About MYALEPTA® ▼ (metreleptin)

Metreleptin, as an adjunct to diet, is the first treatment in Europe specifically licensed for lipodystrophy; a disease that can result in a total lack of subcutaneous fat (fat under the skin), known as generalised lipodystrophy (GL) or a partial lack of subcutaneous fat, known as partial lipodystrophy (PL).[1] This lack of subcutaneous fat can result in a deficiency of the essential hormone leptin.

Metreleptin is a leptin replacement therapy which addresses the complications associated with leptin deficiency. By replacing leptin, metreleptin has the potential to address the many symptoms and metabolic complications associated with the disease.[2] Prior to metreleptin there were no effective treatment options available in Europe to treat the problems associated with leptin deficiency in lipodystrophy. Current treatments (anti-diabetic and lipid-lowering medications, diet and exercise) are ineffective in addressing the associated complications in most cases.

How does metreleptin work?

- Normally the fat under the skin produces a hormone, leptin, which regulates many body functions including energy balance and appetite. In lipodystrophy, the subcutaneous fat is totally or partially absent leading to a deficiency of leptin.[3]
- Leptin controls hunger and how the body uses sugar and fats. Without leptin, patients can have uncontrollable hunger and internal organs may be damaged by an accumulation of fat and by metabolic disorders, such as severe diabetes.
- Metreleptin replaces the missing hormone – leptin – to treat the complications of leptin deficiency in lipodystrophy patients.[4,5,6,7]
- Metreleptin works by binding to and activating the human leptin receptor, restoring leptin levels.[5]
- Metreleptin improves blood glucose and lipid levels, suppresses accumulation of fat in muscles and organs (lipotoxicity), boosts insulin sensitivity and relieves uncontrollable hunger in lipodystrophy patients.[7,8]
- While metreleptin replaces missing leptin, it does not restore the body fat lacking in lipodystrophy patients.

Who can take metreleptin?

The European Commission (EC) has granted a Marketing Authorisation for the use of MYALEPTA® (metreleptin), as an adjunct to diet, to treat the complications of leptin deficiency in lipodystrophy (LD) patients with:

- Confirmed congenital generalised LD (Berardinelli-Seip syndrome) or acquired generalised LD (Lawrence syndrome) in adults and children 2 years of age and above.[5]
- Confirmed familial partial LD or acquired partial LD (Barraquer-Simons syndrome), in adults and children 12 years of age and above for whom standard treatments have failed to achieve adequate metabolic control.[5]

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

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What data supports the use of metreleptin?

The clinical data supporting the Marketing Authorisation of metreleptin demonstrated that metreleptin in both GL and PL patients significantly improved the management of blood sugar and triglyceride (blood lipid) levels which can be severely raised in lipodystrophy patients and are difficult to manage.

In patients with GL, mean reduction, following metreleptin treatment, of HbA1c was 2.2% and triglycerides was 32%. In PL patients, the mean reduction was 0.9% for HbA1c and 37.4% for triglycerides.[5] In addition, some GL patients on metreleptin were able to reduce their need for other treatments with:

41% on insulin at baseline were insulin-free following treatment.

22% on oral anti-diabetic agents at baseline able to discontinue.

24% on lipid-lowering therapy at baseline able to discontinue.[6]

The most common adverse reactions were hypoglycaemia and weight decrease, followed by decreased appetite, headache, abdominal pain, nausea, alopecia, menorrhagia, fatigue, injection site bruising, pain or swelling and neutralising antibodies.[5]

A follow-up study has further demonstrated the therapeutic benefits of metreleptin across a range of potentially life-threatening metabolic complications, as well as in a range of quality of life measures as outlined in the table below.[7] The results showed that one year of treatment with metreleptin was modelled to reduce the quality of life gap between metreleptin-naïve patients and perfect health by:

59% in GL.*

31% in PL.*

*The quality adjusted life years (QALY) values at baseline and after 12 months on metreleptin were modelled to improve from 0.466 to 0.779 in GL and from 0.624 to 0.741 in PL. The QALY value for perfect health is 1.0.

In addition to this, the results showed that treatment with metreleptin markedly improved disease attributes that patients experienced at baseline:

Disease attribute	Prevalence at baseline (GL+PL)	Percentage of these patients who improved from baseline
Hyperphagia	79%	99%
Pancreatitis	39%	98%
Triglycerides (>200mg/dL)	81%	89%
Elevated alanine transaminase (ALT)	51%	84%
HbA1c (>6.5%)	75%	80%
Inability to work/attend school	43%	75%
Elevated aspartate transaminase (AST)	43%	73%
Impaired physical appearance	77%	60%
Hypertension	54%	59%
Elevated 24-hour protein excretion	41%	59%
Disruption to reproductive function in women of reproductive age†	80%	44%
Liver abnormality	94%	36%
Kidney abnormality	63%	27%

†45 patients had disruption of female reproductive function at baseline representing 40% of the entire study population and 80% of 56 females of reproductive capacity. Of these, 20 (44%) experienced improvement on metreleptin.

References

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