Deucravacitinib

Instructions for use

Table 1: Instructions for use (Deucravacitinib)

Pre-treatment

- Physicians are encouraged to enroll their patients in a registry (if available)
- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Medical history and physical examination including prior exposure to treatments, risk factors, signs and symptoms of infection, malignancies.
- Recommended measures include:
    - Check for skin cancer
    - Check for lymphadenopathy
    - Exclusion of tuberculosis (see chapter: “tuberculosis”)
    - Check for evidence of active and chronic infection
    - Check need for vaccinations according to current immunization guidelines
- Laboratory parameters (see Table 2)
- Exclude pregnancy/breastfeeding
- Reliable contraception
- Advise the patient to discontinue the treatment and seek further diagnostic evaluation if they experience muscle pain, tenderness, or weakness, especially if accompanied by malaise or fever.

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)

- Clinical examination including risk factors, signs and symptoms of infection, malignancies.
- Laboratory parameters (see Table 2)
- Reliable contraception

Post-treatment

- After discontinuation of deucravacitinib, patients should be followed up with medical history and physical examination
- For information regarding the ongoing need for contraception immediately following treatment cessation, please see chapter "wish for child / pregnancy"

[1] due to personal-financial conflict of interest 7 abstentions

Recommendations for lab controls

Table 2: Recommended laboratory controls (Deucravacitinib)

	Period in weeks	
Parameter	**Pre-treatment**	**Thereafter, every 3-6 months**
Full blood count	x	x
Liver enzymes	x	x
Creatine phosphokinase (CPK)	x	(x) when indicated on medical history, pre-treatment results or in case of muscle pain during treatment
Lipid profile	x	(x) when indicated on medical history or pre-treatment results
Serum creatinine	x	
Urine status	x	
Pregnancy test (urine or blood)	x	
HBV/HCV	x	
HIV	x	
Interferon gamma release assay (TB exclusion)	x	
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics must be considered. Further specific testing may be required according to clinical signs, risk, and exposure.		
The recommendations are based on expert opinion taking into account that the experience with this drug is still limited. The currently suggested monitoring goes beyond the laboratory controls currently suggested by SmPC. Due to personal-financial conflict of interest 7 abstentions.		

Adverse drug reactions [1-5]

Please see SmPC for complete listing. The guideline subcommittee decided to comment on the following aspects:

The most common adverse drug reactions (occurring in ≥1% and with a higher rate than in the placebo group) in pooled data from POETYK PSO-1 and POETYK PSO-2 trials through week 16 were upper respiratory infections, increased blood creatinine phosphokinase (CPK) levels, herpes simplex, mouth ulcers, folliculitis, and acne (**Table 3**). Headache, diarrhea, and nausea were also reported, with a similar frequency in the deucravacitinib and placebo groups. Through Week 52, no new adverse drug reactions were identified, and their incidence rates did not increase compared to those observed during the first 16 weeks of treatment.

Table 3: Overview of important side effects (Deucravacitinib)

Very common	Upper respiratory infections*
Common	Herpes simplex infections**, oral ulcers***, acneiform rash****, folliculitis
Uncommon	Herpes zoster

* nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, pharyngitis, sinusitis, acute sinusitis, rhinitis, tonsillitis, peritonsillar abscess, laryngitis, tracheitis, and rhinotracheitis
** oral herpes, herpes simplex, genital herpes, and herpes viral infection
*** aphthous ulcer, mouth ulceration, tongue ulceration, and stomatitis
**** acne, dermatitis acneiform, rash, rosacea, pustule, rash pustular, and papule

Infections

Deucravacitinib may increase the risk of infections. The majority of infections were non-serious and mild to moderate in severity upper respiratory tract infections which did not lead to treatment discontinuation. The most common serious infections reported with deucravacitinib included pneumonia and COVID-19, which is attributable to the ongoing pandemic.

Herpes virus reactivation (e.g., herpes zoster, herpes simplex), was reported in clinical studies. Most of the herpes zoster cases were mild to moderate, localized (involved a single dermatome), followed a benign clinical course, and did not lead to discontinuation. During POETYK PSO-1, PSO-2, and the open-label extension trial, 10 out of 18 patients who reported events of herpes zoster were under 50 years of age and there was a case of multidermatomal herpes zoster in an immunocompetent subject who received deucravacitinib. Physicians should educate patients about early signs and symptoms of herpes zoster, advising that treatment should be sought as early as possible, and inform them about the possibility of prevention through vaccination for eligible individuals.

Laboratory Abnormalities

In terms of pooled laboratory abnormality data from clinical trials, treatment with deucravacitinib was associated with increases in creatine phosphokinase (CPK) levels (from asymptomatic to rhabdomyolysis), increases in triglyceride levels and liver serum transaminase elevations ≥ 3 times the upper limit of normal. Interrupt deucravacitinib if myopathy or liver injury is suspected. Patients should be instructed to promptly report any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Malignancies

In pooled data from the entire treatment periods during PSO-1, PSO-2, and the open-label extension trial (total deucravacitinib exposure of 2482 patient–years; PY), malignancies were reported in 22 patients (0.9 per 100 PY) including 11 cases of non-melanoma skin cancer (0.4 per 100 PY) and 3 subjects with lymphoma (0.1 per 100 PY).

Special consideration during treatment [3-7]

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects:

Potential Risks Related to JAK Inhibition

These safety concerns led the FDA and EMA to endorse the measures to minimise risk of serious heart-related events, cancer, blood clots, and death associated with Janus kinase (JAK) inhibitors.
It is not known whether deucravacitinib may be associated with the observed or potential adverse reactions of JAK inhibition. Deucravacitinib is a highly selective TYK2 inhibitor with minimal or no activity against JAK 1/2/3 at clinically relevant doses and concentrations. Allosteric mechanism of TYK2 inhibition reduces the chance of off-target effects and data from PSO-1, PSO-2, and the open-label extension trial demonstrated consistent safety profiles of deucravacitinib in patients with psoriasis. Although further observations are needed to fully characterize the long-term safety of deucravacitinib.

Surgery

There is no data on the management of surgery in patients treated with deucravacitinib. The decision to discontinue of deucravacitinib prior to surgery should be taken case-by-case considering type and risk of surgical procedure, patient characteristics, the risk of infection, the risk of psoriasis worsening. Counselling with the surgeon is advised.

American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty recommend withholding JAK inhibitors for at least 3 days prior to surgery.

Important contraindications [1-3]

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects.

Contraindications:

- Hypersensitivity to the active substance or to any of the excipients
- Active tuberculosis or active serious infections
- Severe hepatic impairment (Child-Pugh C)
- Pregnancy

The risks and benefits of treatment with deucravacitinib should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection, who have been exposed to tuberculosis, with a history of a serious or an opportunistic infection, or with underlying conditions that may predispose them to infection.

Drug interactions [3,8]

Please see SmPC and other sources for complete listing. The guideline subcommittee decided to comment on the following aspects.

Results from healthy volunteer studies showed that no clinically significant differences in the deucravacitinib pharmacokinetics were observed when administered with concomitant medications that inhibit or induce various drug metabolizing enzymes and transporters, including cyclosporine (dual Pgp/BCRP inhibitor), fluvoxamine (CYP1A2 inhibitor), ritonavir (CYP1A2 inducer), diflunisal (UGT1A9 inhibitor), pyrimethamine (OCT1 inhibitor), famotidine (H2 receptor antagonist), or rabeprazole (proton pump inhibitor). No clinically significant differences in the pharmacokinetics of the following drugs were observed when co-administered with deucravacitinib: rosuvastatin, methotrexate, mycophenolate mofetil and oral contraceptives (norethindrone acetate and ethinyl estradiol).

Combination therapy of deucravacitinib with other immunomodulatory agents, including biologics, or phototherapy has not been evaluated in plaque psoriasis.

Overdose/ measures in case of overdose

There is no experience regarding human overdosage with deucravacitinib. In the case of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

References

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