Report Mounjaro® - tirzepatide

Product & Mechanism of action

Substance: tirzepatide

Brand Name: Mounjaro

Originator/licensee: Eli Lilly Nederland B.V.

Classification: NCE

ATC code: A10B

Orphan Status:
Eu: No
Us: No

Mechanism of action:
tirzepatide is a dual GIP and GLP-1 receptor agonist. By means of its action on these receptors, tirzepatide improves glycaemic control through several different mechanisms [1].

Authorized indications Licensing status

Authorized Indication:
EMA: tirzepatide is indicated for the treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise:
- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications;
- in addition to other medicinal products for the treatment of diabetes.

FDA: is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus [2].

Route of administration: SC

Licensing status
EU CHMP P.O. date: 21/07/2022
FDA M.A. date: 13/05/2022

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: Yes

ABBREVIATIONS:
AE: Adverse Event
BMI: body-mass index
CHMP: Committee for Medicinal Products for Human Use
DPP-4: dipeptidyl peptidase-4
GI: gastrointestinal
GIP: glucose-dependent insulinotropic polypeptide
GLP-1: glucagon-like peptide 1
HbA_{1c}: glycated haemoglobin
M.A.: marketing authorization
Pbo: placebo
P.O.: Positive Opinion
Pts: patients
SGLT2: sodium glucose co-transporter 2
T2DM: type 2 diabetes mellitus
TEAE: Treatment Emergent Adverse Event
Vs: versus

Essential therapeutic features

Summary of clinical EFFICACY:
SURPASS-1 (NCT03954834) is a phase III, randomized, double-blind, placebo-controlled trial to compared the efficacy and safety of three tirzepatide doses vs pbo in pts aged ≥ 18 yrs with T2D, inadequately controlled with diet and exercise alone and naïve to injectable diabetes therapy. The eligible pts had an HbA_{1c} of 7% or more (≥ 53 mmol/mol) to 9.5% or less (≤ 80 mmol/mol) at screening.
The primary endpoint was the mean change in HbA_{1c} from baseline at 40 weeks. Pts (N=705) were randomly assigned (1:1:1) to reiceved tirzepatide 5 mg (N=121), tirzepatide 10 mg (N=121), tirzepatide 15 mg (N=121), or pbo (N=115), once a week for 40 weeks.
More pts on tirzepatide than on pbo met HbA_{1c} targets of less than 7.0% (<53 mmol/mol; 87–92% *vs* 20%) and 6.5% or less (≤48 mmol/mol; 81–86% *vs* 10%) and 31–52% of pts on tirzepatide versus 1% on placebo reached an HbA_{1c} of less than 5.7% (<39 mmol/mol) [3].

	Mean HbA_{1c} decreased from baseline	Treatment difference versus placebo (p<0.0001)
Tirzepatide 5mg	1.87% (20 mmol/mol)	-1.91% (-21 mmol/mol)
Tirzepatide 10mg	1.89% (21mmol(mol)	-1.93% (-21 mmol/mol)
Tirzepatide 15mg	2.07% (23 mmol/mol)	-2.11% (-23 mmol/mol)
PBO	+0.04% (+0.4 mmol/mol)	/

Summary of clinical SAFETY:
The proportion of pts reporting any AEs and SAEs were similar between groups [3].

	Tirzepatide 5mg	Tirzepatide 10mg	Tirzepatide 15mg	PBO
Pts with ≥1 TEAE*	83 (69%)	81 (67%)	77 (64%)	76 (66%)
SAEs	5 (4%)	2 (2%)	1 (1%)	3 (3%)
Study drug discontinuation***	4 (3%)	6 (5%)	8 (7%)	3 (3%)
Deaths	0	0	0	1 (1%)

*The most frequent TEAEs (occurring in ≥5 pts) with tirzepatide were: nausea (12%; 13%; 18% *vs* pbo 7%), diarrhoea (12%; 12; 14% *vs* pbo 8%), vomiting (3%; 2%; 6% *vs* pbo 2%); and were mild to moderate in severity and decreased over time in all groups.
***due to gastrointestinal AEs.

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** Yes

Discontinued studies (for the same indication): No

References:

[1]. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/mounjaro
[2]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215866s000lbl.pdf
[3]. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01324-6/fulltext
[4]. https://www.portalediabete.org/epidemiologia-del-diabete/
[5]. https://www.io.nihr.ac.uk/wp-content/uploads/2022/01/28192-Tirzepatide-for-Type-2-Diabetes-Mellitus-V1.0-FEB2020.-non-CONF.pdf
[6]. https://adisinsight.springer.com/drugs/800045287
[7]. https://www.clinicaltrials.gov/

NHS impact

Cost of therapy:
Price is not available yet.

Epidemiology:
The prevalence of T2D is steadily increasing due to the rise in obesity and sedentary lifestyle. In Italy, the prevalence of the disease is around 3-4% [4].

POSSIBLE PLACE IN THERAPY
NICE recommends metformin in pts, who can tolerate it. If triple therapy with metformin and two other oral drugs is not effective, not tolerated or contra-indicated then a GLP-1 receptor agonist may be prescribed as part of a triple combination regimen with metformin and a sulfonylurea.
In pts who cannot tolerate metformin, drug treatment to be offered is one or a combination therapy of the following: a DPP-4 inhibitor, pioglitazone, sulfonylurea, SGLT2 inhibitor, repaglinide [5].

OTHER INDICATIONS IN DEVELOPMENT:
Cardiovascular disorders, heart failure, Obesity, Sleep apnoea syndrome [6].

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: No

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION
Lixisenatide, HSK7653, PB-119 [7].

*Service reorganization: No
*Possible off label use: Yes

Issued on: August 2022