2 SYNOPSIS

Name of Sponsor/Company: Ipsen Ltd	Individual Study Table Referring to Part	*(For national authority use only)*
Name of Product: Somatuline® Autogel®	of the Dossier	
Name of Active Ingredient(s): Lanreotide acetate	Volume: Page:	

Title of study: An observational, multicentre, open label, post-marketing surveillance programme to assess the long-term safety and efficacy of Somatuline® Autogel® in the treatment of acromegaly when administered by patients or their partners ("Home Injection Group") or administered by healthcare professionals.

Investigators: Seven hospital clinicians in the United Kingdom

Study centre(s): Aberdeen Royal Infirmary, Manchester Royal Infirmary, St Bartholomew's Hospital London, Barnsley Hospital, St James's University Hospital Leeds, University Hospital Coventry and Warwickshire, and Churchill Hospital Oxford.

Publication (reference): None at the time of writing this report

Studied period (years):	**Phase of development**:
Date of first enrolment: 09 September 2008 Date of last completed: 25 September 2012	Post marketing

Objectives:

Primary:

To assess the safety and local tolerability of the long-term use of Somatuline Autogel when administered by patients or their partners ("Home Injection Group") and the safety and local tolerability in patients receiving their injection from a healthcare professional (HCP) ("Reference Group").

Secondary:

To assess the efficacy of the long-term use of Somatuline Autogel in both groups.

To evaluate the training requirements for patients / partners to perform home injection of Somatuline Autogel.

To evaluate the acceptability of home injections to patients, partners and healthcare professionals.

Methodology: This was an observational (non-interventional), multicentre post marketing surveillance programme. Patients who had been established on a stable dose of Somatuline Autogel for at least 4 months before entering the programme were asked if they wished to commence home (self or partner) injections. The decision was taken prior to, and independently of, the decision to participate in this post-marketing surveillance (PMS) programme. Patients who were enrolled in this PMS programme and chose to have their injections at home were included in the Home Injection Group, and patients who chose to

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receive their injections from a healthcare professional (HCP) were included in the Reference (HCP) Group. Patients could switch from home injection to HCP injection or from HCP injection to home injection during the observation period.

Number of patients (planned and analysed):

It was planned that approximately 50 patients would be enrolled in this PMS programme. The number of patients enrolled into each group was not mandated. At the end of the data collection period, 42 patients were enrolled, and 40 patients had post-baseline data (intention-to-treat [ITT]/Safety Population). Of the 40 patients with post-baseline data, 14 patients were included in the Home Injection Group of which 7 patients (50.0%) had at least one injection recorded; and 26 patients were included in the Reference (HCP) Group of which 14 patients (53.8%) had at least one injection recorded.

Diagnosis and criteria for inclusion:

Eligible patients were at least 18 years of age and had a diagnosis of acromegaly for which they had received treatment with Somatuline Autogel at a stable dose for at least 4 months. All patients gave written informed consent for their data to be included in the database for this PMS programme and any subsequent analysis. Patients who chose to be in the Home Injection Group had to be able to store Somatuline Autogel safely in a refrigerator in their own home, and either to collect it from their General Practitioner (GP) or Pharmacy on a monthly basis, or to receive the medication by a home delivery service.

Patients who were pregnant or breast-feeding were excluded from the study unless the treating clinician determined that continued treatment with Somatuline Autogel was clearly needed.

Study product dose, mode of administration and batch numbers:

Somatuline Autogel was supplied in pre-filled ready-for-use syringes containing 60, 90 or 120 mg lanreotide as acetate. Study medication was administered by deep subcutaneous injection into either the superior external quadrant of the buttock (HCP or partner injections) or upper, outer thigh (self-injections). Injections could be given by a HCP or by an appropriately trained friend or relative of the patient. Patients who were well motivated and had received appropriate training could self-administer the product.

Injections were generally administered every 28 days, although the 120 mg injection could be given at intervals of up to 56 days to patients whose condition was well controlled. The dose and frequency of administration was determined by the treating clinician in accordance with usual medical practice.

Study medication was obtained from commercial stock and batch numbers were not recorded.

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Name of Active Ingredient(s): Lanreotide acetate	Volume: Page:	

Duration of treatment: Somatuline Autogel is a long-term treatment and no duration of treatment was defined. Participation in the PMS programme for each patient could be up to 4 years, depending on the timing of their enrolment. Participation in the programme ended for all patients 2 years after the last patient was enrolled in the programme.

Reference therapy dose, mode of administration and batch numbers:

There was no comparator compound in this study. The Reference Group consisted of patients whose Somatuline Autogel (60, 90, or 120 mg) was administered by their usual HCP.

Criteria for evaluation:

Safety endpoints:

- Incidence of related treatment-emergent adverse events (TEAEs).
- Incidence of related serious adverse events (SAEs).
- Concomitant medications, therapies and surgical procedures.
- Liver and gall bladder ultrasound imaging, vital signs (heart rate, blood pressure, weight, height), where available.

Efficacy endpoints:

- Growth hormone (GH) plasma levels.
- Insulin-like growth factor (IGF)-1 plasma levels.
- Tumour size.

Additional endpoints:

- Training evaluations for patients in the Home Injection Group, including
  - Number of training sessions required.
  - Nature of training sessions required.
  - Supportive material or documentation used.
  - Length of training sessions.
  - Outcome of training session (patient/partner qualified or not qualified to perform home injections).
- Tolerability evaluations through patient reported comments.
- Acceptability evaluations, including:
  - The proportion of patients/partners who successfully qualified to perform home injections.

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- The proportion of patients who discontinued home injection after successfully qualifying to perform them.
- Treatment compliance.
- Any other issues with administration of injections

Statistical methods:

This was an observational programme. Therefore, no formal statistical analysis was planned or performed. All data were summarised descriptively by administration group and/or by dose and injection interval as appropriate.

Results:

Patients:

Forty-two patients were enrolled in the PMS programme, and 40 patients had post-baseline data: 14 patients in the Home Injection Group and 26 patients in the Reference (HCP) Group. Twenty-two patients (55.0%) were female and 18 patients (45.0%) were male. Mean age was 53.1 years and ranged between 31 and 80 years. Most patients were Caucasian/White (36 patients, 90.0%).

Safety:

A total of 19 related TEAEs were reported for 4 patients (10.0%). Two related TEAEs were reported for 1 patient (7.1%) in the Home Injection Group, and 17 related TEAEs were reported for 3 patients (11.5%) in the Reference (HCP) Group.

The related TEAEs in the Home Injection Group were numbness of the upper extremities (hypoaesthesia) and injection site lump (mass). The intensities were not known or not applicable but the TEAEs were not serious and did not lead to withdrawal of treatment.

In the Reference (HCP) Group, the most frequently reported related TEAE was diarrhoea (3 patients, 11.5%). The other TEAEs were all single cases (3.8%) and were: upper abdominal pain, nausea, injection site pain, and IGF-1 increased. Only 2 related TEAEs were severe in intensity: 1 episode of diarrhoea, and 1 episode of upper abdominal pain.

Two unrelated SAEs were reported in the eCRF database. These have been included in the report listings only as only events considered to be 'related' by the investigator should have been recorded:

- PPD was serious and had fatal outcome. This patient had been receiving PPD, was noted to be terminally ill when PP was seen 2 weeks previously, and the death of this patient was considered unrelated to treatment.
- DVT was serious but the patient recovered and continued in the PMS Programme for a further 1 year 9 months without recurrence of this event.

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One patient discontinued treatment due to multiple episodes of moderate diarrhoea, nausea, and injection site pain after injection.

There were no indications of a relationship between dose or duration of treatment and the frequency or intensity of TEAEs.

There were 5 patients with injection tolerance data, most of whom had no reaction, or had mild or moderate reactions. One patient in the Reference (HCP) Group had severe tenderness, haematoma and pain at various times during PP participation in the PMS Programme (up to 36 months). 'Other symptoms', where reported, were most frequently diarrhoea for 2 to 3 days after injection.

There were no clinically significant changes in laboratory values or physical examinations, including vital signs.

Other information:

Patients in the Home Injection Group required a median of 2 training sessions (range 0 to 3, n=10). The median duration of each training session was 30 minutes (range 20 to 60 minutes, n=8). All 14 patients and their partners were considered to have received adequate training for home injection and were qualified to perform it.

Overall, mean (standard deviation [SD]) GH levels decreased between pre active study to the last visit by -0.43 µg/L (1.63 µg/L). There were no patients with abnormal clinically significant GH values at the last visit. Actual mean (SD) IGF-1 values were unchanged between pre active study to the last visit (change of -0.9 nmol/L [16.2 nmol/L]). Similar results were noted for the normalised mean (SD) IGF-1 change from pre active study to last visit (change of -0.54 nmol/L [49.7 nmol/L]).

Patients in both groups had shifts in acromegaly symptoms; both improvements and worsening were recorded with no indications of a trend either way.

None of the patients permanently switched group during the PMS Programme, although there were indications that 2 patients in the Home Injection Group used HCP administration intermittently. The predominant reason for continuing with home injection was convenience.

There was insufficient data provided on the other endpoints for meaningful comparison between the groups or for conclusions to be drawn. However, there were no individual findings of note.

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Conclusion:
There were no new safety findings in this PMS Programme.
Home injection of Somatuline Autogel was convenient for those patients who chose it.

Date of report: 12 February 2015