

of leuprolide over 6 months (US Food and Drug Administration 2011). A further development included the development of 3.75 mg and 11.25 mg depot formulations for the treatment of endometriosis and fibroids. As with Eligard, the Safety Alert issued in relation to GnRH agonists applies to Lupron Depot™ therefore prescribers are advised to exercise caution. A further formulation development has resulted in the production of Lupron Depot-Ped™ 7.5 mg, 11.25 mg and 15 mg for 1-month and 11.25 mg and 30 mg for 3-month administration for the treatment of children with central precocious puberty (CPP).

Sandostatin LAR is a prolonged-release Octreotide formulation consisting of PLGA and NMP. Octreotide is a synthetic analogue of somatostatin that is used to treat acromegaly by controlling the levels of growth hormone (GH) and IGF-1, which reduces the size of tumors and regulates symptoms. It is also used in the treatment of gastroenteropancreatic neuroendocrine tumors (GEP NETs) by controlling gastrointestinal hormone secretion. FDA approval of the LAR formulations was granted to Novartis Pharmaceuticals Corporation on 25th November 1998, with Novartis Pharmaceuticals UK Limited trading as Sandoz Pharmaceuticals granted marketing authorizations by the MHRA for 10, 20 and 30 mg formulations in June 2007 (Novartis Pharmaceuticals UK Ltd. 2011). This product is injected intramuscularly and the prolonged release nature of the formulation allows for monthly dosing, regardless of dose.

Modlin et al. in 2010 reviewed a number of articles that focused on the use of Sandostatin LAR in the treatment of GEP NETs, as well as other SST analogues. The review consisted of examining 15 previously published studies, which included 481 patients. They determined that the use of Sandostatin LAR accomplished symptomatic relief in 74.2%, biochemical response in 51.4% and tumour response in 69.8% (Modlin et al. 2010). A multicenter study conducted which was published in 2002, compared patient outcomes in relation to GH levels, IGF-1 levels and tumor size after treatment of acromegaly with the subcutaneous or long acting octreotide formulations. Before treatment, the mean GH level was 30 mU/litre but with the initial 24 weeks of subcutaneous treatment, GH levels were reduced to less than 5 mU/litre in 9 patients, with IGF-1 levels being reduced to normal in 8 patients. A tumor size decline of 49% was seen in those patients with microadenomas and a 43% reduction in those with macroadenomas. Upon completion of the study, 79% of patients showed a mean serum GH level of less than 5 mU/litre, 53% had normalized IGF-1 levels and a 23% reduction in tumor volume was reported in 73% of patients (James et al. 2002).

## **Current Issues with Solvent-Induced SPI**

Although SPI are an attractive alternative to other currently used methods of drug delivery, they do however face a number of problematic issues. The first to consider is the susceptibility to burst release. As shown, this can be extensive within the first 24 hours after injection. A large initial release may result in drug levels that are above the therapeutic window and could be toxic. This is obviously more problematic for those drugs that have narrow therapeutic window. As this review has shown, many