapy in selected cases, such as in young women who wish to retain fertility.

It should be noted that one expert involved in compiling this response declared a personal non–specific interest in relation to pegvisomant for the indication under consideration.