Surrey & North West Sussex Area Prescribing Committee

Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath), Crawley CCG and Horsham & Mid-Sussex CCG

REVIEW AND UPDATE OF EXISTING APC POLICY STATEMENT:

1. **Tacrolimus (topical) for atopic dermatitis**
2. **Pimecrolimus (topical) for atopic dermatitis**

MEDICINE DETAILS[1,2,3]		
Name and brand	Tacrolimus: Protopic® 0.1% ointment Protopic® 0.03% ointment Various generics	Pimecrolimus: Elidel® 10mg/g cream
Manufacturer	Leo Laboratories Limited	Mylan
Licensed indication	Treatment of moderate to severe atopic dermatitis: Protopic 0.03% ointment is indicated in adults, adolescents and children from the age of 2 years. Protopic 0.1 % ointment is indicated in adults and adolescents (16 years of age and above) Please refer to SPC for details.	Treatment of patients aged 2 years and over with mild or moderate atopic dermatitis where treatment with topical corticosteroids is either inadvisable or not possible. This may include: • Intolerance to topical corticosteroids • Lack of effect of topical corticosteroids • Use on the face and neck where prolonged intermittent treatment with topical corticosteroids may be inappropriate
Formulation	Ointment	Cream
Usual dosage	Please refer to SPC for details.	Please refer to SPC for details.

EXISTING APC POLICY STATEMENT[2]			
1. Tacrolimus (topical)			
Details	**Policy no**	**Date of issue**	**Review date**
	PCN 236-2016	December 2016	December 2019
Recommendations and key considerations			
The PCN recommends tacrolimus (topical) as a treatment option for the treatment of atopic dermatitis. Tacrolimus (topical) will be initiated by GPs with a specialist interest in dermatology or secondary care dermatology specialists. Transfer of prescribing (to primary care) may be considered following the 1st prescription from the specialist. Tacrolimus (topical) will be considered **BLUE (with no information sheet)** on the traffic light system. **Key Considerations:** • Information in relation to prescribing is available in the license at www.medicines.org.uk			
2. Pimecrolimus (topical)			
Details	**Policy no**	**Date of issue**	**Review date**
	PCN 235-2016	December 2016	December 2019
Recommendations and key considerations			
The PCN recommends Pimecrolimus (topical) as a treatment option for the treatment of atopic dermatitis. Pimecrolimus (topical) will be initiated by GPs with a specialist interest in dermatology or secondary care dermatology specialists. Transfer of prescribing (to primary care) may be considered following the 1st prescription from the specialist. Pimecrolimus (topical) will be considered **BLUE (with no information sheet)** on the traffic light system. **Key Considerations:** • Information in relation to prescribing is available in the license at www.medicines.org.uk			

REVIEW

Changes in product characteristics including comparators

None.

Changes in efficacy

None.

Changes in cost implications to the local health economy

Drug tariff price	30g	60g	100g
Protopic 0.03% ointment	£23.33	£42.55	-
Protopic 0.1% ointment	£17.26	£34.52	-
Generic tacrolimus 0.1% ointment	£17.26	£34.52	-
Elidel® 1% cream	£19.69	£37.41	£59.07

Drug tariff prices from the BNF May 2020.

Changes due to new guidelines/advice/NICE TA published after date of issue of existing policy statement

No changes since initial review but NICE TA82 guidance and Do Not Do Recommendation do not seem to have been considered in the current policy statements.

NICE: Tacrolimus and pimecrolimus for atopic eczema
Technology appraisal guidance [TA82] Published date: 25 August 2004[4]

Guidance

1.1 Topical tacrolimus and pimecrolimus are not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.

1.2 Topical tacrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate to severe atopic eczema in adults and children aged 2 years and older that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

1.3 Pimecrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

1.4 For the purposes of this guidance, atopic eczema that has not been controlled by topical corticosteroids refers to disease that has not shown a satisfactory clinical response to adequate use of the maximum strength and potency that is appropriate for the patient's age and the area being treated.

1.5 It is recommended that treatment with tacrolimus or pimecrolimus be initiated only by physicians (including general practitioners) with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options.

Do Not Do Recommendation[5]

Topical tacrolimus and pimecrolimus are not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.

Trust formulary status

June 2020:

	Tacrolimus	Pimecrolimus
Ashford and St Peter's Hospital NHS Trust (ASPH)	Restricted: Dermatology	Restricted: Dermatology
Royal Surrey Hospital NHS Foundation Trust (RSH)	BLUE Indications: •Eczema Short-term treatment of moderate to severe atopic eczema (including flares) in patients unresponsive to, or intolerant of conventional therapy (initiated by a specialist), •Prevention of flares in patients with moderate to severe atopic eczema and 4 or more flares a year who have responded to initial treatment with topical tacrolimus (initiated by a specialist) •Short-term treatment of facial, flexural, or genital psoriasis in patients unresponsive to, or intolerant of other topical therapy (initiated under specialist supervision) NB: Tacrolimus (topical) is a treatment option for atopic dermatitis. Tacrolimus (topical) will be initiated by GPs with a specialist interest in dermatology or secondary care dermatology specialists. Transfer of prescribing (to primary care) may be considered following the 1st prescription from the specialist	BLUE Indications: • Short-term treatment of mild to moderate atopic Eczema (including flares) when topical corticosteroids cannot be used. RSCH: Restricted Item For Dermatology Consultants Only NB: The PCN recommends that Pimecrolimus (topical) will be initiated by GPs with a specialist interest in dermatology or secondary care dermatology specialists. Transfer of prescribing (to primary care) may be considered following the 1st prescription from the specialist.
Epsom and St Helier University Hospital NHS Trust (ESHUT)	Initiation by Dermatologists only To be prescribed by dermatologists and paediatricians only in accordance with NICE guidance Tacrolimus and Pimecrolimus for moderate to severe atopic eczema (Aug 2004) 0.03% & 0.1% for vitiligo from 2 years onwards (unlicensed indication) 0.03% for eczema in infants & children under 2 years (unlicensed indication) 0.1% for eczema in children 2-15 years (unlicensed indication)	Initiation by Dermatologists only To be prescribed by dermatologists and paediatricians only in accordance with NICE guidance Tacrolimus and Pimecrolimus for moderate atopic eczema (Aug 2004)
Frimley Park Hospital NHS Foundation Trust (FPH)	AMBER without shared care. INDICATION: moderate to severe atopic eczema. RESTRICTION: To be initiated by dermatology consultants and GPs with	AMBER without shared care. Topical pimecrolimus is not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.

	specialist interest only.	Pimecrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy. NICE TA82: Atopic dermatitis (eczema) – pimecrolimus and tacrolimus
Surrey and Sussex Healthcare NHS Trust (SASH)	**RESTRICTED for DERMATOLOGY CONSULTANT** use only. See NICE Guidance	**RESTRICTED** for **DERMATOLOGY CONSULTANT** use only

Other reviews or changes identified on the PAD

- Tacrolimus and pimecrolimus (both calcineurin inhibitors) are not licensed for short-term treatment of facial, flexural, or genital psoriasis[1,2,3] (off-label use). Although they are not mentioned in the NICE CKS Psoriasis Prescribing Information[6], they are included in the following:

1. The BNF includes an unlicensed use for short-term treatment of facial, flexural, or genital psoriasis in patients unresponsive to, or intolerant of other topical therapy (initiated by a specialist), together with dose information[7].
2. Psoriasis: assessment and management. Clinical guideline [CG153][8] which states:
   'For adults with psoriasis of the face, flexures or genitals if the response to short-term moderate potency corticosteroids is unsatisfactory, or they require continuous treatment to maintain control and there is serious risk of local corticosteroid-induced side effects, offer a calcineurin inhibitor applied twice daily for up to 4 weeks. Calcineurin inhibitors should be initiated by healthcare professionals with expertise in treating psoriasis.' The guidance advises that 'the prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information'.
3. British Association of Dermatologists patient leaflet information entitled 'Topical treatments for Psoriasis'[9].
4. The Guildford and Waverley Joint Formulary[10] which considers this as BLUE.
5. Psoriasis primary care pathway on the PAD[11] which was due for review in February 2019.

Consultative partners

Consultant Dermatologists across trusts in Surrey Heartlands ICS.

Additional comments

The ESHUT formulary also includes the following as off-label uses:

- 0.03% & 0.1% for vitiligo from 2 years onwards (unlicensed indication)
- 0.03% for eczema in infants & children under 2 years (unlicensed indication)
- 0.1% for eczema in children 2-15 years (unlicensed indication).

Summary: what is the APC being asked to do and why

Recommendations from the review:

1. **The current policy statements (issued Dec 2016) do not take into account the NICE guidance on tacrolimus and pimecrolimus for atopic eczema (TA84) published 25 August 2004.**

   The APC is therefore asked to agree on one policy statement for tacrolimus and pimecrolimus based on this NICE TA.

   Proposed policy statement:

Tacrolimus and pimecrolimus (topical use) for atopic eczema.
The APC recommends the use of tacrolimus and pimecrolimus in atopic eczema as BLUE and as per NICE TA82: Topical tacrolimus and pimecrolimus are <u>not recommended</u> for the treatment of *mild* atopic eczema or as *first-line treatments* for atopic eczema of any severity. Tacrolimus: Topical tacrolimus <u>is recommended</u>, within its licensed indications, as an option for the *second-line treatment* of *moderate to severe* atopic eczema in *adults and children aged 2 years and older* that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy. Pimecrolimus: Pimecrolimus <u>is recommended</u>, within its licensed indications, as an option for the *second-line treatment* of *moderate* atopic eczema on the *face and neck in children aged 2 to 16 years* that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy. For the purposes of this guidance, atopic eczema that has not been controlled by topical corticosteroids refers to disease that has not shown a satisfactory clinical response to adequate use of the maximum strength and potency that is appropriate for the patient's age and the area being treated. It is recommended that treatment with tacrolimus or pimecrolimus be *initiated only by physicians (including general practitioners) with a special interest and experience in dermatology*, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options. In addition it has been decided locally that the transfer of prescribing from the specialist to primary care may be considered *following the first prescription from the specialist*. Key considerations: • Tacrolimus and pimecrolimus for atopic eczema. Technology appraisal guidance [TA82] Published date: 25 August 2004

2. There is no policy statement for the established use (off-label) of tacrolimus and pimecrolimus in facial, flexural, or genital psoriasis.

The APC is therefore asked to agree on a policy statement for this indication.

Proposed policy statement:

Tacrolimus and pimecrolimus (topical use) for short-term treatment of facial, flexural, or genital psoriasis in patients unresponsive to, or intolerant of other topical therapy
The APC recognises the *off-label use* of tacrolimus and pimecrolimus (topical use) for short-term treatment of facial, flexural, or genital psoriasis in patients unresponsive to, or intolerant of other topical therapy as per the NICE clinical guidance (CG153) Psoriasis: assessment and management. This is considered as BLUE, with the following taken from the guidance: • Calcineurin inhibitors should be initiated by healthcare professionals with expertise in treating psoriasis • The prescriber should follow relevant professional guidance, taking full responsibility for the decision • The patient (or their parent or carer) should provide informed consent, which should be documented • See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information. In addition, it has been decided locally that the transfer of prescribing from the specialist to primary care may be considered *following the first prescription from the specialist.* Key considerations: • NICE Psoriasis: assessment and management. Clinical guideline [CG153]. Published date: 24 October 2012. Last updated: 01 September 2017. • The British National Formulary.

3. Does the APC require another policy statement along the same lines as the above for the off-label uses of tacrolimus and/or pimecrolimus listed below from the ESHUT formulary?

- 0.03% & 0.1% for vitiligo from 2 years onwards (unlicensed indication)
- 0.03% for eczema in infants & children under 2 years (unlicensed indication)
- 0.1% for eczema in children 2-15 years (unlicensed indication).

For information:

- The cBNF[12] includes information on the following for tacrolimus:
  - short-term treatment of moderate to severe atopic eczema (including flares) in patients unresponsive to, or intolerant of conventional therapy (initiated by a specialist)
  - Prevention of flares in patients with moderate to severe atopic eczema and 4 or more flares a year who have responded to initial treatment with topical tacrolimus (initiated by a specialist)

  with dosage recommendation for children ages 2-15 and 16-17.

— The cBNF also includes information on the use of pimecrolimus for the short-term treatment of mild to moderate atopic eczema (including flares) when topical corticosteroids cannot be used (initiated by a specialist), for children aged 2-17. — There is no information in the cBNF for tacrolimus or pimecrolimus for use in vitiligo.
Accompanying papers (please list)
None.

References:

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12. Medicines Complete. cBNF. Available at: https://www.new.medicinescomplete.com/#/content/bnfc/_351442497?hspl=tacrolimus and https://www.new.medicinescomplete.com/#/content/bnfc/_258083646 <accessed 18.6.20>

Declaration of interests:

	Name	Title	Organisation	Date	Declaration of interest
Prepared by	Tejinder Bahra	Lead Commissioning Pharmacist	Surrey Heartlands ICS	28.5.20	None
Reviewed by					

Version control sheet:

Version	Date	Author	Status	Comment
V1	11.6.20	T Bahra	Draft	Initial review
V2	2.7.20	T Bahra	Final	Out for clinical comment