BRS
Belgian Retina Society

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Belgian guidelines for the treatment of non-infectious uveitis (NIU) - 2017

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Addendum - 2020

Belgian guidelines for the treatment of non-infectious uveitis (NIU)

Panel:
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General considerations:

1. Topical treatment in anterior uveitis and as adjuvant treatment in intermediate/posterior uveitis and panuveitis

2. Parabulbar/intravitreal injections in intermediate/posterior uveitis and panuveitis and as adjuvant treatment in anterior uveitis.

3. Systemic (oral, intravenous) treatment in bilateral moderate or severe or severe unilateral intermediate/posterior uveitis or panuveitis. Systemic treatment only indicated in very selected cases of anterior noninfectious uveitis.

4. The use of systemic steroids and other immunomodulatory agents is associated with various side effects, some of them being very severe and potentially fatal. A multidisciplinary approach is recommended. In every case, patients should be correctly informed.

Systemic treatment:

1. Corticosteroids continue to have a vital role in the acute phase of NIU, but their use as a maintenance therapy is limited by their associated side effects. The American Uveitis Society expert consensus recommendations suggest a maintenance dose of ≤ 7.5 mg if possible and no more than 10 mg oral prednisolone equivalent per day, and this is broadly in line with guidelines from other inflammatory diseases.

2. The oral corticosteroids loading dose is usually 1 mg/kg/day with a minimum of 0.5mg/kg/day. Tapering of long standing treatment has to be executed for at least 12 weeks. Depending on inflammation severity and the presence of sight

threatening lesions, starting with an intravenous treatment may be necessary in the acute stage of severe sight threatening uveitis.

3. In uveitis not responding to corticosteroids, or when there is a need for corticosteroid sparing treatment in patients unable to reduce oral prednisolone under 8 mg daily, an immunosuppressive agent alone or in combination with low doses of oral prednisolone ≤ 7.5 mg daily) is indicated.

Inadequate response can be defined by worsening of one or more of the following criteria:

- ✓ Active chorioretinal or retinal vascular lesions OK
- ✓ Anterior chamber cells OK
- ✓ Vitreous haze OK
- ✓ (Macular edema: considered now as a complication of uveitis)
- ✓ (Best corrected visual acuity (BCVA): can be due to cataract of glaucoma)

4. Addition of immunosuppressive/immunomodulatory agents might also be proposed in patients with a good steroid response but who developed unacceptable side effects.

5. Suggested immunosuppressive/ immunomodulatory medication:

- ✓ Methotrexate (MTX): starting dose of 7.5-12.5mg/week, to titrate to a maximal dosage of 20-(25) mg/w following systemic toxicity and clinical response. Treatment for at least 3 months.
  - o Lag time of 4–6 weeks from initiation of treatment to full therapeutic effect.
  - o Side effects include gastrointestinal symptoms, cytopenia, and hepatotoxicity; lung fibrosis.
- ✓ Azathioprine (AZA): starting dose of 2–3 mg/kg/day, titrated according to response and side effects. Treatment for at least 6 weeks.
  - o Genotype screening for TPMT (thiopurine methyltransferase) deficiency is recommended before starting azathioprine to avoid important drug toxicity.
  - o Efficacy is achieved within 4–12 weeks after commencing treatment.
  - o Side effects include gastrointestinal upset and myelosuppression for which regular monitoring of blood count and liver enzymes is required.
- ✓ Mycophenolate mofetil (MMF): starting dose of 500 mg twice daily, increased to 1 g twice daily after 2 weeks provided that side effects are acceptable. Treatment for at least 6 weeks.

- Efficacy is achieved within 2–12 weeks after commencing treatment.
- Side effects include gastrointestinal disturbance, elevation of liver enzymes, leukopenia and thrombocytopenia.

✓ Cyclosporine (CSA): 2.5– 3 mg/kg daily (max 5 mg)/kg daily for at least 4 weeks. Needs to be tapered slowly to avoid rebound of the uveitis.

- Fast acting, reaching peak efficacy within 7–15 days of initiation of therapy.
- Side effects include hypertension, renal impairment, gingivitis, and hirsutism.

6. In patients with an inadequate response to one immunosuppressive/immunomodulatory treatment, or in which this treatment is inappropriate, a combination of two immunomodulatory agents with or without low doses of oral prednisolone ($\leq$ 7.5 mg daily) can be an option. In such patients, biological medicines such as TNF-alfa blocking agents can be indicated either as a unique immunomodulatory therapy or in combination with a classical drug (usually, prednisolone, MTX , AZA or MMF).

Indications for primary combination therapy (corticosteroids + add-on):
1. Absolute indications for primary immunomodulatory therapy following the American Academy of Ophthalmology (AAO):

✓ Behçet's disease
✓ Juvenile idiopathic arthritis
✓ VKH/sympathetic ophthalmia
✓ Serpiginous choroiditis
✓ Wegener granulomatosis

2. Indication for primary biological therapy:

✓ Behçet's disease

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Belgian guidelines for the treatment of non-infectious uveitis (NIU): 2020 addendum

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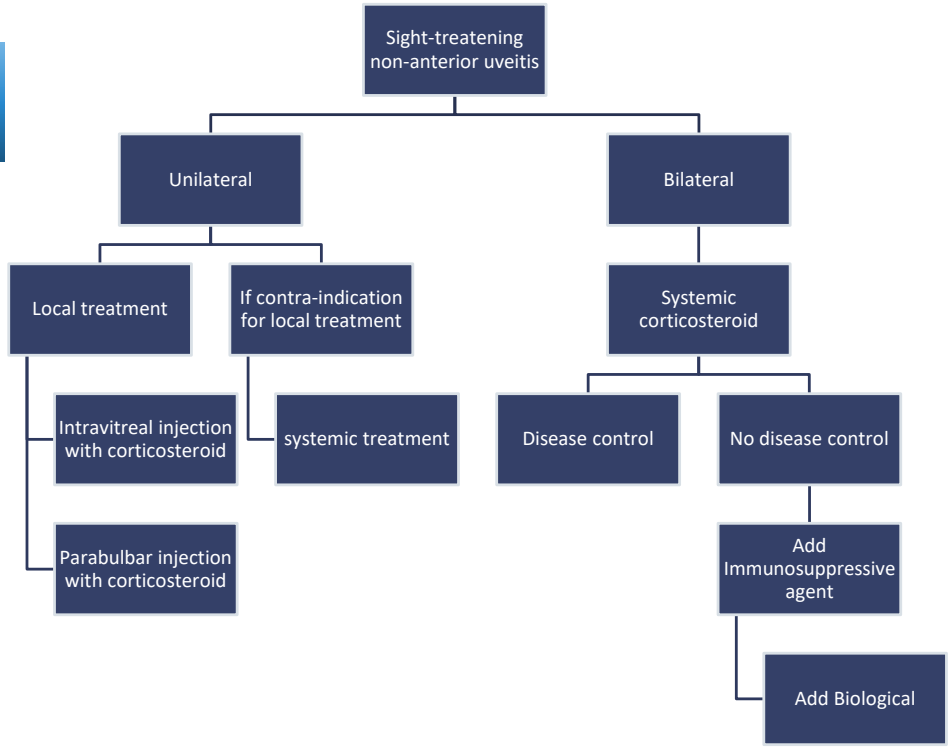
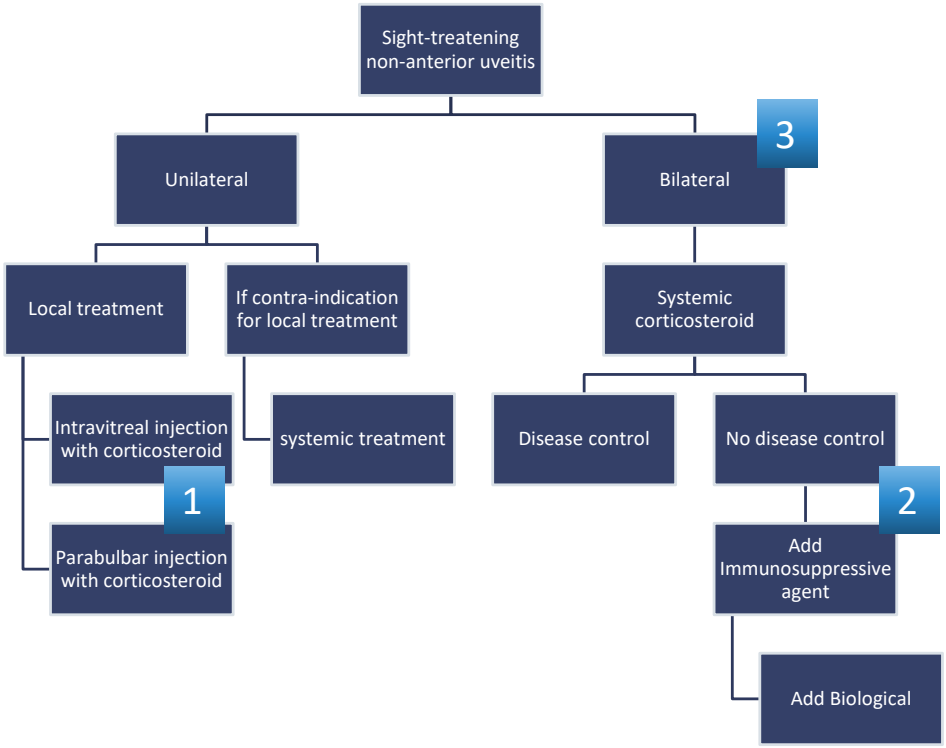
Belgian guidelines for the treatment of non-infectious uveitis (NIU): 2020 addendum

Adopted from 2017 consensus document



Belgian guidelines for the treatment of non-infectious uveitis (NIU): 2020 addendum

Consensus obtained by uveitis expert panel discussion in 2020



Consensus obtained by uveitis expert panel discussion in 2020

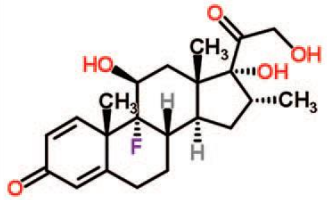
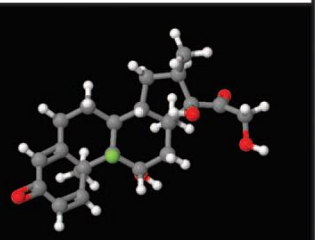
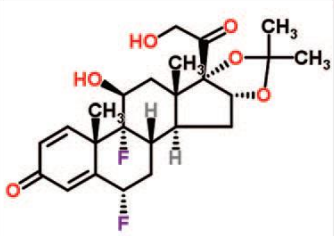
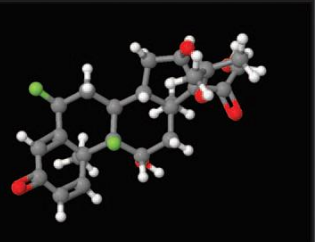
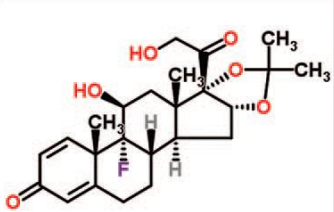
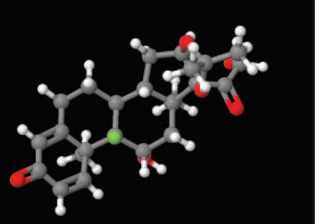
1. Agreement on using intravitreal corticosteroids as first line in unilateral sight-threatening non-anterior uveitis. Take into account:
   - ✓ Age (no reimbursement < 18yo)
   - ✓ The presence or absence of systemic inflammatory disease
   - ✓ Absence of contra-indication

2. Agreement on using intravitreal corticosteroids when a first immunosuppressive agent is insufficient in controlling bilateral non-anterior uveitis. In selected patients, intravitreal corticosteroids can be injected when recurrence occurs after systemic corticosteroids. 3 options:
   - ✓ Increase oral corticosteroid dosage
   - ✓ Switch immunosuppressive agent
   - ✓ Add intravitreal corticosteroid, depending on reimbursement criteria

3. Agreement on using intravitreal corticosteroids in bilateral non-anterior uveitis as first line agent. Consensus argumentation:
   - ✓ Definite agreement if contra-indication for systemic treatment can be objectified
   - ✓ Alternative approach: it might be an option for using bilateral intravitreal corticosteroids after excluding systemic inflammatory disease. Take also the age of the patient into account.
   - ✓ Otherwise, systemic treatment has to be maintained

Available steroids for intravitreal injection in uveitis patients

- Ozurdex
- Iluvien/ Retisert (No EMA label)
- Triamcinolone (off label)

Corticosteroid	Two-dimensional structure	Three-dimensional structure
Dexamethasone		
Fluocinolone acetonide		
Triamcinolone acetonide		

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2020 Uveitis expert panel:

Chairs:

- Dr. J. Van Calster — UZLeuven
- Prof. F. Willermain — CHU Saint Pierre / CHU Brugmann

Panel:

- Dr. S. Bonnet — CHR Citadelle
- Dr. L. Judice — ULB Saint Pierre / CHU Brugmann
- Dr. N. Kisma — ULB Erasme
- Dr. A. Kozyreff — UCL Saint Luc
- Dr. G. Lepiece — CHR Citadelle
- Dr. D. Makhoul — ULB Saint Pierre / CHU Brugmann
- Dr. J. Thys — CHU Liège
- Dr. L. Van Os — UZAntwerpen / Turnhout

Excused:

- Dr. I. De Schrijver — UZGent
- Dr. P.-P. Schauwvliege — UZLeuven / Middelheim