

## Enc 7 Appx 3

### Clinical Expert Summary Pasireotide (as pamoate) (Signifor<sup>®</sup>▼) 20 mg, 40 mg, 60 mg powder and solvent for suspension for injection

Pasireotide (as pamoate) (Signifor<sup>®</sup>▼) for the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with another somatostatin analogue

#### 1. Existing guidelines

It was highlighted that there are no UK-specific guidelines; the most recently published guideline is from the American Endocrine Society:

Katznelson L, Laws Jr ER, Melmed S et al. Acromegaly: An Endocrine Society clinical practice guideline. *Journal of Endocrinology and Metabolism* 2014; 99 (11): 3933-51.

#### 2. Disease prevalence/incidence

The estimated prevalence of acromegaly is approximately 60 per million (incidence 3–4 per million annually), equating to approximately 185 patients in Wales with the disease at any one time. Of these patients, it is estimated that fewer than five would be considered for treatment with pasireotide.

#### 3. Current treatment options

It was estimated that 95% of patients with acromegaly would undergo transsphenoidal pituitary surgery as the initial treatment, of which about 70% would be expected to achieve biochemical cure. The other 5% of patients would not undergo surgery either because the risk is considered too great or because a patient does not wish to consider this option.

In the 30% of patients not cured by surgery, and for the 5% who have not undergone surgery at all, a somatostatin analogue (octreotide LAR or lanreotide autogel) may then be considered. A dopamine agonist (cabergoline) alone or in combination with a somatostatin analogue may be considered for a small number of patients (approximately 10%) with co-existing hyperprolactinaemia or 'mild' biochemical excess. For those patients treated with medical therapy, adequate biochemical control would be expected in 70% (stated to be greater for somatostatin analogue than dopamine agonist). Patients with inadequately controlled disease at this stage may switch from octreotide to lanreotide, or vice versa, if they are intolerant of one preparation or in an attempt to gain control but this is only considered in a very small number of our patients.

For the residual patients, the treatment option would be radiotherapy, in the absence of availability of pegvisomant in Wales. About 60% of patients would normalise biochemistry following radiotherapy (stereotactic or conventional), but this often takes many years; therefore, medical therapy may need to continue until this is achieved. In practice, it would be this small group of patients where pasireotide (or pegvisomant if available) would be considered. Even in this group, clinicians would usually distinguish between 'mild' growth hormone excess (slightly raised IGF-1 with few symptoms) where a 'watch and wait' approach might be followed, and more severe acromegaly which would definitely need treatment.

#### 4. Unmet needs

Clinical expert opinion highlighted that there is a definite unmet need for the minority of patients, who are not controlled despite surgery, somatostatin analogues, dopamine agonists or radiotherapy. Patients often have disabling symptoms (e.g. sweating, arthralgia, changes in appearance) and comorbidities (hypertension, glucose intolerance/diabetes, cardiomyopathy) leading to impaired quality of life and premature

mortality. It is this small group which causes the greatest concern and it would be useful to have access available to additional medical therapies (pegvisomant, pasireotide) which might offer an alternative approach.

#### **5. Knowledge of product in given indication**

It was stated that pasireotide would be used in patients with uncontrolled disease (IGF-1 above normal and GH > 1 micrograms/l) despite treatment with surgery, somatostatin analogues, dopamine agonists (if considered) and radiotherapy. As radiotherapy is associated with inevitable hypopituitarism, pasireotide might be considered before this in a small number of selected cases (for example young women who wish to retain fertility).

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