dupilumab (DUPIXENT°) and nasal polyps

POSSIBLY HELPFUL

For adults with very troublesome nasal polyposis which is not sufficiently relieved by intranasal corticosteroids, oral corticosteroid treatment, given for the shortest possible duration, is one option. *Dupilumab* appears to be an alternative, because it has a different adverse effect profile. However, it has only been shown to have modest efficacy, which has not been demonstrated in patients whose symptoms are refractory to oral corticosteroids. There are still many unknowns regarding its adverse effect profile, particularly in the long-term.

DUPIXENT° - *dupilumab* solution for subcutaneous injection

- **300 mg** of *dupilumab* per prefilled syringe or pen

■ **monoclonal antibody inhibiting interleukin 4 and 13 receptors**

■ **New indication:** "*severe chronic rhinosinusitis with nasal polyposis for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control*", in adults, as an add-on therapy with intranasal corticosteroids. [EU centralised procedure]

Nasal polyposis is a chronic inflammatory condition of the nasal mucosa, with the development of polyps. Patients are troubled, sometimes considerably, by the sensation of having a blocked nose, a partial or complete loss of the sense of smell, taste disturbances and occasionally nasal discharge. Complications are rare (1).

The first-choice treatment is an intranasal corticosteroid (1-3). In very troublesome cases, an oral corticosteroid for a short period is sometimes an option (1). Surgery may be resorted to after failure of drug treatment, but recurrences are frequent (1,3).

Dupilumab (Dupixent°, Sanofi Aventis) is an immunosuppressant monoclonal antibody directed against a subunit of the receptors for interleukin 4 and 13, which are cytokines involved in the inflammatory response (4). Already authorised in the European Union for some forms of atopic dermatitis and asthma, *dupilumab* has now been authorised, as an addition to intranasal corticosteroid, for adults with very troublesome nasal polyposis, when an oral corticosteroid is not sufficiently effective or in case of recurrence after surgery (4-6).

Evaluation of *dupilumab* is based on two randomised, placebo-controlled, double blind trials in a total of 724 adults suffering from moderate to severe symptoms despite use of intranasal corticosteroids, and who were not receiving systemic corticosteroid therapy. One trial lasted 24 weeks and the other 52 weeks. Intranasal corticosteroid treatment was continued throughout the trials (3). The protocol stipulated that patients must have undergone surgery (with no limit on the time between the operation and inclusion in the trial) or that they must have received a systemic corticosteroid in the preceding two years. However, recent failure of oral corticosteroid treatment was not an inclusion criterion, and the number of patients with polyposis that was actually refractory to systemic corticosteroids was not specified in the documents identified by our literature search (3,7).

In both trials, the severity of nasal congestion was assessed by the patients, using a score ranging from 0 (no nasal congestion) to 3 (maximum nasal congestion). At inclusion, the patients had an average score of about 2.4. After six months, the average reduction in the score was 1.3 in the *dupilumab* groups versus 0.4 in the placebo groups ($p<0.0001$) (3). This difference is statistically significant, but it is not known whether it is clinically meaningful, because there was no clinical interpretation of the differences in the scores in the documents identified by our literature search (3,7).

Dupilumab also improved other symptoms such as loss of smell (3). Recourse to a systemic corticosteroid was also less frequent in the *dupilumab* groups (9% of patients versus 31% in the placebo groups), as well as recourse to surgery (1% versus 8%) (7).

In the 52-week trial, after the first 6 months, the 295 patients in the *dupilumab* group were randomised to continue to receive 300 mg either every 2 weeks, or every 4 weeks (3). Six months later (i.e. one year after trial initiation), the improvement in clinical symptoms was sustained, with no difference between the two dosage regimens (6).

The known adverse effects of *dupilumab* include injection site reactions, ocular disorders (mainly conjunctivitis), hypersensitivity reactions, herpes infections and eosinophilia (4,5). The immunosuppressant action may increase the risk of cancer in the long-term. Comparative trials in nasal polyposis have not revealed any previously unrecognised adverse effects of *dupilumab* (5).

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Literature search up to 6 July 2020

In response to our request for information, Sanofi Aventis provided us with no documentation on its product.

1- Prescrire Editorial Staff "Nasal fluticasone, nasal mometasone: no better than beclometasone" *Prescrire Int* 2006; **15** (84): 135.
2- Prescrire Rédaction "Polypose nasale de l'adulte" *Rev Prescrire* 2002; **22** (224): 9.
3- EMA - CHMP "Public assessment report for Dupixent. EMEA/H/C/004390/II/0017" 19 September 2019: 238 pages.
4- Prescrire Editorial Staff "Dupilumab - Dupixent°. In adults with atopic dermatitis: an option for very troublesome eczema after failure of ciclosporin" *Prescrire Int* 2019; **28** (204): 121.
5- Prescrire Rédaction "dupilumab (Dupixent°) et asthme sévère. Aussi peu d'intérêt que les anticorps monoclonaux anti-IgE ou anti-IL5" *Rev Prescrire* 2020; **40** (442): 571-573.
6- European Commission "SPC-Dupixent" 25 June 2020: 62 pages.
7- Bachert C et al. "Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials" *Lancet* 2019; **394**: 1638-1650 (+ annexes: 56 pages).