OPINION ON MEDICINAL PRODUCTS

177 Lutecium oxodotreotide
LUTATHERA 370 MBq/mL,

Solution for infusion

Reassessment

Adopted by the Transparency Committee on 29 June 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement only for the treatment of well-differentiated (G1 and G2), progressive, inoperable or metastatic intestinal neuroendocrine tumours (NETs) expressing somatostatin receptors in adults.

Therapeutic improvement?

Therapeutic improvement with respect to octreotide.

Role in therapeutic strategy?

The Committee points out that the initiation of LUTATHERA (^{177}Lutecium oxodotreotide) treatment must be discussed within the framework of multidisciplinary review meetings as part of the NET-specific national network, RENATEN, designated by INCa.

The treatment of intestinal NETs consists of tumour syndrome management, along with the management of any potentially associated secretory syndrome, which has a significant impact on patient quality of life and morbidity.

Considering the updated data from the NETTER-1 study, showing no new safety signals of concern, and despite the lack of evidence of a benefit in terms of overall survival, vectorised internal radiotherapy with LUTATHERA remains a 2nd-line treatment, after disease progression with octreotide. This therapy is envisaged as a 1st-line treatment following a multidisciplinary review in specific cases of patients presenting with tumours that are progressive from the outset or with a large liver tumour mass (> 50%).

Failing comparative data, the role of Radio Ligand Therapy (RLT) with respect to everolimus in not known.

LUTATHERA must be co-administered with a hyperosmolar amino acid solution. Due to prolonged serotonin secretion from NETs, capable of damaging heart valves (right heart valve stenosis), co-administering this solution may induce a sudden water/salt overload potentially causing acute decompensation on the damaged heart. For the initial pre-treatment assessment for digestive tract NETs, the TNCD recommends performing echocardiography on patients presenting with carcinoid syndrome or elevated 5HIAA (5-hydroxyindolacetic acid, the main catabolite of serotonin) levels in urine, with a view to analysing heart valve status.

Note that LUTATHERA is a radiopharmaceutical medicinal product requiring compliance with radioprotection rules.

Special recommendations

The Committee recommends that the initiation of LUTATHERA (^{177}Lutecium oxodotreotide) treatment must be discussed within the framework of regional multidisciplinary review meetings as part of the NET-specific national network, RENATEN, designated by INCa.

Committee's conclusions

Clinical Benefit

- Gastroenteropancreatic neuroendocrine tumours, particularly when intestinal and metastatic, are severe, potentially life-threatening diseases.
- The proprietary medicinal product LUTATHERA (^{177}Lutecium oxodotreotide) is a curative medicinal product.
- The efficacy/adverse effect ratio is significant.
- Therapeutic alternatives are available.
- It is a first- or second-line treatment for well-differentiated (G1, G2) progressive, metastatic intestinal NETs expressing somatostatin receptors.

Public health benefit

Considering:

– the severity of gastroenteropancreatic neuroendocrine tumours,
– the incidence of GEP NETs of approximately 1.1/100,000 in men and 0.9/100,000 in women,
– the medical need for medicinal products demonstrating their superiority over conventional therapies in terms of overall survival and quality of life for these patients.
– the demonstrated impact of LUTATHERA in terms of progression-free survival with respect to octreotide LP 60 mg, and therefore the response provided to the partially met medical need,
– the lack of demonstrated impact on quality of life and on mortality,
– the impact on the delivery of care with respect to available alternatives, given the radioprotection constraints associated with the characteristics of the radiopharmaceutical medicinal product and co-administering a hyperosmolar amino acid infusion,

LUTATHERA (^{177}Lutecium oxodotreotide) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of LUTATHERA (^{177}Lutecium oxodotreotide) remains significant for the treatment of well-differentiated (G1 and G2), progressive, inoperable or metastatic intestinal neuroendocrine tumours (NETs) expressing somatostatin receptors, in adults.

Clinical Added Value

Considering:

- the evidence of the superiority of LUTATHERA, in association with octreotide LP 30 mg, in terms of progression-free survival, with respect to octreotide LP 60 mg alone, the clinically relevant comparator (median not yet reached in the LUTATHERA group, in association with octreotide LP 30 mg, and 8.5 months in the comparator group; HR = 0.18; $CI_{95\%}$ = [0.11; 0.29]; p<0.0001),
- the context of these diseases, which particularly include slowly progressing forms, and for which progression-free survival may be considered as a clinically relevant outcome measure in view of the effect size observed in the NETTER-1 study.
- long-term survival, maintaining quality of life, is a significant therapeutic endpoint, which controlling the disease, tumour and secretory syndrome, is likely to help achieve;
- and despite the lack of difference in terms of overall survival between the 2 treatment groups in the context of the final analysis (median overall survival of 48 months in the LUTATHERA group ($CI_{95\%}$: [37.4; 55.2]) versus 36.3 months in the octreotide group ($CI_{95\%}$: [25.9; 51.7]), HR=0.84 ($CI_{95\%}$: [0.6; 1.17]),
- the additional safety data not showing any new signal of concern,
- the medical need to have effective, and well-tolerated, alternatives,

the Committee deems that LUTATHERA (^{177}Lutecium oxodotreotide) still provides moderate clinical added value (CAV III) with respect to octreotide LP 60 mg administered alone, for the treatment of well-differentiated (G1 and G2), progressive, inoperable or metastatic intestinal neuroendocrine tumours (NETs) expressing somatostatin receptors, in adults.