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NEW FIXED-DOSE COMBINATION / NEW ROUTE

Pertuzumab + trastuzumab (PHESGO°) by subcutaneous injection, in certain types of breast cancer

OFFERS AN ADVANTAGE

Subcutaneous injection is quicker than intravenous administration. In Europe, this drug is restricted to hospital use. The harm-benefit balance of *pertuzumab* + *trastuzumab* is only favourable in women with inoperable breast cancer.

PHESGO° – *pertuzumab* + *trastuzumab* solution for subcutaneous injection

• **600 mg** or **1200 mg** of *pertuzumab* + **600 mg** of *trastuzumab*, in 10 ml or 15 ml of solution per vial

Roche

■ **Antineoplastics; anti-HER2 monoclonal antibodies**

■ **Indications**: HER2-positive breast cancer, in combination with cytotoxic chemotherapy, as neoadjuvant treatment or adjuvant treatment before or after surgery, or as first-line treatment for inoperable disease. [EU centralised procedure]

■ **Dosage**: one subcutaneous injection every 3 weeks, using 1200 mg of *pertuzumab* + 600 mg of *trastuzumab* for the first injection (given over 8 minutes), and 600 mg of *pertuzumab* + 600 mg of *trastuzumab* for subsequent injections (given over 5 minutes).

Both *pertuzumab* and *trastuzumab* are anti-HER2 monoclonal antibodies. In the European Union, they are authorised for combined use in women with breast cancer that overexpresses the HER2 protein, added to cytotoxic chemotherapy, in a variety of clinical situations (1-4). *Pertuzumab* and *trastuzumab* were initially marketed as two separate products; *pertuzumab* was administered by intravenous (IV) infusion and *trastuzumab* by IV infusion or subcutaneous (SC) injection (4).

A solution for SC injection containing both *pertuzumab* and *trastuzumab* (i.e. a fixed-dose combination) has been authorised in the European Union (5).

This fixed-dose combination was mainly evaluated in a study in 500 patients treated surgically for breast cancer, versus the same combination of drugs administered separately by IV infusion (4). As the outcome measures were mainly pharmacokinetic variables, and all the patients received *pertuzumab* + *trastuzumab*, this study provides no new information about the efficacy of this combination. We previously concluded that the harm-benefit balance of this combination is only favourable in women with inoperable breast cancer (1-3).

The data from this study on adverse effects are of low quality, because the study was not blinded. A serious adverse event was reported in 20% of patients, with no difference between the groups (4). As would be expected, injection site reactions (mainly pain and erythema, none considered serious) were more common in the group receiving SC injections (reported in 16% of patients, versus 1% of patients receiving IV infusions); while systemic reactions linked to administration were less common with SC injections (1% versus 11%) (4,5).

Patients preferred the subcutaneous route. An IV infusion of *pertuzumab* or *trastuzumab* lasts 60 to 90 minutes (4). The recommended duration of a SC injection of the *pertuzumab* + *trastuzumab* combination is 8 minutes for the first injection and 5 minutes for subsequent injections (5). The frequency of administration is the same, i.e. once every 3 weeks (1-3,5).

A non-blinded "crossover" trial in 160 patients compared subcutaneous use of *pertuzumab* + *trastuzumab* as a fixed-dose combination, versus the same combination of drugs but with each component administered separately by the IV route. Patients were asked their opinion about their treatment at a time when none were receiving cytotoxic medication (6). 85% of the patients preferred the SC route (6).

In the European Union, the fixed-dose combination for SC use is restricted to hospital use, as are the solutions for IV infusion. The time spent in hospital must also take into account a period of observation after the injection (15 to 30 minutes) and the time required to administer any concomitant cytotoxic drugs.

► Translated from *Rev Prescrire* January 2022
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Literature search up to 10 October 2021

In response to our request for information, Roche provided us with administrative documents, published articles and packaging items.

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