SUMMARY

Normal human immunoglobulin (co-administered with recombinant human hyaluronidase)

HYQVIA 100 mg/ml,

solution for infusion for subcutaneous use

Reassessment at manufacturer's request

Original French opinion adopted by the Transparency Committee on 22 November 2023

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

For adults

- Immune deficiencies requiring immunoglobulin replacement therapy are uncommon serious life-threatening conditions.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio remains high.
- This is a first-line treatment.

Public health benefit

In view of:

- the seriousness of immune deficiencies requiring immunoglobulin replacement therapy;
- their low prevalence;
- the medical need already met by the alternatives but also considering recurrent supply tensions;
- the lack of evidence of:
  - an additional impact in terms of morbidity-mortality and quality of life on account of the selected outcome measures only relating to safety, and in the absence of any comparative studies compared to other normal human immunoglobulins;
  - an additional impact on the delivery of healthcare or on patients' care and life pathway. Indeed, the pharmacokinetic properties of HYQVIA allow a monthly dose interval, but in

exchange 2 injections are required (a first injection of recombinant human hyaluronidase followed by a second injection of normal human immunoglobulin), which effectively entails increased administration time and volume.

HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) 100 mg/ml, for subcutaneous use, remains substantial in the MA indications.

The Committee approves continued inclusion of HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) 100 mg/ml, for subcutaneous use, in the list of covered drugs for inpatients in the indications and at the MA dosages.

For children and adolescents (aged 0 to 18 years)

- Immune deficiencies requiring immunoglobulin replacement therapy are uncommon serious life-threatening conditions.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio is high.
- This is a first-line treatment.

Public health benefit

In view of:

- the seriousness of immune deficiencies requiring immunoglobulin replacement therapy;
- their low prevalence;
- the medical need already met by the alternatives but also considering recurrent supply tensions;
- the lack of evidence of:
  - an additional impact in terms of morbidity-mortality and quality of life on account of the selected outcome measures only relating to safety, and in the absence of any comparative studies compared to other normal human immunoglobulins;
  - an additional impact on the delivery of healthcare or on patients' care and life pathway. Indeed, the pharmacokinetic properties of HYQVIA allow a monthly dose interval, but in exchange 2 injections are required (a first injection of recombinant human hyaluronidase followed by a second injection of normal human immunoglobulin), which effectively entails increased administration time and volume.

HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) 100 mg/ml, for subcutaneous use, is substantial in the MA indications.

The Committee approves the inclusion of HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) 100 mg/ml, for subcutaneous use, in the list of covered drugs for inpatients in the indications and at the MA dosages.

Clinical Added Value

For adults

In view of:

- the currently met medical need, on account of the presence of numerous available therapeutic alternatives;
- the lack of new clinical efficacy data;
- an overall positive safety profile of HYQVIA marked by adverse events, of which the most frequent have been infections (in particular sinusitis, bronchitis, upper respiratory tract infection) and general injection-related disorders (in particular fever, injection site pain) based on the latest post-authorisation safety studies (European study 161302, US study 161406), and severe acute bacterial infections only occurring in PID patients (FIGARO observational study);
- the presence of anti-rHuPH20 antibodies with a titre ≥ 160 (positive test) occurring in a small number of patients included in the studies, with an overall positive anti-rHuPH20 antibody binding test estimated between 0.04 and 0.317 cases per patient-year;
- the set-up of a prospective pregnancy registry (PASS study 161301) including only 9 pregnant women of whom 7 received HYQVIA replacement therapy, in which the findings showed a negative anti-rHuPH20 antibody binding test for the 4 patients who were tested;

the Committee deems that HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) provides no clinical added value (CAV V) in relation to other normal human immunoglobulins administered intravenously or subcutaneously.

For children and adolescents (aged 0 to 18 years)

In view of:

- the partially met medical need, on account of the presence of numerous available therapeutic alternatives;
- the lack of comparative clinical efficacy data in relation to other immunoglobulins administered intravenously or subcutaneously;
- an overall positive safety profile of HYQVIA marked by local adverse events (in particular pain and infusion site pruritus) and general injection-related disorders (in particular fatigue, fever and headaches), based on the latest post-authorisation safety (European study 161504 and U.S. study 161406) and efficacy (U.S. Study 161503) studies;
- the lack of follow-up in particular in safety in 5 infants exposed in utero to HYQVIA, and followed up for the first two years of their lives (PASS study 161301)
- the presence of anti-rHuPH20 antibodies with a titre ≥ 160 (positive test) occurring in one patient (U.S. study 161503) and with no reports of neutralising antibodies detection during all of the additional 2-year follow-up visits, without however eliminating uncertainty in respect of the effects of concomitant hyaluronidase administration on fertility;

the Committee deems that HYQVIA (normal human immunoglobulin co-administered with recombinant human hyaluronidase) provides no clinical added value (CAV V) in relation to the therapeutic alternatives.