Report Etrasimod –VELSIPITY®

Product & Mechanism of action

Substance:etrasimod

Brand Name: Velsipity®

Originator/licensee:

Classification:NCE

ATC code:L04AE05

Orphan Status:
Eu: No
Us: No

Mechanism of action:
etrasimod is a selective immunosuppressant. The mechanism by which etrasimod exerts therapeutic effects in UC is unknown, but it may involve the reduction of lymphocyte migration into sites of inflammation, as selective binding of etrasimod to S1P receptors 1,4 and 5 partially and reversibly blocks the capacity of lymphocytes to egress from lymphoid organs [1].

Authorized indications Licensing status

Authorized Indication:
EMA:etrasimod is indicated for the treatment of patients 16 years of age and older with moderately to severely active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biological agent [1].

FDA: etrasimod is a sphingosine 1-phosphate receptor modulator indicated for the treatment of moderately to severely active UC in adults [2].

Route of administration:os

Licensing status
EU CHMP P.O. date:14/12/2023
FDA M.A. date:12/10/2023

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

ABBREVIATIONS:
AE: adverse event
JAK: Janus Kinases
MMS: modified Mayo score
P: p-value
Pbo: placebo
Pts: patients
SAE: Serious adverse event
UC: ulcerative colitis

Essential therapeutic features

Summary of clinical EFFICACY:
The efficacy and safety of etrasimod were evaluated in two independent randomized, multicenter, double-blind, pbo-controlled, phase III trials (ELEVATE UC 52 and ELEVATE UC 12, NCT03945188 and NCT03996369,respectively).
Eligible pts were 16 to 80 years old with moderately to severely active UC (confirmed by endoscopy with ≥ 10 cm rectal involvement and on the basis of a MMS of 4-9 with a centrally read endoscopic subscore ≥2 and rectal bleeding subscore ≥1) and a documented history of inadequate response, loss of response, or intolerance of at least one therapy approved for the treatment of UC.
ELEVATE UC 52 comprised a 12-week induction period followed by a 40-week maintenance period with a treat-through design. ELEVATE UC 12 independently assessed induction at week 12.
The primary efficacy endpoints were the proportion of pts with clinical remission at weeks 12 and 52 in ELEVATE UC 52 and week 12 in ELEVATE UC 12.
In both trials, pts wererandomly assigned (2:1) to etrasimod 2mg or pbo, stratified by previous exposure to biologicals or JAK inhibitors therapy (yes *vs* no), baseline corticosteroid use (yes *vs* no), and baseline disease activity (MMS; 4-6 *vs* 7-9).

Table 1: N of eligible pts

	Tot of pts	Etrasimod	pbo
ELEVATE UC 52	433	289	144
ELEVATE UC 12	354	238	116

In ELEVATE UC 52, a significantly greater proportion of pts in the etrasimod group achieved clinical remission compared with pts in the pbo group at completion of the 12-week induction period (74 [27%] of 274 pts *vs*10 [7%] of 135 pts; p<0.0001) and at week 52 (88 [32%] of 274 pts *vs*9 [7%] of 135 pts; p<0.0001)
In ELEVATE UC12, 55 (25%) of 222 pts in the etrasimod group had clinical remission compared with 17 (15%) of 112 pts in the pbo group at the end of the 12-week induction period (p=0.026) [3].

Summary of clinical SAFETY:
In both ELEVATE UC 52 and ELEVATE UC 12, etrasimod showed a favourable safety profile consistent with previous studies. Most events were considered mild or moderate. The most frequently reported AE (≥1% of pts) included anemia, headache, and worsening of ulcerative colitis or ulcerative colitis flare. AEs of special interest were similar between the two trials and occurred in up to 3% of pts: cardiovascular disease (hypertension, sinus bradycardia, atrioventricular block) and infection (tuberculosis, cytomegalovirus infection, herpes zoster events). These events were considered either mild or moderate, were localized and did not lead to discontinuation from the study [3].

Table 2: Summary of clinical safety

	ELEVATE UC 52		ELEVATE UC 12	
	Etrasimod group (N=289)	Pbo group (N=144)	Etrasimod group (N=238)	Pbo (N=116)
Any AE	206 (71%)	81 (56%)	112 (47%)	54 (47%)
Any SAE	20 (7%)	9 (6%)	6 (3%)	2 (2%)
Any AE leading to study treatment discontinuation	12 (4%)	7 (5%)	13 (5%)	1 (1%)

Ongoing studies[4]:
- ***For the same indication:***No
- ***For other indications:***Yes

Discontinued studies (for the same indication): No

References:

[1]. https://www.ema.europa.eu/en/medicines/human/EPAR/velsipity
[2]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216956s000lbl.pdf
[3]. Sandborn WJ et al. Etrasimod as induction and maintenance therapy for ulcerative colitis (ELEVATE): two randomised, double-blind, placebo-controlled, phase 3 studies. Lancet. 2023 Apr 8;401(10383):1159-1171. doi: 10.1016/S0140-6736(23)00061-2. Epub 2023 Mar 2. Erratum in: Lancet. 2023 Mar 25;401(10381):1000. PMID: 36871574.
[4]. https://adisinsight.springer.com/drugs/800037849
[5]. https://pubmed.ncbi.nlm.nih.gov/33784448/
[6]. https://www.io.nihr.ac.uk/wp-content/uploads/2022/10/23880-TSID_10636-Risankizumab-for-Ulcerative-Colitis-v1.0-OCT2022-NONCONF.pdf
[7]. https://www.nice.org.uk/guidance/ta828/resources/ozanimod-for-treating-moderately-to-severely-active-ulcerative-colitis-pdf82613377539781

NHS impact

Cost of therapy:
The estimated cost of etrasimod is not yet known.

Epidemiology:
In Italy, a review based on 16 studies reported incidence rates of UC as 10-15 cases per 100,000 inhabitants per year [5].

POSSIBLE PLACE IN THERAPY
NICE currently recommends thefollowingtreatment options for moderateto severe UC:
- Tofacitinib
- Vedolizumab
- Infliximab, adalimumab, golimumab
- Filgotinib
- Ustekinumab
- Ozanimod [6-7].

Etrasimov could be another option, which role has to be defined.

OTHER INDICATIONS IN DEVELOPMENT: Atopic dermatitis; Crohn's disease [4].

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

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:
Ontamalimab, SHR03302, Cobitolimod [8].

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

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