Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

HERTFORDSHIRE AND WEST ESSEX AREA PRESCRIBING COMMITTEE (APC)

IVERMECTIN 10MG/G CREAM FOR PAPULOPUSTULAR ROSACEA (PPR)

RECOMMENDED

Name: generic (trade)	What it is	Indication	Date Decision last revised	Decision Status	NICE / SMC Guidance
Ivermectin 10mg/g cream (Soolantra®)	Topical anthelmintic	Inflammatory lesions of papulopustular rosacea	HMMC September 2016	Final	NICE - none SMC – accepted for moderate to severe PPR where topical appropriate

Ivermectin 10mg/g cream (Soolantra®) is RECOMMENDED as a topical treatment option in moderate to severe papulopustular rosacea (PPR). For initiation and prescribing in primary or secondary care.

EFFICACY

- Trials have demonstrated that ivermectin was more effective than vehicle and metronidazole for improvements in severity score and lesion count.
- All trials included patients with moderate or severe PPR. No data for mild PPR.
- No studies vs azelaic acid or oral antibiotics.

SAFETY

- Most commonly reported adverse reactions are skin burning sensation, irritation, pruritis and dry skin (<1% in trials). These are typically mild/moderate and usually decrease on continuation.
- No interaction studies have been performed but caution is advised with potent CYP3A4 inhibitors.
- Limited information in pregnancy – SPC advises avoid.
- No studies in renal or hepatic impairment. SPC states caution should be exercised in patients with severe hepatic impairment.

COST

- Soolantra® 45g tube costs £27.43.
- Average cost of generic scripts for topical metronidazole in Herts per 28 days is £11.38 which is higher than ivermectin cost: £9.15.
- Azelaic acid gel and some topical metronidazole products prescribed by brand are lower cost than ivermectin.
- Economic modelling by SMC and AWMSG has suggested decreased healthcare resource costs over a 3 year time period (moderate to severe PPR)

PATIENT FACTORS

- There are no clear data on prevalence of rosacea. Reported rates are 1 - 22%. PPR is thought to be the most prevalent subtype. One estimate suggests 25% are moderate to severe.
- Ivermectin cream offers an additional topical option in the symptomatic treatment of PPR.
- Ivermectin cream is licensed for once daily use, in contrast to twice daily topical metronidazole or azelaic acid.
- A potential reduction in oral antibiotic use could aid a reduction in the growth of antimicrobial resistance.

Background Information

- Ivermectin 10mg/g cream (Soolantra®), Galderma UK, is an anthelmintic licensed as a once daily topical therapy to treat inflammatory lesions of papulopustular rosacea (PPR) in adults. It was launched June 2015.
- It has anti-inflammatory actions and antiparasitic effects against *Dermodex folliculorum* mites (which may be present in up to 80% rosacea sufferers). The role of these mites is unknown, but is currently thought to be an aggravating rather than causative factor in the disease.
- **Ivermectin cream is applied once daily for up to 4 months. Courses may be repeated as many times as required with no minimum interval. In the case of no improvement after 3 months, treatment should be stopped.**
- CKS advises mild to moderate PPR (limited papules, pustules, no plaques) is managed with topical metronidazole or azelaic acid. Moderate to severe disease (extensive papules, pustules or plaques) is managed with systemic antibiotics oral tetracycline or erythromycin but note that not all are licensed for this indication, and limited RCT data to support use.
- Azelaic acid gel is an alternative to metronidazole cream and may be more effective, however it may cause transient stinging.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness

- Refer to efficacy box.
- Ivermectin was significantly more effective than vehicle in 2 identical double blind RCTs. Improvement noted in rosacea severity score and inflammatory lesion count.
- An RCT of ivermectin v metronidazole 0.75% showed superiority of ivermectin at improving rosacea severity score and reducing lesion count.
- There is limited longer term efficacy and safety data. Initial efficacy trials of 12 or 16 weeks were followed by a 40 week extension study.

Safety

- Refer to safety box.

Cost of treatment and Cost Effectiveness

- Refer to cost box
- Shelf life of Soolantra® is 2 years (once open discard after 6 months). Shelf life varies for other treatments (for example Acea® 0.75% metronidazole gel states discard 8 weeks after opening, some other products do not state a timescale)
- SMC considered a manufacturer submitted cost utility analysis comparing ivermectin to metronidazole and azelaic acid for PPR in moderate to severe cases over 3 years. Costs included weighted drug costs, GP visits and specialist visits. Ivermectin was estimated to be dominant v both metronidazole and azelaic acid cream and resulted in incremental savings of £73 and £37 and incremental QALY gain of 0.0091 and 0.0113 respectively.
- AWMSG considered a company submitted cost utility analysis & concluded that over 3 years ivermectin is marginally less costly v metronidazole or azelaic acid. AWMSG noted that the model only related to moderate to severe PPR.

The needs of the population

- Refer to patient factors box.

The needs of the community

- The cost impact is uncertain. Estimated drug costs for each CCG may increase by £2.5k in year 1 and £6k in year 5 (figures extrapolated from SMC budget impact analysis). Cost utility analysis by Wales and Scotland for topical treatments suggested that increased drug costs are more than offset by a reduction in healthcare costs. However, it is noted in Herts, generically written metronidazole gel scripts and Metrogel® scripts (accounting for the majority of metronidazole) are currently more costly than the estimated monthly cost of ivermectin.
- In general ivermectin topical costs are higher than those of oral antibiotics.
- Availability of an additional topical treatment may reduce the use of oral antibiotics. Use of oral antibiotics is associated with antimicrobial resistance, drug and food interactions (common with tetracyclines and erythromycin) and systemic side effects.
- It has been suggested that the availability of ivermectin as an option for prescribing in primary care may result in fewer referrals to specialists.

Policy Drivers

- All Wales Medicines Strategy Group (AWMSG) (Final Appraisal Recommendation Feb 2016): Recommends ivermectin as an option for topical treatment of inflammatory lesions of PPR in adults.
- Scottish Medicines Consortium (SMC) (Nov 2015): Ivermectin accepted for restricted use. 'The treatment of moderate to severe inflammatory lesions of rosacea where a topical treatment is considered appropriate'

Equity

- No impact anticipated.

Implementability

- No issues anticipated

Selected References (full reference list available in HMMC evaluation)

- NICE Evidence Summary New Medicine (Jan 2016) https://www.nice.org.uk/advice/esnm68/chapter/Key-points-from-the-evidence
- All Wales Medicines Strategy Group (Final Appraisal Recommendation Feb 2016) http://www.awmsg.org/awmsgonline/app/appraisalinfo/1627
- Scottish Medicines Consortium (Advice Nov 2015) https://www.scottishmedicines.org.uk/SMC_Advice/Advice/1104_15_ivermectin_Soolantra/ivermectin_Soolantra
- Regional Drug and Therapeutics Centre RDTC New Drug Evaluation (Oct 2015) http://rdtc.nhs.uk/sites/default/files/publications/nde_146_ivermectin_v2.pdf

Version	2.0 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: • Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers • Review date removed and replaced with standard statement.
Developed by	HMMC
Approved by	HMMC
Date approved/updated	September 2016
Review date:	The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.
Superseded version	1.0