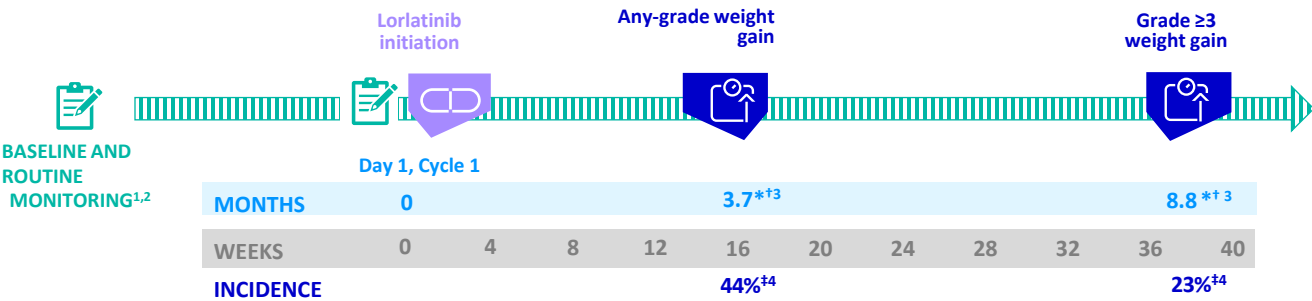


# Weight Management with 3rd Gen TKIs

## Monitoring, Management and Counselling Factsheet

Counsel patients, family and care partners about the possibility of weight gain and expectations for monitoring (measured at each clinical visit)<sup>1,2</sup>

The CROWN study reports both **any-grade** and **grade ≥3 weight gain** that can present at **different stages during lorlatinib therapy**<sup>1,3</sup>



In CROWN,\* **baseline body weight did not influence subsequent weight gain** (Grade 2/3 weight gain: n=55; No grade 2/3 weight gain: n=94), and **no patients discontinued treatment with lorlatinib because of weight gain**<sup>3</sup>

In CROWN, **weight was measured at the start of lorlatinib treatment (Day 1, Cycle 1)**<sup>2</sup>

- Some patients may have lost weight unintentionally due to their underlying disease. Thus, some HCPs may prefer to choose a baseline that is the patient's healthy weight prior to cancer diagnosis, rather than their nadir weight<sup>1</sup>

A **proper baseline assessment** is important<sup>1</sup>:

- The degree that the patient is bothered by the AE is subjective and based on baseline function, daily lifestyle and activities
- The greater the degree to which the patient experiences bothersome symptoms and functional detriment, the greater the likelihood that intervention will be needed

\*CROWN 5-year expanded safety analysis; n=149<sup>3</sup>; †Median time to onset<sup>3</sup>; ‡CROWN 5-year analysis; n=149.<sup>4</sup>

Accurate grading of lorlatinib AEs, including weight gain as an AE, is important for implementing informed management decisions<sup>1,5</sup>

CTCAE grade definitions <sup>5</sup>				
AE	Grade 1	Grade 2	Grade 3	Grade 4
Weight gain	5% to <10% from baseline	10% to <20% from baseline	≥20% from baseline	N/A

## Discussion guide

Patients with weight gain as an AE, along with their care partners, may initially see this as a sign of health improvement and not realize that these symptoms could be related to lorlatinib treatment<sup>6,7</sup>

Conducting a baseline assessment and using open-ended questions during ongoing monitoring with your patients and/or their care partners can help uncover changes in symptom burden and severity, which can impact their daily life

How bothersome is weight gain to you?

- Are you experiencing any discomfort or self-consciousness related to the weight gain?
- Has the weight gain affected your overall sense of well-being or self-esteem?

How is weight gain impacting your ability to perform daily activities or chores?

- Do you find it harder to complete tasks that require physical exertion, such as climbing stairs or lifting objects?
- Has the weight gain affected your energy levels or motivation to carry out daily responsibilities?

How does weight gain affect your participation in sports or hobbies?

- Have you noticed any changes in your performance or enjoyment of physical activities?
- Are there any hobbies or sports you have had to adjust or give up due to weight gain?

**Clinical practice self-reflections**

Are you monitoring weight gain at baseline vs at each clinical visit?

When do you recommend non-pharmacologic vs pharmacologic interventions?

## Lorlatinib doses can be modified. Dose reduction did not seem to impact PFS or IC efficacy\*<sup>1</sup>

\*CROWN post hoc analysis in patients who had a dose reduction (from 100 mg to 75 mg) within the first 16 weeks.<sup>1,2</sup>

### Recommended dose modifications for weight gain AEs:

#### Per Local PI<sup>3</sup>

If grade 1/2

Continue lorlatinib at the same dose or at a reduced dose

If grade 3/4

Withhold lorlatinib

After symptoms resolve to grade  $\leq 2$  or baseline

Resume lorlatinib at a reduced dose level\*

\*If not considered a safety risk for the patient.<sup>4</sup>

### Per the Pragmatic Guide for Management of Adverse Events Associated with Lorlatinib<sup>5</sup>

Weight gain may become bothersome, which can impact patient QoL. Therefore, the routine assessment of this relationship is important

#### How bothersome is the toxicity for the patient?

Not  
bothersome

Mildly to moderately  
bothersome

Severely bothersome

Reassess  
(regularly until  
stable/improved)



Lifestyle modification and management of weight gain



If worse:

If stable,  
or better:

Legend



Continue: maintain the same lorlatinib dose



Reduce: lorlatinib dose reduction  
(by 25 mg decrements)

## Counsel patients, family and care partners about the possibility of lorlatinib-associated oedema, and how to differentiate it from lorlatinib-associated weight gain<sup>5,6</sup>

Body weight increases and oedema are sometimes experienced concurrently. If weight gain and oedema are experienced together, oedema should be managed first, as a reduction in oedema can influence body weight.<sup>5</sup>



In CROWN,\* weight gain and oedema seem to correlate in 40% of patients<sup>†7</sup>



Oedema-related swelling is typically localized to peripheral extremities (arms, legs, hands and feet)<sup>‡5,6</sup>

\*CROWN 5-year expanded safety analysis; n=149<sup>8</sup>; <sup>†</sup>Weight gain and oedema seem to correlate in a fraction of patients, suggesting different mechanisms for these AEs<sup>8</sup>; <sup>‡</sup>Facial and periorbital oedema have also been reported.<sup>5</sup>

## Lifestyle modifications, as a non-pharmacologic intervention, can be beneficial for managing weight gain and improving QoL. These modifications can be tailored to the patient's ability to and interest in making changes<sup>5</sup>

### Non-pharmacological mitigation strategies<sup>5,6</sup>

- **Food intake counselling\***: eg referral to an oncology-certified dietitian or bimonthly check-ins with a nutritionist
- **Dietary advice**: eg use of a food diary, meal planning support and access to simple, healthy recipes
- **Exercise advice**: eg use of an app that can track steps or activity
- **Follow up with an endocrinologist, weight management clinic and/or dietitian** if these do not yield results



### Pharmacological mitigation strategies<sup>5</sup>

- **Lorlatinib dose modifications**: recommended only if weight gain continues to be severely bothersome after lifestyle modifications
- **Weight loss medications (e.g. GLP-1 inhibitors)**: there are limited data supporting their use for lorlatinib-associated weight gain. Any use should be per approved indications under expert physician supervision of potential AEs



\*An increase in appetite has been reported by some lorlatinib-treated patients; however, a cause-and-effect relationship has not been established between an increased appetite and lorlatinib-associated weight gain.<sup>4</sup>

AE=adverse event; GLP-1=glucagon-like peptide-1; IC=intracranial; PFS=progression-free survival; QoL=quality of life.

1. Solomon BJ, et al. J Clin Oncol. 2024;42:3400-3409; 2. Pfizer. CROWN Protocol (B7461006). December 6, 2022; 3. Local Prescribing Document for LORLATINIB version 7 Pfizer India \_LPDLOR072024. 4. Bauer TM, et al. Oncologist. 2019;24:1103-1110. 5. Liu G, et al. Lung Cancer. 2024;191:107535. 6. Reed M, et al. Adv Ther. 2020;37:3019-3030; 7. Bauer TM, et al. Presented at: WCLC Annual Meeting; September 7-10, 2024; San Diego, CA; 8. Solomon BJ, et al. J Clin Oncol. 2024;42:3400-3409. Supplementary Appendix;

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