



## Question: How is short-acting octreotide converted to long-acting lanreotide?

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### Summary

Sandostatin® and Sandostatin® LAR contain octreotide. Somatuline® Autogel and Somatuline® LA contain lanreotide. Sandostatin® LAR and Somatuline® LA are administered by intramuscular injection. Somatuline® Autogel is administered by deep subcutaneous injection. Unfortunately, there are no licensed recommendations available to direct the conversion of short acting octreotide to long acting lanreotide. However, an indirect conversion may be used as a guide. The information outlined in detail below summarises the conversion of short acting preparations of octreotide and lanreotide to their equivalent long-acting preparations. If the patient is controlled on a short acting preparation of octreotide, the patient is switched to octreotide LAR 20mg, and the dose is adjusted according to the response. Considering the information outlined below, the following conversions may be used as a guide;

- Octreotide LAR 20mg converts to Somatuline® Autogel 90mg
- Octreotide LAR 10mg convert to Somatuline® Autogel 60mg

This conversion should only be carried out by a practitioner with experience of doing so. The patient should be monitored carefully during the change in therapy.

## Detailed Information

### 1. Octreotide (Sandostatin®)

#### 1.1 Recommended starting doses by subcutaneous (SC) injection/infusion

Depending on the indication, the initial dose of octreotide varies between 50 micrograms once or twice daily to 200 micrograms three times daily (higher initial doses are required exceptionally).<sup>1,2,3,4,5,6</sup>

#### 1.2 Maintenance doses

Maintenance doses are variable. The American Hospital Formulary Services (AHFS) advises that for carcinoid tumours, the median maintenance dosage in clinical studies was approximately 450 micrograms daily.<sup>5</sup> Clinical and biochemical benefits were obtained with as little as 50 micrograms daily in some patients, while others required dosages up to 1500 micrograms daily.<sup>5</sup> However, experience with dosages exceeding 750 microgram daily is limited.<sup>5</sup> The Palliative Care Formulary (PCF) states that a maximum dose of 6000micrograms daily has been used for hormone secreting tumours.<sup>6</sup>

#### 1.3 Switching from an octreotide infusion to an octreotide LAR preparation

It is recommended that once control has been established, maintenance therapy with a depot preparation may be considered.<sup>1,4,6</sup> An initial dose of 20mg by intramuscular injection (IM) every 4 weeks is suggested.<sup>1,3,4,5,6,7</sup> In acromegaly, the SC octreotide is stopped when the first long acting dose is administered.<sup>1,3,5,6,7</sup> However, for other neuro-endocrine tumours, SC injection with a rapid-acting preparation should be continued for 2 weeks after the first depot injection to provide symptomatic cover,<sup>1,3,4,5,6,7</sup> and in some cases, subcutaneous therapy may be need to be continued for 3–4 weeks to avoid exacerbation of disease symptoms.<sup>5</sup> After 2 to 3 months, maintenance doses of the depot preparation may be adjusted to between 10 and 30mg every 4 weeks, as necessary.<sup>1,3,4,5,7</sup> In patients who have achieved satisfactory symptom relief with the 20mg dose, a reduction to 10mg IM once every 4 weeks may be attempted.<sup>3,5,7</sup> On the other hand, if adequate symptom control has not been achieved with 20mg, an increase to 30mg IM once every 4 weeks may be necessary.<sup>1,3,4,5,7</sup> If adequate control has not been achieved at 30mg dose the dose may be further increased to 40mg IM every 4 weeks.<sup>3,4,5,7</sup> Doses above 40mg have not been evaluated and are not recommended.<sup>5</sup>

## **2. Lanreotide (Somatuline®)**

### **2.1 Recommended starting doses;**

#### **Somatuline® LA**

Initially one intramuscular injection (Somatuline® LA 30mg) is administered every fourteen days.<sup>8,9,10</sup> In acromegaly and symptomatic neuroendocrine tumours, this may be increased, if necessary, to 30mg every 7 to 10 days and in thyroid tumours it may be increased to 30mg every 10 days.<sup>8,10</sup> Frequency of administration may vary according to the indication and the individual patient's response.<sup>9</sup>

#### **Somatuline® Autogel**

For the treatment of acromegaly, the recommended starting dose is 60 to 120 mg administered every 28 days by deep subcutaneous injection.<sup>11</sup> For the treatment of neuroendocrine tumours the recommended starting dose is 60 to 120 mg administered every 28 days.<sup>8,10,11</sup>

### **2.2 Switching from Somatuline® LA to Somatuline® Autogel**

In patients previously treated with Somatuline® LA 30 mg every 14 days, the initial dose of Somatuline® Autogel should be 60 mg every 28 days, and in patients previously treated with Somatuline® LA 30 mg every 10 days, the initial dose of Somatuline® Autogel should be 90 mg every 28 days.<sup>10,11</sup> Thereafter, the dose should be individualised according to the response of the patient.<sup>11</sup>

## **3. Long Acting Octreotide or Long Acting Lanreotide?**

Octreotide and lanreotide have comparable efficacy and have similar molecular structure and mechanisms of action.<sup>12</sup> Several small studies have been conducted observing clinical endpoints in treatment of acromegaly with various forms of lanreotide and octreotide; no study has been large enough or adequately powered to demonstrate superiority of one drug over another.<sup>12</sup> Sandostatin® LAR (octreotide) and Somatuline® LA (lanreotide) are administered by intramuscular injection.<sup>7,9</sup> Somatuline® Autogel (lanreotide) is administered by deep subcutaneous injection.<sup>11</sup> Subcutaneous administration may be preferable for palliative care patients.<sup>6</sup>

#### **4. Switching between Octreotide and Lanreotide**

There have been no studies of patients treated with short-acting octreotide who have subsequently been switched directly to Somatuline<sup>®</sup> Autogel, therefore guidance has to be derived from other information.<sup>13</sup> There is however, data available relating to switching between octreotide LAR and Somatuline<sup>®</sup> Autogel.<sup>13,14,15</sup> When switching between these agents two factors should be taken into consideration; firstly a suitable dose should be calculated and secondly an assessment should be made of whether or not to overlap the treatments.<sup>13</sup>

##### **4.1 Dose calculation**

##### **Switching from SC Octreotide to Somatuline<sup>®</sup> Autogel (via Sandostatin<sup>®</sup> LAR dose calculation)**

There is no information available to support a direct conversion from SC octreotide to Somatuline<sup>®</sup> Autogel.<sup>13</sup> As outlined above patients who are controlled with SC octreotide should be switched to 20mg of Sandostatin<sup>®</sup> LAR, irrespective of the daily dose of SC octreotide used previously. Subsequent treatment adjustments are recommended after 3 months of treatment, if considered necessary. As information is available to guide the switch from Sandostatin<sup>®</sup> LAR to Somatuline<sup>®</sup> Autogel, this information could be extrapolated to guide the switch from SC octreotide to Somatuline<sup>®</sup> Autogel<sup>13</sup>

- Ashwell et al<sup>14</sup> conducted a study with the aim of comparing the efficacy of Somatuline<sup>®</sup> Autogel and Sandostatin<sup>®</sup> LAR in order to establish clinically equivalent doses and to generate guidelines on switching patients.<sup>14</sup> Twelve acromegaly patients previously treated and stabilised with depot octreotide LAR 20mg were switched to 90 mg Somatuline<sup>®</sup> Autogel, given every 28 days. The authors concluded that the results suggested that the majority of patients switched from 20mg octreotide LAR to Somatuline<sup>®</sup> Autogel 90mg would have equivalent or better disease control.<sup>14</sup>

On the basis of the above data, a suggestion for transferring patients from monthly octreotide LAR to monthly Somatuline<sup>®</sup> Autogel would be to initiate patients as follows:

Sandostatin<sup>®</sup> LAR 20mg convert to Somatuline<sup>®</sup> Autogel 90mg<sup>13,14</sup>

Based on the data from the Ashwell study, a further suggestion for conversion from other doses of Sandostatin® LAR would be as follows:

Sandostatin® LAR 10mg convert to Somatuline® Autogel 60mg<sup>13</sup>

The suggested conversion doses above are supported by two further studies in acromegalic patients, which have switched patients on different doses of Sandostatin® LAR to Somatuline® Autogel.<sup>13,15</sup>

#### **4.2 Switching method**

As mentioned previously, there are no clinical data available relating to a direct conversion from SC octreotide to Somatuline® Autogel. However, data relating to the pharmacokinetics of Somatuline® Autogel is useful in establishing how to initiate treatment.<sup>13</sup>

Due to the rapid attainment of peak plasma levels following injection with Somatuline® Autogel<sup>11,13</sup> it may be possible to switch from octreotide SC without crossover of therapy. Peak plasma levels are generally achieved during the first day after administration.<sup>11</sup> Therefore; the patient should be given their first dose of Somatuline® Autogel in place of their next octreotide SC dose.<sup>13</sup>

After this initial conversion, for all patients, the dose should be individualised according to the response of the patient.<sup>13</sup> The dose may be increased or decreased as required.<sup>13</sup> It should be noted that steady state levels of Somatuline® Autogel are achieved after approximately 6 monthly injections.<sup>13</sup> Patients reviewed before this time point may not have achieved steady state lanreotide levels and this should be taken into account when assessing a patient's response to treatment.<sup>13</sup>

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